THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

CONTENTS

This Issue in the Journal

Editorial

Original Articles

Clinical Correspondence

100 Years Ago in the NZMJ

Methuselah

Letters

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

This Issue in the Journal

Demographic predictors of cervical cancer screening in Chinese women in New Zealand
Wanzhen Gao, Janis Paterson, Ruth DeSouza, Tongjing Lu

Research is scarce about the cervical cancer screening uptake of Asian or Chinese migrants in New Zealand; however coverage is thought to be lowest among Asian women. We surveyed 234 Mainland Chinese women living in Auckland to ascertain the uptake of cervical screening programme. Of the respondents, 65% reported having ever been screened in New Zealand and 56% reported they were screened in the last 3 years. For the sociodemographic factors, women aged under 30 or above 50 years and short duration of residence in New Zealand were associated with lower uptake of the screening programme. The study highlights the information needs of this group.

Prospective 10-year study of postmenopausal women with asymptomatic primary hyperparathyroidism
Mark J Bolland, Andrew B Grey, Brandon J Orr-Walker, Anne M Horne, Margaret C Evans, Judy M Clearwater, Greg D Gamble, Ian R Reid

Primary hyperparathyroidism is common in older women. It is uncertain what the best form of management is (surgery or conservative management without surgery). To see whether they could be managed without surgery, we followed 23 women with primary hyperparathyroidism who did not have symptoms related to the disorder for up to 10 years. Despite 19 out of 23 women meeting the standard criteria for surgical management, few developed clinical events related to the disorder during follow-up. This suggests that many women with primary hyperparathyroidism who do not have symptoms from the disorder do not develop symptoms or complications of primary hyperparathyroidism over time and therefore can be managed without surgery.

The maternal outcome in placenta accreta: the significance of antenatal diagnosis and non-separation of placenta at delivery
Hong Soo Wong, John Hutton, Jane Zuccollo, John Tait, Kevin C Pringle

Placenta accreta (PA) refers to adherent placenta, which requires manual separation after delivery of the infant and is associated with severe haemorrhage during this procedure. It occurs at a rate of 1 in 1660 deliveries. Although previous Caesarean delivery appears to be a risk factor, PA also occurs in patients without it, and the location of the adherent placenta may not be related to the previous Caesarean scar. Diagnosis of the condition before delivery allows the decision to be made not to separate the placenta in selected cases, which results in improved maternal outcomes in terms of less blood loss and less units of blood transfused at delivery and a reduced risk of emergency hysterectomy, without an increase in other morbidity including DIC, ICU admission, infection, and the length of stay in the hospital.

Changes in cause of neonatal death over a decade
Annie Wong, Dawn Elder, Jane Zuccollo

Accurate assessment of the reason for deaths in the first month of life allows monitoring of change in cause of deaths in this age group over time. This review of neonatal deaths in Wellington over a 10-year period shows less neonatal deaths from congenital anomaly in this age group in the second 5-year period of review. This is likely due in part to better antenatal diagnosis with parents deciding to terminate the pregnancy but improved prognosis for liveborn infants with life threatening congenital anomalies is also a likely contributor. An increase in death secondary to infection is at least in part explained by the improved early survival of extremely preterm infants who remain vulnerable to infection particularly in the first month of life.

Unusual primary manifestations of multiple sclerosis
Yeşim Yetimalar, Yaprak Seçil, Ayşen Kendir İnceoğlu, Şölen Eren, Mustafa Başoğlu

Muliple sclerosis (MS) lesions in the brain and spinal cord can damage every function of the central nervous system. The protean symptoms included fatigue as well as disturbed function in sensory, motor, bladder, bowel, sexual, cerebellar, brainstem, optic nerve, and cognitive realms in other series. Most physicians consider the diagnosis of MS only in the presence of usual symptoms or signs and this may reflect underdiagnosis. Physicians should pay attention to those symptoms and consider they be the first manifestation of MS.

Cystic lesions of the liver: 6 years of surgical management in New Zealand
Jonathan B Koea

Cystic liver lesions can represent a spectrum of underlying conditions and liver cysts are very common. All cysts require investigation and complex cysts or symptomatic simple cysts require further treatment usually with minimally invasive surgery.

Risk and severity of injury in a population of BASE jumpers
Erik Monasterio, Omer Mei-Dan

BASE jumping is a high-risk adventure sport that developed out of skydiving, and uses specially adapted parachutes to jump from fixed objects. The research, which focuses on an international population of BASE jumpers, has been conducted by medical specialists with an interest and experience in adventure sports, and examines the risks of injury. BASE jumpers tend to participate in other adventure sports and are at significant risk of serious injury (from BASE jumping). The results are from a broader study that has also examined the personality characteristics of BASE jumpers. The long term goal of the researchers is to determine the risks associated with a range of other adventure sports, practiced in New Zealand.

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Screening the hard to reach: improving morbidity and mortality from cervical cancer in New Zealand

Peter Sykes, Lynn Sadler, Patricia Priest

Cervical cancer is arguably the most preventable common cancer. Indeed, since the introduction of our National Cervical Screening Programme (NCSP), we have seen a dramatic reduction in new diagnoses and deaths from this disease in New Zealand.[1,2] However we still report around 200 cases and 65 deaths per year.

Cervical cancer is clearly more common and has a worse outcome in definable groups of women. These include Māori women, older women, and the socioeconomically disadvantaged. This is probably due to both an increase in risk factors and to lower screening frequency among these groups. There may also be increased rates among other ethnic minorities.[3–6]

We now stand on the threshold of a new era in the prevention of cervical cancer. The Ministry of Health has signalled its intention to implement an HPV vaccination programme, and the NCSP is contemplating the implementation of liquid-based cytology and human papilloma virus (HPV) testing. However due to incomplete coverage of the eligible population, the NCSP is not currently performing to its potential.

HPV vaccination has the potential to reduce the risk of cervical cancer by about 70% but only in those vaccinated prior to HPV exposure. To be of significant national benefit, it will need to target young women prior to the onset of sexual activity and to reach women who are currently poorly accessed by the screening programme.

A fully funded school-based vaccination programme will be very expensive, however it is likely to be a cost-effective intervention[7,8] , despite the benefits of reduced cancer rates taking more than a decade to be realised.

When the vaccine is introduced, all women who have been exposed to HPV due to prior sexual activity will remain at risk of cervical cancer, and some cases will still occur. Those at greatest risk will be the unscreened and unvaccinated.

Liquid-based cytology and HPV testing may improve the efficiency and sensitivity of the NCSP at a yet to be determined cost. However, it will have minimal impact on morbidity and mortality from cervical cancer.[9,10]

The NCSP recommends that eligible women have a smear taken every 3 years. The taking of regular smears not only prevents cancers, it also ensures that greater proportions of cancers are detected at an earlier stage when the cancer is likely to be cured.

The New Zealand Cervical Cancer Audit revealed that 50% of women with cervical cancer were unscreened during the 3 years prior to their diagnosis, and 80% were not screened regularly. The Audit also found that 75% of the women with stage 2 or more advanced cervical cancer had not been screened in the 3 years prior to their diagnosis.

Screening data from the NCSP (IMG Annual report 2004) reveal that 30% of eligible New Zealand women are unscreened in the preceding 3 years. It is likely, therefore, that 50% of women with cervical cancers and 75% of those with advanced disease are seen in the 30% of women who were not screened at their last 3 yearly screening interval.

Screening rates are considerably lower among Māori and older women, who are at higher risk of cervical cancer. Screening rates may also be lower in other ethnic minorities as suggested by Wanzhen Gao, Janis Paterson, Ruth DeSouza, and Tongjing Lu in this issue of the *NZMJ* (*Demographic predictors of cervical cancer screening in Chinese women in New Zealand*; http://www.nzma.org.nz/journal/121-1277/3133).

Indeed, immigrant populations will be particularly at risk, if they are not regularly screened prior to immigration and, in the future, do not have access to HPV vaccination prior to sexual activity. It is therefore important that Gao et al's work is recognised. The study is preliminary and the sample is limited but it gives us some insight into the likely reasons for poor compliance with cervical screening in the Chinese immigrant population.

Issues relating to education, access, cost, and appropriateness of services were identified as barriers to screening. This information offers a springboard for further information gathering and hence interventional studies. It also raises the issue that while Asian women constitute one of New Zealand's largest ethnic minority groups their data are not reported uniquely in evaluations of the NCSP.

The most significant impacts on the burden of cervical cancer in New Zealand are likely to require attempts to reach the at risk, unscreened and potentially poorly vaccinated populations. A recent model commissioned by the NCSP predicts an increase in coverage from 70 to 90% would save an additional 27 lives per year (personal communication, NCSP, 2008). Although the difficulties in screening these populations are a cause for nihilism in some, it needs to be remembered they are hard but not impossible to reach.

Studies have shown that some interventions including the direct invitation of non participating women can improve coverage rates.[11,12] Interventions clearly need to be tailored to the poorly screened populations.

If the NCSP operated a population-based registry, this would at least ensure all eligible women are invited. The crucial role of primary healthcare providers and other health professionals must not be forgotten. Many unscreened women see health professionals for other reasons and these opportunities for education and screening should not be missed.

In summary, despite technological advances, improving screening rates would, in the short term, be the most effective way to reduce morbidity and mortality from cervical cancer. This fact must not be overlooked and it is essential that there is further investment into the development of strategies to access poorly screened populations and individuals.

Competing interests: None known.

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Demographic predictors of cervical cancer screening in Chinese women in New Zealand

Wanzhen Gao, Janis Paterson, Ruth DeSouza, Tongjing Lu

Abstract

Objective This pilot study examined the cervical cancer screening practices of Chinese women living in Auckland and the association with social demographic factors.

Methods A community-based survey was conducted and 234 questionnaires were administrated to ascertain the uptake of cervical screening. Participants were asked whether they had ever been screened in New Zealand and whether it had occurred in the previous 3 years.

Results One hundred and fifty-two (65.0%; 95% CI: 58.5–71.1) respondents reported having been screened in New Zealand and 56.0% (95% CI: 49.4–62.4) reported they were screened in the last 3 years. Factors independently associated with cervical cancer screening practice included age and duration of residence in New Zealand. The most frequently cited reason for never having had a smear test was that "thought it is unnecessary" (39%), followed by "don't know where to go" (36.6%).

Conclusion The uptake of cervical cancer screening is lower among women migrants from Mainland China living in New Zealand than that of the national New Zealand average. In addition, it is lower than that of Chinese women living in North America. The study highlights the information needs of new immigrants and older or younger women.

The Asian ethnic group was New Zealand's fourth largest major ethnic group after European, Māori, and Other ethnicity, totalling 9.2% in 2006. Two-thirds of people who identified with the Asian ethnic group lived in the Auckland Region; that is, almost 20% people in the Auckland Region identified with Asian ethnic group, the highest proportion of all the regions, and the second largest ethnic group in the Auckland region. [1] According to 2001 census data, the Chinese are the largest Asian group, making up 45% of all Asian people in the Auckland region.[2]

Cancer of the cervix uteri is the second most common cancer among women worldwide.[3] Invasive cervical cancer is the second leading cancer among women in mainland China.[4]Studies have suggested that Chinese women living in North America have higher cervical cancer incidence rates than the general population,[5,6] and that this higher prevalence is due in part to inadequate cervical screening.[7,8]

Some barriers to cervical screening appear to be universal for most women, such as perceptions that a cervical smear test is unnecessary, fear of a cancer diagnosis, embarrassment with the test procedure, and the lack of a physician referral.[9] However, it has been demonstrated that individual barriers to screening, and their relative importance, differ markedly between population groups.[10]

International studies have found that 76% to 81% Chinese women reported ever having a cervical smear test, and 57% to 61% reported having a smear test within the last 2 years.[7,8,11] Several sociodemographic factors were identified to be associated with having fewer smear tests, including older age, single marital status, being born in mainland China, lower education, lower household income, and less acculturation.[7,8,11]

New Zealand National Cervical Screening Programme (NCSP) reported a screening coverage of 73% overall for the last 5 years. However, the coverage varied by ethnic groups with the lowest coverage of 45% or so among Asian women.[12] Despite this low coverage, there are no published statistics on cervical cancer in Asian or Chinese immigrant women in New Zealand.

Women from mainland China have very little experience of screening because there is no organised population health programme in China, although some women are screened through annual health examinations arranged by their employers.

In response to the lack of research on the details of screening uptake and the reasons for the low rates of uptake of cervical screening in Asian population in New Zealand, we conducted a pilot study focusing on mainland Chinese women to investigate the:

- Cervical screening practices in Chinese immigrants;
- Barriers of and facilitators to cervical screening that could be used to develop intervention strategies for Chinese women; and
- Knowledge of cervical screening and cervical cancer risk factors in this immigrant population.

This brief report focuses on the description of cervical screening practice in the study population and the association with social demographic factors.

Methods

This was a community-based pilot survey that was followed up with a focus group interview.

Study sample—We aimed to recruit 260 women with the consideration of a 20% dropout rate. This was based on the finding of the screening rate of 45% for Asian women.[11] We allowed 15% of the desired margin of error, with 95% probability that the estimate was within the margin of error of the population value, thus establishing that two-hundred and ten women were needed for this study.

Survey recruitment—We partnered with the Chinese New Settlers Services Trust (CNSST), a local non-government organisation, to assist in the principal method for recruiting participants through access to their database. The researchers also utilised their considerable personal networks and affiliations in ethnic community organisations.

To promote the survey and enhance recruitment, information about the study was publicised in Chinese-language posters distributed in community settings and in Chinese newspapers. Women were eligible to participate in the study if they were (1) born in mainland China; (2) currently resided in Auckland New Zealand; (3) were aged 20 to 69.

The survey was conducted between November 2006 and February 2007. Once potential participants were identified, phone contact was made to confirm the address with potential participants, check the eligibility and invite them to participate in the study if eligible. The eligible women were asked to complete the self-administered survey and return the completed form to CNSST or to AUT using a postage-paid envelope. Ethics approval from AUT Ethics Committee was obtained before the recruitment started.

Survey instrument—The survey questions were developed in English, translated into Chinese, piloted, revised, and back translated to ensure lexical equivalence. Sociodemographic information were

collected regarding the woman's age, marital status, educational level, employment, income, and housing status (owned, rented), duration of residence in New Zealand and their fluency of English speaking.

Participants were asked whether they had ever been screened with a cervical smear test in China and in New Zealand, and, if so in New Zealand, whether they had been recently screened (within the last 3 years). They were also asked the reasons for never being screened or not being screened recently.

A pilot test of the survey questionnaire was conducted with eight Mainland Chinese women (they were not recruited as participants in the final study) and the questionnaire was further refined with input and feedback from Women's Nursing, Education and Health Promotion (WONS) and the NSCP team.

Statistical analysis—Descriptive analysis was conducted to summarise the characteristics of the sample. Primary analyses included the comparison of ever being screened with a cervical smear test of women with different sociodemographic characteristics. In a second analysis, we compared the proportion of being recently screened. The Chi-squared test and, when necessary, Fisher's exact test was used to assess statistical significance in bivariate comparisons. Multiple logistic regression analysis was performed to summarise the independent effects of sociodemographic factors on cervical cancer screening participation while adjusting for the possible confounding factors; specifically, due to the relatively small sample size, a method of forward selection of variables was used. The crude and adjusted odds ratios and 95% confidence intervals were reported for the effects. A significance level of α=0.05 was used to determine statistical significance for all calculations.

Results

Two hundred and sixty questionnaires were sent to eligible participants and 234 were received. Of these 234, 190 were recruited through CNSST, 33 through personal networks, and 11 through an advertisement. The mean age (SD) of the participants was 41 (10.6) with the range of 20 to 69 , 80.3% reported legally married, 80.7% had tertiary or postgraduate education, 47% were employed, 62.4% could converse in English, 38% had religion beliefs, the mean duration of living in New Zealand was 6 years (SD=3.8).

The rate of uptake of cervical screening—Ninety-eight respondents (41.9%; 95% CI: 35.5–48.5) reported ever being screened with a cervical smear test in China. 152 (65.0%; 95% CI: 58.5–71.1) reported ever being screened in New Zealand and 56.0% (95% CI: 49.4–62.4) reported they were recently screened in New Zealand. There was no statistical difference for the rate of ever being screened in New Zealand between women who were screened in China and who were not (64.3% vs 64.7%, p=0.953); no difference was found for being recently screened between these two groups (55.1% vs 55.6%, p=0.935).

Associations between having ever been screened with a cervical smear test in New Zealand and socio-demographic factors—In the bivariate analyses, statistically significant associations were found between women who had ever being screened in New Zealand and most of the sociodemographic variables examined in Table 1 except for education level, employment, and religion beliefs. Compared with women who were less than 30 years of age, middle-age women (30–49 years old) were more likely to report having ever being screened (77.6% vs 20.8%; OR: 13.19, 95% CI: 4.61–37.80); odds ratio of 1.65 for women aged 50 years old suggested an increased odds of being screened but it was not statistically significant.

Table 1. Numbers (row percentages), and crude and adjusted odds ratios of reporting ever being screened with cervical smear test in New Zealand by sociodemographic variables

Variable	Category	Total	Ever screened		Crude		Adjusted	
		N	n	%	OR	(95% CI)	OR	(95% C)I
Age (years)	20–29	24	5	20.8	1.00		1.00	
	30–49	161	125	77.6	13.19	(4.61–37.80)‡	9.65	(3.16–29.49)‡
	50+	33	10	30.3	1.65	(0.48–5.67)	0.97	(0.26–3.65)
	unknown	16	12	75.0	11.40	(2.54–51.11)‡	8.95	(1.59–50.47)*
Marital status	Married	188	130	69.1	1.00			
	Unmarried/single	36	16	44.4	0.36	(0.17–0.74) †		
	Unknown	10	6	60.0	0.67	(0.18–2.46)		
Education	Secondary or under	31	17	54.8	1.00			
	Tertiary or above	189	126	66.7	1.65	(0.76–3.56)		
	Unknown	14	9	64.3	1.48	(0.40–5.45)		
Income (weekly)	$0–$400	100	53	53.0	1.00			
	$401–$600	33	22	66.7	1.77	(0.78–4.04)		
	>$600	36	30	83.3	4.43	(1.70–11.59)†		
	Unknown	65	47	72.3	2.32	(1.18–4.53)*		
House tenure	Owned	121	92	76.0	1.00			
	Rented	113	60	53.1	0.36	(0.20–0.62) ‡		
Employment	Unemployed	91	53	58.2	1.00			
	Employed	110	78	70.9	1.75	(0.97–3.14)		
	Unknown	33	21	63.6	1.26	(0.55–2.86)		
Years lived in NZ	0–4	98	44	44.9	1.00		1.00	
	5–9	75	55	73.3	3.38	(1.77–6.45) ‡	4.15	(1.95–8.85) ‡
	10+	53	47	88.7	9.61	(3.76–24.57)‡	7.28	(2.63–20.10)‡
	Unknown	8	6	75.0	3.68	(0.71–19.15)	1.78	(0.25–12.43)
Can converse in English	No	77	40	51.9	1.00			
	Yes	146	104	71.2	2.29	(1.29–4.06) †		
	Unknown	11	8	72.7	2.49	(0.61–10.01)		
Religion	No	134	87	64.9	1.00			
	Yes	89	58	65.2	1.01	(0.58–1.77)		
	Unknown	11	7	63.6	0.95	(0.26–3.40)		
Age at immigration	0–39 years	163	117	71.8	1.00			
	40+ years	52	20	38.5	0.25	(0.13–0.47) ‡		
	Unknown	19	15	78.9	1.47	(0.47–4.68)		
Screened in China	No	133	86	64.7	1.00			
	Yes	98	63	64.3	0.98	(0.57–1.70)		

*P<0.05; † P<0.01; ‡ P<0.001

Single, never married, divorced, or separated women had a decreased odds of reporting having ever been screened compared to currently married women (44.4% vs 69.1%; OR: 0.36; 95% CI: 0.17–0.74). Women who were renting a property, who immigrated into New Zealand at the age of 40 years old or older were less likely to be screened.

The odds of having ever been screened increased for women who had a higher income ($600 or above weekly), and for those who could converse in English. A dose-response relationship was identified for the duration of residence in New Zealand, the odds were 3.38 (95% CI: 1.77–6.45) and 9.61 (95% CI: 3.76–24.57), respectively, for

women living in New Zealand for 5–9, and 10 years or more compared to those living in New Zealand for less than 5 years.

Table 2. Numbers (row percentages), and crude and adjusted odds ratios of reporting being recently screened with cervical smear test in NZ by sociodemographic variables

Variable	Category	Total	Ever screened		Crude		Adjusted	
		N	n	%	OR	(95% CI)	OR	95% CI
Age (years)	20–29	24	5	20.8	1.00		1.00	
	30–49	161	109	67.7	7.97	(2.82–22.51)‡	6.55	(2.28–18.83)‡
	50+	33	7	21.2	1.02	(0.28–3.72)	0.73	(0.19–2.80)
	unknown	16	10	62.5	6.33	(1.54–26.00)†	5.83	(1.24–27.43)†
Marital status	Married	188	112	59.6	1.00			
	Unmarried/single	36	14	38.9	0.43	(0.21–0.90)*		
	Unknown	10	5	50.0	0.68	(0.19–2.42)		
Education	Secondary or under	31	14	45.2	1.00			
	Tertiary or above	189	109	57.7	1.65	(0.77–3.55)		
	Unknown	14	8	57.1	1.62	(0.45–5.78)		
Income (weekly)	$0–$400	100	45	45.0	1.00			
	$401–$600	33	20	60.6	1.88	(0.84–4.19)		
	>$600	36	23	63.9	2.16	(0.99–4.75)		
	Unknown	65	43	66.2	2.39	(1.25–4.56) †		
House tenure	Owned	121	82	67.8	1.00			
	Rented	113	49	43.4	0.36	(0.21–0.62) ‡		
Employment	Unemployed	91	47	51.6	1.00			
	Employed	110	65	59.1	1.35	(0.77–2.37)		
	Unknown	33	19	57.6	1.27	(0.57–2.84)		
Years lived in NZ§	0–4	98	43	43.9	1.00		1.00	
	5–9	75	46	61.3	2.03	(1.10–3.74) *	2.10	(1.16–3.80) *
	10+	53	37	69.8	2.96	(1.46–6.01) †		
	Unknown	8	5	62.5	2.13	(0.48–9.42)	1.08	(0.19–6.26)
Can converse in English	No	77	36	46.8	1.00			
	Yes	146	89	61.0	1.78	(1.02–3.11)*		
	Unknown	11	6	54.5	1.37	(0.38–4.86)		
Religion	No	134	76	56.7	1.00			
	Yes	89	49	55.1	0.94	(0.55–1.60)		
	Unknown	11	6	54.5	0.92	(0.27–3.15)		
Age at immigration	0–39 years	163	101	62.0	1.00			
	40+ years	52	17	32.3	0.30	(0.15–0.58) ‡		
	Unknown	19	13	68.4	1.33	(0.48–3.68)		
Screened in China	No	133	74	55.6	1.00			
	Yes	98	54	55.1	0.98	(0.58–1.65)		

*P<0.05; † P<0.01; ‡ P<0.001; §The adjusted OR was calculated by combing the two middle groups of "5–9" and "10+".

Multiple logistic regression analyses generated two variables in the final step, namely, age and years lived in New Zealand. The adjusted OR and 95% confidence intervals are presented in Table 1. After controlling for confounding factors, women aged 30–49 years old were nearly 10 times more likely to report being screened in comparison with the young group (20–29 years of age). A fourfold and sevenfold odds of having

been screened were found for women living in New Zealand for 5–9 years and 10 years or more in comparison with those living in New Zealand for less than 5 years.

Associations between being recently screened in New Zealand and sociodemographic factors—As seen above, age, marital status, income, house type, duration of residence in New Zealand, age at immigration and English ability were found to be statistically associated with having been recently screened. The dose-response relationship for the duration of residence in New Zealand was not evident in the multivariable analysis. Thus, a group of '5+' was redefined to combine '5–9' and '10+' and the new category was used for the multiple logistic regression.

Again, age and the duration of residence in New Zealand were selected into the final multiple Logistic regression model. Table 2 shows that an adjusted odds ratio of 6.55 (95% CI: 2.28–18.83) was found for women of 30 to 49 years of age relative to women aged 20–29; the odds of be recently screened with cervical smear test doubled for the women who had lived in New Zealand for more than 5 years in comparison with those recent immigrants (<5 years) after controlling for age.

Table 3. Reasons reported never being screened with a cervical smear test (N=82)

Reason	N	%	(95% CI)
Feel embarrassed	6	7.3	(2.7–15.2)
It might be painful	7	8.5	(3.5–16.8)
Thought it is unnecessary	32	39.0	(28.4–50.4)
Scared about the results	2	2.4	(0.3–8.5)
Can't afford it	6	7.3	(2.7–15.2)
Unable to attend due to work	14	17.1	(9.7–27.0)
Language barrier	11	13.4	(6.9–22.7)
Don't know where to go	30	36.6	(26.2–48.0)
No woman GP / nurse smear-taker	1	1.2	(0–6.6)
Other	6	7.3	(2.7–15.2)

Reasons for never being screened or not being recently screened in New Zealand—Reasons reported for never being screened with cervical smear test were wide ranging. Table 3 shows that of those who had never had a smear test, the most frequently cited reason was that "thought it is unnecessary" (39%), followed by "don't know where to go" (36.6%), "unable to attend due to work" (17.1%), and "language barrier" (13.4%).

Twenty-one respondents reported that they had at least one smear test, but the test was not undertaken within the last 3 years. The main reasons were "thought it is unnecessary" (23.8%) and "unaware it is needed every 3 years" (19%). See Table 4.

Table 4. Reasons that cervical smear test was not conducted within the last 3 years (N=21)

Reason	N	%	(95% CI)
Pregnant	0	0	NA
Unable to attend due to work	2	9.5	(1.2–30.4)
Thought it is unnecessary	5	23.8	(8.2–47.2)
Unaware it is needed for every 3 years	4	19.0	(5.4–41.9)
Can't afford it	1	4.8	(0.1–23.8)
Had a bad experience with the last test	0	0	NA
Language barrier	1	4.8	(0.1–23.8)
Don't know where to go	2	9.5	(1.2–30.4)
No woman GP / nurse smear-taker	2	9.5	(1.2–30.4)
Other	0	0	NA

Discussion

We found that over one-third (35%) of the women who participated in this community-based survey had never been screened for cervical cancer in New Zealand, and 44% had not been screened within the last 3 years. The uptake is not only lower than that of the national level in New Zealand,[12] but also lower than that of Chinese women living in North America.[7,11]

In New Zealand, one of the goals of the New Zealand Health Strategy is to monitor the health of all New Zealanders and monitor inequalities in health between ethnic groups.[13] Much progress has been made over the past decade towards monitoring the health of Māori, European, and Pacific ethnic groups, but little has been conducted for Asian peoples.[14] The available research conducted in late 2004 to inform the development of communication strategies to promote greater use of cervical screening services omitted the Asian population.[15]

The different uptake between our sample and Chinese women living in North America might possibly be, in part, due to the different sampling methods. We only included Chinese immigrants who came from Mainland China. These women were relatively new immigrants with a mean duration of living in New Zealand of 6 years. It is likely that they were less acculturated into traditional New Zealand life in comparison with their counterparts who had lived in North America for a longer period of time[11] and who had immigrated from mainland China and other countries. In addition, it is envisaged that in North America, extensive and tailored educational programs and research to target underserved communities may have played a major role in reducing the gap across ethnic communities.[16–18]

Our findings that age and duration of residence are the most important factors associated with both having ever been screened and being recently screened are in line with other studies.[7,19] Women aged under 30 or above 50 years old were less likely to be screened compared to their middle-age group counterparts. A possible explanation is that women in the middle-age group were more likely to be integrated into the dominant culture through study, work and social activities. Through our focus group interview, it was also apparent that for many women aged between 40 to 50 the beginning of physical symptoms was a catalyst for being proactive about their

wellbeing. Some viewed taking care of their personal health as a prerequisite for being able to look after the whole family including the care of children and ageing parents.

The finding that young women had the lowest uptake of cervical screening could be related to their perceived view that they are relatively healthy and not at risk for cervical cancer or other gynaecologic problems. Another possible reason could be that some of them are not sexually active. Unfortunately, our survey did not contain information on sexual activity. If underuse of screening is limited to young women who are not sexually active, it may not represent a public health problem. Internationally, it has been suggested that unmarried Asian immigrants are less sexually active than unmarried US-born women;[20] however, a recent domestic study has showed that 56% of Chinese students living in New Zealand had their first sexual experience between 16–24 years old.[21] It is possible that some single and sexually active women simply did not want to attend the cervical screening programme to avoid people's awareness of their sexual behaviour.

Duration of residence appeared to be an important factor in screening uptake. The strong dose-response relationship suggested that new immigrants may be less aware of the cervical screening programme and the resources available to them for health care maintenance in their new country. Our findings that neither educational level nor whether being screened in China was significantly associated with the uptake in New Zealand suggested that it is not critically important whether women were aware of cervical cancer and related health services before immigration, but more important that information is available and accessible to them.

Although not entered into the multiple regression models, marital status, age at immigration, income, housing tenure as well as English ability were all significantly associated with cervical screening in the bivariate analysis. Studies have shown that these are very important predictors,[7,11] reflecting the association between socioeconomic status and screening participation. One possible explanation for the fact that age at immigration was not independently associated with the uptake of cervical screening programme in our study might be due to its co-linearity with the current age.

Of the 152 women who had ever been screened, 21 (13.8%) did not follow the screening time frame, that is, they did not get screened when they were due for a new smear test. One of the most important reasons they gave was same as the one given by those who had never been screened, that is, they thought it was unnecessary. The second important reason of 'don't know where to go' given by those who never had a smear test and of being 'unaware it is needed for every 3 years' given by those who were not followed up regularly with the screening programme suggested the lack of appropriate information provided for Chinese women and the need for a sound reminder process.

The strengths of this study include the community-based sampling method that included Chinese community services providers and a focus group as a component of the study. However, several limitations should be acknowledged. First, we only included women living in Auckland regional area, where there is a high density of Chinese residents. It is unknown to what extent our findings can be generalised to other geographic areas, where there are fewer Chinese residing.

Second, our principal method of recruitment via CNSST networks could have caused a selection bias. It is possible that our respondents had different uptakes of cervical screening compared to those who are not engaged with an ethnic community organisation and were less visible or to those who were approached but refused to participate.

Third, there may have been measurement error as a result of using a self-reported assessment of screening. A previous study found that there was a concordance of 78% between the patient report and medical record. Most discordance was from women who reported having had a test but had no record of testing.[22] The possible bias could partly explain the higher uptake rate in our sample compared to government statistics.[14]

Fourth, self-administered questionnaire may have also acted as a bias, because this method may have excluded women who may have found difficult to answer a questionnaire, even if it was in their own language. Last, as a pilot study, our sample size was small, which limited the power to identify the independent effects of some important socio-demographic factors.

In conclusion, our study has provided valuable baseline data of the uptake of cervical cancer screening among Chinese women in the Auckland area. It is hoped that the findings contribute to further research, health promotion and making services more accessible and acceptable. Efforts should be made to encourage enrolment and retention in the screening programme for all Chinese women between 20–69 years of age and increase the levels of understanding for the need for screening. The study highlights the information needs of new immigrants and older or younger women.

Competing interests: None known.

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Prospective 10-year study of postmenopausal women with asymptomatic primary hyperparathyroidism

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Abstract

Aim There are few prospective studies of people with asymptomatic primary hyperparathyroidism (PHPT) who have not had parathyroidectomy. We followed a group of postmenopausal women with asymptomatic PHPT for up to 10 years to determine whether they could be managed conservatively without parathyroidectomy.

Methods A 10-year, prospective, longitudinal study of 23 postmenopausal women with asymptomatic PHPT initially enrolled into a 4-year randomised controlled trial of hormone replacement therapy. Serum total and ionised calcium, biochemistry, urine calcium, and bone mineral density were measured every 6–12 months.

Results Serum ionised calcium, creatinine, and urine calcium:creatinine remained stable throughout follow-up. In contrast, there was a steady increase in the total and adjusted serum calcium and a small rise in serum PTH. Only one woman had an adjusted serum calcium >3.0 mmol/L during follow-up. There were few other clinical events possibly related to PHPT (1 possible episode of nephrolithiasis, 4 fractures, 1 severe osteoporosis). Three women underwent parathyroidectomy, although 19/23 women met the updated criteria for parathyroidectomy from the 2002 NIH-sponsored workshop during follow-up.

Conclusions Many postmenopausal women with asymptomatic PHPT do not develop symptoms or complications of PHPT, and their biochemical parameters remains stable. Therefore, such asymptomatic women with PHPT can often be managed conservatively without parathyroidectomy.

Primary hyperparathyroidism (PHPT) is a common condition with a prevalence of approximately 3/1000.[1] It occurs most commonly in postmenopausal women where the prevalence may be as high as 21/1000.[1] Most women with PHPT are asymptomatic but the management of such asymptomatic patients remains controversial.

The United States' National Institutes of Health (NIH)-sponsored consensus conference on the management of asymptomatic PHPT in 1990 recommended that parathyroidectomy be undertaken in asymptomatic patients if the patient was aged <50 years, serum calcium was >0.25–0.4 mmol/L above the reference range, creatinine clearance was reduced >30% compared to age-matched normal values, 24h urine calcium was >10 mmol/day, there was a history of nephrolithiasis, or a bone mineral density (BMD) Z-score was <-2.0.[2]

For those patients with PHPT who did not meet these criteria it was recommended that management include 6-monthly measurement of serum calcium, annual

measurement of 24h urine calcium, creatinine clearance, serum creatinine and BMD, and annual abdominal X-ray.[2]

In 2002, at a NIH-sponsored workshop, the recommendations for management were updated. Parathyroidectomy was recommended if the serum calcium was >0.25 mmol/L above the reference range or if the BMD T score was <-2.5 at the spine, hip, or distal radius. For those patients who did not meet the criteria for parathyroidectomy, annual measurements of 24h urinary calcium and creatinine clearance, and annual abdominal X-rays were no longer recommended.[2]

Despite these recommendations, the optimal management of mild PHPT remains controversial. A number of editorialists recommend that almost all people diagnosed with PHPT should undergo parathyroidectomy.[3–5]

There are only a small number of prospective longitudinal studies of asymptomatic PHPT without parathyroidectomy.[6–8] These studies show that the serum calcium and serum creatinine remain stable over time, and that most patients do not develop new symptoms or complications, suggesting that most asymptomatic patients with PHPT do not require parathyroidectomy. We have closely followed a group of postmenopausal women with asymptomatic PHPT for up to 10 years. Here we report the clinical, biochemical, and BMD data from this group of women.

Methods

Participants—In 1992 we searched the records of our Endocrinology Department for patients with PHPT; 73 postmenopausal women with asymptomatic PHPT were subsequently invited to take part in a 2-year randomised controlled study of the effects of hormone replacement therapy (HRT) on BMD.

The protocol has been previously published.[9] In brief, women with elevated serum ionised calcium and parathyroid hormone (PTH) levels were eligible to take part. Women were excluded if they had systemic illness, untreated thyroid disease, hepatic or renal dysfunction, undiagnosed genital bleeding, or recent use of bone-active medication including thiazide diuretics, oestrogen, glucocorticoids, fluoride, or bisphosphonates; 42 women agreed to take part.

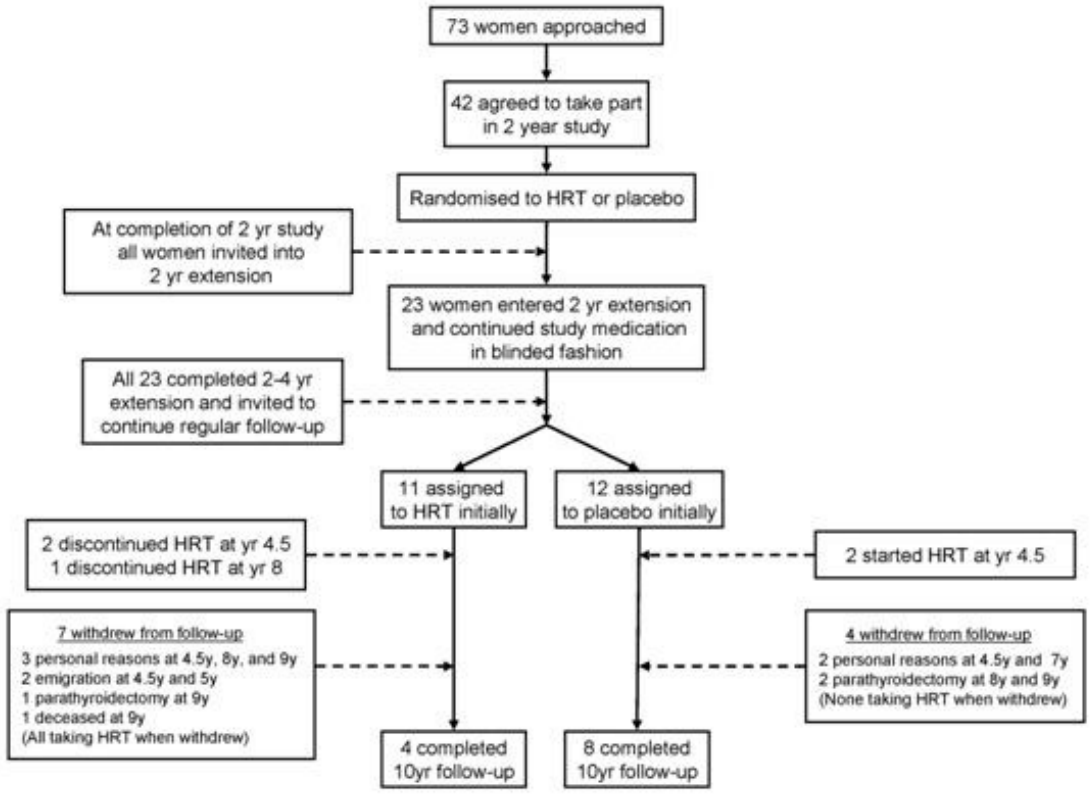
At completion of the study, all participants were invited to continue into a 2-year extension where they continued their study medication in a blinded fashion;[10] 23 participants agreed to enter this extension study, at the end of which (at year 4), all participants were invited to continue regular follow-up at the Endocrinology Department (Figure 1).

During the first 6 years of follow-up, participants were seen every 6 months and for the last 4 years they were seen on an annual basis. Here we present the results of the 23 women who entered the years 2–4 extension study and were followed for up to a total of 10 years.

Eleven of these women were initially randomised to treatment with HRT and 12 women to placebo. At year 4, the treatment allocation was discussed with each participant. Two women initially randomised to HRT opted to discontinue HRT, while two women initially randomised to placebo chose to start HRT at that time (Figure 1).

Over the 10-year observation period, the mean (SD) duration of HRT was 6.8 (2.2) years in the 11 women initially randomised to treatment with HRT, and 5.3 (1.0) years in the 2 women initially randomised to treatment with placebo.

Figure 1. Flow of participants



Note: The mean (SD) duration of follow-up was 8.5 (2.0) years.

Controls—For comparison, we selected a control group from our previously reported 10-year study of normal postmenopausal women.[11] In that study, women who had volunteered for a study of calcium supplementation were invited for a repeat measurement of BMD 10 years after their first assessment. From this group of 102 women, we selected a control group comprising 28 postmenopausal women aged >60 years who had not taken any medication likely to impact on bone density (including oestrogen, bisphosphonates, fluoride or prednisone) over this 10-year period; 15/28 women took calcium supplements for a mean (SD) of 6.5 (3) years.

Measurements—At each visit we inquired about specific complications related to PHPT, and height and weight were measured. BMD of the lumbar spine, total body, proximal femur, and forearm, and body composition were measured using a dual energy X-ray absorptiometer (DPX-L, Lunar, Madison, WI), and fasting blood and urine samples were collected at each visit.

Serum biochemistry (including ionised calcium), serum albumin, and serum alkaline phosphatase were performed at baseline, 6 months, 2 years, 4 years, 4.5 years, 5 years and then annually. 25-hydroxyvitamin D, PTH, fasting urine calcium and urine creatinine, and 24-hour urine calcium and creatinine were performed at baseline, 6 months, 2 years, 4 years, 8 years, 9 years, and 10 years. Serum calcium was measured using an automated analyser (Roche), and serum ionised calcium using an automated ion-selective electrode (Bayer). PTH was measured using a two-site immunoradiometric assay (Nichols Institute Diagnostics) for years 0–8 and then using an electrochemiluminescence immunoassay (E170, Roche) for years 9-10. Serum albumin was measured with a bromocresol green assay (Roche).

Statistics—Differences between baseline and final results, and between participants and controls were compared using Student's t-test for continuous variables or the Chi-squared test for categorical variables. Since the length of follow-up differed among participants, we used linear regression to

calculate a line of best fit for each participant for serum ionised calcium, adjusted serum calcium and BMD with respect to time. The means of the slopes were calculated to give an average line of best fit for the cohort for the 10-year period which represents the average change in ionised calcium, adjusted calcium, or BMD with time.

Statistical significance was set at $p<0.05$ and all tests were two-tailed. All statistical analyses were performed using SAS statistical software (SAS Institute, Cary, NC version 9.1).

Results

Patient characteristics—The characteristics at study entry of the 23 women with PHPT and the 28 controls are shown in Table 1. The mean (SD) duration of known PHPT was 3.0 (2.8) years. As we have previously reported,[12] the women with PHPT were heavier than the controls. The controls had higher BMD at the femoral neck and total body. In total, 11 women withdrew from the study between years 2 and 10 of the study (Figure 1). The characteristics at study entry of the women who completed 10 years of follow-up were not significantly different from those who did not. The mean (SD) duration of follow-up was 8.5 (2.0) years.

Possible PHPT complications—During the 10-year follow-up period there were a number of events potentially related to PHPT. These events are shown in Table 2 along with the events in the healthy controls for comparison. 4/23 women with PHPT suffered fractures compared with 11/28 healthy controls. One woman with adjusted serum calcium at baseline of 2.76 mmol/L developed persistent adjusted serum calcium >3.0 mmol/L after 7 years.

She underwent parathyroidectomy for hypercalcaemia at 8 years. No other participants had adjusted serum calcium >3 mmol/L at any time. Two other women underwent parathyroidectomy—one for hypercalcaemia at 9 years [baseline adjusted serum calcium 2.58 mmol/L, mean (range) over 9 years: 2.75 (2.57–2.96) mmol/L], and one at 9 years because of osteoporosis (baseline BMD: lumbar spine 0.95 g/cm^2, femoral neck 0.80 g/cm^2, mid-forearm 0.55 g/cm^2; change over 9 years lumbar spine -3%, femoral neck -10%, mid-forearm -7%; during the study period she received HRT for 9 years). There were no other potential complications of PHPT reported.

Biochemistry and anthropometry—Previously, we reported that HRT did not cause any sustained effects on anthropometric or biochemical parameters in postmenopausal women with PHPT.[9,10] Therefore, we analysed the cohort as a whole for all these parameters. Data from the three women who underwent parathyroidectomy were included until the last visit before surgery. Table 1 shows the baseline biochemical and anthropometric parameters and the changes at the final visit for the women with PHPT. Data from the healthy control group is included for comparison.

The mean level of serum ionised calcium did not change during the period of observation in the women with PHPT, whereas the adjusted serum calcium increased by 0.23 mmol/L. Figure 2 shows the mean serum ionised calcium and mean adjusted serum calcium over time and the average lines of best fit for the group.

In the women with PHPT, mean serum PTH increased steadily while serum 25-hydroxyvitamin D decreased steadily. In the women with PHPT, body weight, fat mass, and lean mass tended to decrease over time, whereas in the controls, body weight increased while lean mass was stable and fat mass tended to increase.

Table 1. Anthropometric, bone density, and biochemical characteristics at study entry and changes over time in 23 women with primary hyperparathyroidism (PHPT) and 28 healthy controls

	Primary hyperparathyroidism (n=23)			Controls (n=28)			Between-groups differences	
	Baseline	Difference at final visit	P[a]	Baseline	Difference at 10 years	P[a]	Baseline P[b]	Change from baseline P[c]
Age (years)	66 (7)			64 (3)			0.09	
Bone density (g/cm^2)								
L24	1.00 (0.17)			1.02 (0.09)			0.24	
Femoral neck	0.79 (0.13)			0.82 (0.08)			**0.02**	
Total body	0.99 (0.10)			1.04 (0.05)			**<0.001**	
Weight (kg)	77 (16)	-3.5 (8.4)	0.06	63 (8)	2.1 (4.8)	**0.03**	**<0.001**	**0.005**
Fat mass (kg)	35 (12)	-2.8 (7.8)	0.10	24 (6)	1.3 (3.9)	0.10	**<0.001**	**0.02**
Lean mass (kg)	38 (4)	-0.4 (2.1)	0.38	37 (4)	0.0 (1.5)	0.88	0.19	0.49
Body mass index (kg/m^2)	30 (6)	-0.8 (3.0)	0.23	24 (3)	1.1 (1.8)	**0.003**	**<0.001**	**0.007**
Total serum calcium (mmol/L)	2.59 (0.13)	0.10 (0.15)	**0.006**	2.38 (0.07)	-0.02 (0.08)	0.24		
Adjusted serum calcium (mmol/L)	2.49 (0.12)	0.23 (0.14)	**<0.001**	2.36 (0.07)	-0.04 (0.07)	**0.006**		
Serum ionised calcium (mmol/L)	1.40 (0.07)	-0.03 (0.09)	0.18	1.23 (0.04)	N/A			
Albumin (g/L)	45 (2)	-5.3 (3.8)	**<0.001**	44 (2)	-1.4 (2.1)	**0.002**	**0.02**	**<0.001**
Serum creatinine (mmol/L)	0.09 (0.01)	-0.01 (0.01)	**0.007**	0.09 (0.01)	0.00 (0.01)	0.07	0.67	0.16
Alkaline phosphatase (U/L)	107 (31)	-7 (35)	0.35	73 (16)	12 (12)	**<0.001**	**<.0001**	**0.02**
25 hydroxyvitamin D (nmol/L)	57 (24)	-16 (28)	**0.01**	N/A	N/A			
Parathyroid hormone (pmol/L)	7.9 (3.2)	3.5 (4.8)	**0.002**	N/A	N/A			
24 hour urine calcium (mmol/day)	7.6 (3.1)	-1.4 (3.6)	**0.07**	N/A	N/A			
Urine calcium/creatinine	0.5 (0.5)	0.0 (0.5)	0.90	0.2 (0.2)	0.1 (0.2)	0.09	**<0.001**	0.69

Data are mean (SD). The mean (SD) duration of follow-up in the women with primary hyperparathyroidism was 8.5 (2.0) years.

[a] P values are for the within-groups changes from baseline.

[b] P values are for the between-groups differences between baseline variables.

[c] P values are for the between-groups differences in the change from baseline.

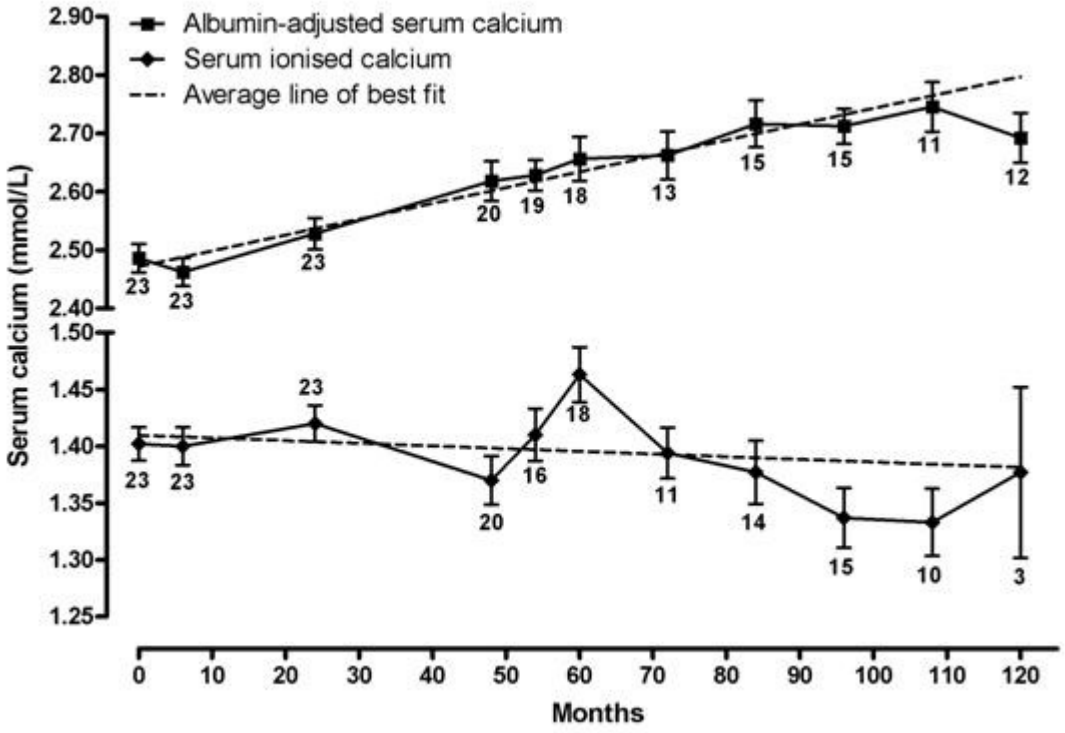
N/A: not available.

Table 2: Events during the study potentially related to primary hyperparathyroidism (PHPT)

Event	PHPT by initial treatment assignment		Healthy controls
	HRT (n=11)	Placebo (n=12)	n=28
Fractures (number, site)	1 fibula	1 fibula, 1 hip, 1 humerus	7 wrist, 1 foot, 1 hand, 2 finger
Kidney stones	1 possible episode	0	0
Hypercalcaemia (> 3.0 mmol/L)	0	1	0
Parathyroidectomy (number, indication)	1 osteoporosis	2 hypercalcaemia	0
Death (number, cause)	1 congestive heart failure	0	N/A

HRT=hormone replacement therapy; N/A=only controls completing 10 years of follow-up were included.

Figure 2. The mean serum ionised calcium and mean adjusted serum calcium for the group of women with PHPT, and the average lines of best fit for the group



Note: The average line of best fit was calculated using the mean intercept and slope of the individually calculated lines of best fit. The error bars represent the standard error of the mean. The number of women at each time point is listed next to the individual point.

In both groups serum creatinine remained stable and serum albumin decreased, although the decline in serum albumin was greater in the women with PHPT than the controls.

Bone mineral density—Previously we reported that treatment with HRT produced a 3.6–6.6% increase in BMD after two years and 4.6–8.2% after 4 years,[9,10] therefore

we restricted analyses involving BMD to those 12 women initially assigned to placebo. Two of these women later opted to take HRT and 1 woman an oral bisphosphonate, and so only their results until the commencement of HRT or the bisphosphonate were included in analyses.

The average change in BMD at the lumbar spine was 0.3%/year (95% confidence interval -0.1 to 0.6) for the PHPT group and 0.3%/year (0.0 to 0.5) for the healthy controls (p>0.9). At the femoral neck the annual change was -1.3%/year (-2.0 to -0.5) for the PHPT group and -0.3%/year (-0.6 to -0.1) for the controls (p=0.02).

At the total body, the annual change was -0.1%/year (-0.3 to 0.2) for the PHPT group and -0.2%/year (-0.3 to -0.1) for the controls (p=0.4). At the mid-forearm the annual change in the PHPT group was -0.4%/year (-0.9 to 0.0).

Discussion

The results from this small group of postmenopausal women with PHPT closely followed prospectively for up to 10 years suggest that biochemical parameters remain stable over at least 8.5 years. During follow-up, the serum ionised calcium, serum creatinine, and measures of urine calcium excretion remained stable.

While serum PTH levels increased over time, only one woman had an adjusted serum calcium >3.0 mmol/L at any time during the study, and, after a mean follow-up of 8.5 years, the mean adjusted serum calcium was 2.72 mmol/L which is similar to the reported mean serum calcium from other studies of PHPT.[7,8,13] There was a discrepancy between serum ionised calcium results, which remained stable throughout follow-up, and serum total and adjusted calcium results, which steadily increased over time.

There were few clinical events potentially related to PHPT during the follow-up period and only three women had parathyroidectomy performed. In those women who were initially assigned to placebo treatment, the annual change in BMD was similar to that observed in eucalcaemic controls at the spine and total body but there was greater loss of BMD at the femoral neck.

If we had applied the updated criteria for parathyroidectomy from the recent NIH-sponsored workshop[2] to our group of women, 19/23 would have met these criteria during follow-up: 8 women had at least one adjusted serum calcium >2.8 mmol/L (0.25 mmol above the reference range of 2.10-2.55 mmol/L); no woman had a creatinine clearance 30% less than healthy matched controls; 7 women had at least one 24 hour urine calcium >10mmol/day; and 15 women had at least one BMD T-score <-2.5 at the spine, femoral neck, or forearm. Since there were few clinical events during follow-up, and few patients required parathyroidectomy, a conservative approach appears to be justified.

There are few prospective longitudinal studies of patients with asymptomatic PHPT who have been closely followed but not had parathyroidectomy.

Scholz et al followed 142 patients with PHPT and serum calcium <2.75 mmol/L for up to 10 years:[6] 33 had parathyroidectomy, 67 were excluded because of previous negative neck exploration, or loss to follow up, thus leaving 42 patients with complete data for 10 years. Thirty had persistent but stable disease with no significant

worsening of hypercalcaemia or renal function, while 12 were normocalcaemic at follow-up.

Rao et al followed 80 asymptomatic patients with PHPT and serum calcium <3.0 mmol/L.[7] Over a mean duration of follow-up of 4 years, serum calcium, PTH, urine calcium, and renal function remained stable. The rate of bone loss at the forearm, as measured by single photon absorptiometry, was within the expected range. Four patients underwent parathyroidectomy, although none met those authors' criteria for surgical intervention.

Silverberg et al studied 101 asymptomatic patients with PHPT;[8] 49 had parathyroidectomy because they met the NIH consensus conference criteria. The remaining 52 patients were followed for up to 10 years. The mean duration of follow-up was not stated, but 73%, 47%, 35%, and 23% of participants completed 1, 4, 7, and 10 years of follow-up respectively. The serum calcium, PTH, urine calcium, and BMD remained stable during follow-up; 14/52 patients had progression of disease during follow-up, defined as the development of one or more new indications for parathyroidectomy (2 developed serum calcium >3 mmol/L, 8 developed urinary calcium >10 mmol/day, and 6 developed forearm BMD Z score <-2).

The findings of these prospective longitudinal studies that serum calcium, creatinine, and bone density remain stable over time are in agreement with other prospective and retrospective reviews of patients managed in clinical practice,[13–20] patients identified at health screening surveys and followed up 14–17 years later,[21,22] and two more recent randomised controlled trials of surgery versus observation.[23,24]

Our findings of stable but persistent disease over time are in broad agreement with these previous studies. One striking difference was that, although serum ionised calcium levels remained stable, there was a steady rise in serum adjusted calcium over the follow-up period, from a mean level of 2.49 mmol/L at baseline to 2.72 mmol/L at the final visit. This was accompanied by an increase in PTH but not in alkaline phosphatase, the latter suggesting the absence of progressive bone disease and implying that the ionised calcium is providing a more accurate indication of disease activity.

The dissociation of total/adjusted and ionised calcium implies a change in protein binding of calcium and/or the complexed calcium fraction, both possibilities suggesting a change in acid-base status towards a more alkalotic state. This is not an expected consequence of parathyroid hormone excess, so remains unexplained.

Ladenson reviewed determination of calcium in PHPT and concluded that ionised calcium levels are more sensitive and are more likely to be elevated in PHPT than adjusted serum calcium levels,[25] but to our knowledge, such a discrepancy between ionised and adjusted calcium levels over time has not previously been reported.

The reason for the greater sensitivity of ionised calcium levels in the diagnosis of PHPT is also unknown but is not explained by differences in serum proteins, albumin or pH in patients with PHPT.[25] Our data suggest that any early rise in serum calcium levels in the course of the disease is artefactual, as serum ionised calcium levels are likely to be elevated but stable. Additionally, our data suggest some women may have had elevated serum ionised levels for a considerable time before serum total calcium levels become increased.

The discrepancies between serum total and ionised calcium may also explain the common occurrence of normocalcaemia in follow-up of cohorts with PHPT.[6,22] In the Mayo clinic series, 12/42 patients with PHPT who had not undergone parathyroidectomy had normal levels of total/adjusted serum calcium after 10 years of follow-up.[6]

Palmer et al reported that 48/95 people with PHPT who had not undergone parathyroidectomy were normocalcaemic after 14 years of follow-up.[22] In addition, elevated serum ionised calcium but normal adjusted serum calcium has been reported in people with PHPT and surgically proven parathyroid adenomas.[25,26]

Our data support the routine use of ionised calcium in the diagnosis and monitoring of PHPT.[25,27] All our participants had serum ionised calcium above the reference range at baseline whereas only 6/23 had elevated adjusted serum calcium levels. Use of the adjusted serum calcium would have led to underdiagnosis of PHPT and the erroneous impression of worsening hypercalcaemia over time. However, measurement of ionised calcium is more technically challenging and costly than measurement of total serum calcium.

We also found that the change in BMD over time was similar to that occurring in healthy controls at the spine and total body but accelerated at the femoral neck. The accelerated loss may have been contributed to by the weight loss that occurred in the women with PHPT.

The present findings differ from those of Silverberg et al who found stable BMD at all sites, but the mean age of subjects in that study was 58 years, 8 years younger than the mean age in our study.[8] These data suggest that recommendations to measure BMD annually[2] in patients with PHPT are excessive.

We believe that measurement of BMD should be undertaken at diagnosis in postmenopausal women with PHPT, and repeated after a 3–5 year interval in those women managed without parathyroidectomy. The occurrence of osteoporosis and/or fragility fracture should prompt intervention, which might reasonably involve either anti-resorptive therapy or parathyroidectomy, which both lead to increases in BMD in patients with PHPT.[8–10,20,28–32]

Previously we reported that patients with PHPT have greater body weight than their eucalcaemic healthy peers,[12,33] and body weight is positively correlated with PTH levels in eucalcaemic postmenopausal women.[34] A possible explanation for this observation is that excess PTH could promote insulin resistance, thereby inhibiting lipolysis by adipocytes leading to greater fat mass and body weight. Our results do not support this hypothesis because women with PHPT lost an average of 3.5 kg over 10 years in contrast to the controls who gained a similar amount of weight.

These findings of weight loss over time, along with the decrease in serum albumin, suggest that excess PTH secretion over time does not lead to increased fat mass or body weight, but rather is associated with catabolic changes. Another hypothesis to explain the weight differences is that increased body weight may cause PHPT.[33] Increased body weight is associated with lower 25-hydroxyvitamin D levels[35–39] which may lead to parathyroid autonomy and eventually PHPT by prolonged stimulation of the parathyroid glands.[40, 41]

We observed a 28% decrease in serum 25-hydroxyvitamin D levels over time in the women with PHPT which may have contributed to the increase in serum PTH levels.

There are some limitations to our results. Firstly the sample size was small. Out of the original group of 42 women, 23 entered the extension study and 12 completed the full 10 years of follow-up. The loss of participants during the study may have biased our results in either direction.

Women who had poorer health may have been more likely to withdraw from the study because of these health issues. Alternatively, women with better health may have been more likely to withdraw from the study because they had fewer health issues and therefore perceived there to be fewer benefits from continued participation. The study was restricted to postmenopausal women and the results are not generalisable beyond this group.

Despite these limitations, the study has a number of strengths—particularly the prospective study design, the close follow-up of participants, and the prolonged duration of follow-up (mean duration 8.5 years).

In conclusion, our study suggests that many asymptomatic postmenopausal women with PHPT remain asymptomatic with stable biochemical parameters over time. Bone loss may be slightly accelerated at the proximal femur. Therefore most such asymptomatic women with PHPT can be managed conservatively without parathyroidectomy.

Application of the updated criteria for parathyroidectomy from the NIH-sponsored workshop would have led to almost all our group being referred for parathyroidectomy; the reassuring results from this and other longitudinal studies of mild PHPT suggest that adherence to these criteria may promote unnecessary intervention.

Competing interests: None known.

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The maternal outcome in placenta accreta: the significance of antenatal diagnosis and non-separation of placenta at delivery

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Abstract

Aim To evaluate the effects of antenatal diagnosis and subsequent placental non-separation at delivery on the maternal outcome in confirmed cases of placenta accreta.

Method The perinatal database and medical records for women who delivered in the period 2000–6 in a teaching hospital in New Zealand with a diagnosis of placenta accreta or postpartum haemorrhage or hysterectomy were reviewed. In confirmed placenta accreta cases, the amount of blood loss and blood transfused at delivery and subsequent emergency hysterectomy were analysed in respect to the presence/absence of antenatal diagnosis and the management at delivery.

Results 16 women had placenta accreta confirmed (15 histologically and 1 visually). Antenatal diagnosis was made in 7 women, elective Caesarean delivery planned in all, hysterectomy to follow in 5 (4 elective, 1 emergency preterm), and elective placental separation in 2 women. When an antenatal diagnosis was not made (n=9), attempted placental separation led to emergency hysterectomy for all (p=0.001). Antenatal diagnosis and placental non-separation resulted in less mean blood loss (1.4 L vs 3.6 L, p=0.003; 1.0 L vs 3.4 L, p<0.001) and mean units of blood transfused (1.2 vs 5.1, p= 0.005) in the latter.

Conclusion In placenta accreta, antenatal diagnosis and avoidance of placental separation may result in better maternal outcome.

Placenta accreta is a well-known cause of maternal morbidity and mortality.[1] The incidence of placenta accreta (including increta and percreta) may have risen 10-fold in the past 50 years,[2] and recent reports suggest a frequency per delivery between 1:2500 and 1:110.[1–3].

The maternal risk appears to occur at the time of placental separation resulting in severe haemorrhage, disseminated intravascular coagulation, massive blood transfusion, need for intensive care, hysterectomy, and occasionally maternal death.[4–6]

Conservative management by leaving the placenta *in situ* at the time of delivery has been proposed to lessen the risk of severe haemorrhage and hysterectomy.[7–9] However, when conservative management is carried out based on the clinical suspicion of placenta accreta at the time of delivery, there may not be histological confirmation or proof of the condition.[7] It is therefore difficult to attribute a better outcome for conservative management to the treatment method alone.

The aim of this retrospective analysis was to determine the incidence of confirmed placenta accreta in our institution and to examine the effects of an antenatal diagnosis and the subsequent non-separation of the placenta during the third stage on maternal outcomes.

Methods

Women who delivered in the second and third trimesters in the period 1 January 2000 to 31 December 2006, with a diagnosis of placenta accreta or postpartum haemorrhage or hysterectomy, were identified from a perinatal database at Wellington Hospital (Wellington, New Zealand).

The medical notes were examined and checked with the database for the following:

- Any confirmation of diagnosis placenta accreta and the basis for the confirmation including clinical observation or histologic findings;
- The women's risk factors for placental accreta;
- Any antenatal diagnosis made by ultrasound and/or magnetic resonance imaging (MRI);
- The recorded blood loss (litres, measured and estimated);
- The blood units transfused (around 300 ml per unit);
- Requirement for other blood products (fresh frozen plasma and/or cryoprecipitate);
- Intensive Care Unit (ICU) admission;
- Diagnosis of disseminated intravascular coagulation (DIC);
- Operative interventions and complications (such as hysterectomy and bladder injuries); and
- The length of stay after delivery.

The diagnosis of placenta accreta in those women identified was checked against the histological findings by the Pathology Department.

As this retrospective analysis conforms to the standards established by the NHMRC for ethical quality review, ethics approval was not sought.

The statistical software package SPSS 12.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Independent samples t-test, Fisher exact test and Mann-Whitney U test were applied where appropriate. A p value <0.05 was regarded as statistically significant.

Results

Sixteen women were identified from the perinatal database, hospital records, and the Pathology Department as having confirmed placenta accreta in this 7-year period during which there were 26,556 deliveries—an incidence of 1 per 1660 deliveries.

Of these 16 women, 15 had histological confirmation (based on hysterectomy specimens in 14, and the placental specimen in 1) and 1 had clinical confirmation by laparotomy with placenta percreta being observed. There were 2 cases of placenta percreta (Cases A and G). The clinical details and the pregnancy outcomes of these sixteen women are listed in Table 1.

There were 4 women with no previous Caesarean section. In the 12 women with previous Caesarean section(s), 4 did not have placenta previa in the index pregnancy. In the remaining 8 patients with previous Caesarean section(s) and placenta previa, the location of the placenta was Type IV (i.e. both anteriorly and posteriorly located) in 3, anterior in 4, and posterior in 1.

Table 1. Summary of the demographic data and pregnancy outcomes in women diagnosed with placenta accreta

Woman ID	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Age (years)	29	36	33	34	40	30	33	31	30	44	32	40	36	36	30	33
Gravidity	3	4	4	3	5	2	6	5	4	2	5	2	7	7	5	6
Parity	2	3	3	2	4	1	5	1	3	1	4	0	3	3	3	3
No. of previous C/S	2	0	3	2	3	1	4	1	3	1	1	0	1	1	0	0
No. of previous curettage	0	0	0	0	0	0	0	3	0	0	0	1	2	3	1	4
No. of previous MROP	0	2	0	0	0	0	0	0	0	0	0	0	0	1	1	0
Previous history of ‘placenta accreta’	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N
Placenta previa in current pregnancy	Y	N	Y	Y	N	Y	Y	Y	N	N	Y	N	Y	N	Y	Y
Antenatal diagnosis	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	N	N	N	N	N
Gestation at delivery (weeks)	37	37	34	38	36	37	32	38	38	36	24	38	32	26	18	33
Attempted placental separation	N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Total blood loss (ml)	500	800	1500	500	1500	1500	3400	5000	1500	3500	3500	3000	4000	5400	5310	1500
No. of units of blood transfused	0	0	3	0	3	2	8	6	0	7	4	4	8	6	9	2
Other blood products	N	N	N	N	Y	N	N	N	N	N	Y	Y	Y	N	Y	N
Hysterectomy	N	El	El	El	Em	N	El	Em	Em	Em	Em	Em	Em	Em	Em	Em
Bladder injury	N	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N
Infection	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y
DIC	N	N	N	N	Y	N	N	Y	N	Y	Y	Y	N	N	Y	N
ICU admission	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	Y	N
Length of postnatal stay (days)	18	4	10	5	7	5	11	7	4	5	5	6	7	18	5	32

C/S=Caesarean section; MROP=manual removal of placenta; DIC=disseminated intravascular coagulation; ICU=Intensive Care Unit; Y=yes; N=,no; El=elective; Em=emergency.

Placenta accreta was not screened in the first half of the study period. An antenatal diagnosis of placenta accreta had been made by ultrasound and/or magnetic resonance imaging (MRI) in seven women—six were delivered by elective Caesarean section and one as a preterm emergency because of antepartum haemorrhage.

After effecting delivery of the infant, the placenta was left unseparated in five of these seven women, of whom four had a hysterectomy, and the fifth (Woman A), with placenta percreta, had combined methotrexate treatment and uterine artery embolisation.[10]

The normal practice of the use of syntocinon bolus after delivery of the infant was avoided in cases where the placenta was not separated electively. The placenta was separated as planned in two of these seven cases at the time of delivery; at elective Caesarean section in a case with antenatal diagnosis of partial placenta accreta (Woman F), and during dissection at elective Caesarean hysterectomy (confirmed placenta percreta histologically) in the other (Woman G). Thus, in the group with an antenatal diagnosis, hysterectomy was planned following Caesarean delivery in five of the seven women, and the uterus was conserved in two.

In nine cases an antenatal diagnosis was not made. Separation of the placenta was attempted in all nine women at the time of delivery (p=0.005) leading to emergency hysterectomy in all (p=0.001). Compared with the group with an antenatal diagnosis of placenta accreta, women who had not had an antenatal diagnosis of placenta accreta had significantly more haemorrhage (mean total blood loss of 3.6 L vs 1.4 L, p=0.003) (Table 2).

Table 2. The maternal outcome in relation to antenatal diagnosis of placenta accreta

Variables	Antenatal diagnosis		P value
	Yes (n=7)	No (n=9)	
Attempted placental separation	2	9	0.005‡*
Total blood loss (litres) (mean ± SD)	1.4 ± 1.0	3.6 ± 1.3	0.003†*
Number of units of blood transfused	2.3 ± 2.9	5.1 ± 2.9	0.07†
Other blood products required	1	4	0.31‡
DIC	1	5	0.15‡
Emergency hysterectomy	1	9	0.001‡*
Bladder injury	1	1	1.0‡
ICU admission	1	1	1.0‡
Infection	0	3	0.21‡
Length of postnatal stay (days) (mean ± SD)	8.6 ± 4.9	9.9 ± 9.3	0.92∫

*Statistically significant; †2-tailed independent sample t-test not assuming equal variance; ‡2-tailed Fisher Exact Test; ¶2-tailed Mann-Whitney U test; DIC=disseminated intravascular coagulation; SD=standard deviation.

Attempts at placental separation were made in 11 women (Table 1 and 3).

Two of these 11 women had been diagnosed with accreta antenatally as described above. These 11 women had significantly more blood loss (3.4 L vs 1.0 L, p <0.001) and more units of blood transfused (5.1 units vs 1.2 units, p=0.005) compared to the 5 women who had an antenatal diagnosis but had hysterectomy without attempted

placenta separation (4), or had the placenta left *in situ* with methotrexate therapy and uterine artery embolisation (Woman A)[10] (Table 3).

Table 3. The maternal outcome in relation to attempted placental separation at delivery

Variables	Placental separation		P value
	Yes (n=11)	No (n=5)	
Total blood loss (litres) (mean ± SD)	3.4 ± 1.5	1.0 ± 0.5	<0.001†*
Number of units of blood transfused	5.1 ± 2.9	1.2 ± 1.6	0.005†*
Other blood product required	4	1	0.62‡
DIC	5	1	0.59‡
Emergency hysterectomy	9	1	0.04‡*
Bladder injury	2	0	1.0‡
ICU admission	2	0	1.0‡
Infection	3	0	0.51‡
Length of postnatal stay (days) (mean ± S.D.)	9.6 ± 8.5	8.8 ± 5.6	1.0¶

*Statistically significant; †2-tailed independent sample t-test not assuming equal variance; ‡2-tailed Fisher Exact Test; ¶2-tailed Mann-Whitney U test; DIC=disseminated intravascular coagulation; SD=standard deviation.

There were two bladder injuries: in one the injury occurred at elective hysterectomy after an antenatal diagnosis (a case of placenta percreta, injury related to disease pathology), and the other from dissection of the lower segment of the uterus at emergency hysterectomy, and this was considered to be related to a previous Caesarean section rather than the placenta accreta. The use of ureteric stent was useful intraoperatively when bladder involvement was suspected.

Three women who had had placental separation developed infection postnatally, and all three did not have an antenatal diagnosis of placenta accreta. In two woman, intrauterine infection occurred after the placenta was removed partially; one following a vaginal delivery and hysterectomy was required 2 weeks post delivery due to recurrent haemorrhage (Woman N), and the other following an elective Caesarean section for placenta previa and the adherent portion of placenta was removed by hysterectomy four weeks later (Woman P). In the third woman, vault infection followed hysterectomy that was performed for severe haemorrhage at manual removal of placenta after a second trimester abortion.

No other significant morbid associations were noted (Table 2 and Table 3).

Discussion

In a recent study[7] where conservative management of placenta accreta was reported to be associated with less maternal morbidity, the diagnosis of placenta accreta was made either clinically or histologically. This retrospective analysis showed that there were 16 cases of confirmed placenta accreta in the seven year study period in our institution—15 histologically and one on direct observation at laparotomy (a case of placenta percreta where the obtaining of a specimen for histologic confirmation would have been hazardous). The incidence of placenta accreta in our study of 1:1660 was within the range of other reports.[1–3]

Hysterectomy was undertaken in most of the women (14 of 16) either electively or as an emergency. All but one had had children previously (Woman L, in whom hysterectomy was performed as a life-saving procedure due to severe haemorrhage).

In nearly half of our cases, the diagnosis of placenta accreta was made antenatally. An antenatal diagnosis allowed patient counselling and management to be planned, including the choice and timing of elective delivery, the decision as to whether to separate the placenta at the time of delivery and the use of prophylactic or alternative strategies (e.g. internal iliac artery ligation at the time of surgery, uterine artery embolisation, and the use of methotrexate after delivery).[11]

The degree of haemorrhage in this group of patients was low and resulted in a decreased risk of emergency/unplanned hysterectomy.

In all our cases, the deliveries or the third stage were supervised by obstetric consultants because of the presence of risk factors of placenta accreta (e.g. placenta previa or previous Caesarean section).[1,3,4] Four units of blood were made available routinely when the patient was at high risk or diagnosed of placenta accreta. In each of the 9 cases where placenta accreta was not diagnosed antenatally, heavy bleeding resulted from attempted placental separation at the time of delivery.

Efforts to arrest bleeding (including the use of syntocinon, prostaglandin or uterine sutures) were often made before resorting to emergency hysterectomy, and may account for the significantly larger amount of blood loss and blood transfused in this group.

In the second half of the study period, screening of placenta accreta in women with identifiable risk factors allowed antenatal diagnosis and planned management, with better clinical outcome observed. An antenatal diagnosis of placenta accreta can be made with ultrasound and/or MRI.[12–21]

The reported diagnostic criteria ultrasound include marked thinning/absence[12] or obliteration[13] of the retroplacental hypoechoic/clear zone/space,[12,13] thinning, irregularity or focal disruption of the hyperechoic uterine serosa-bladder wall complex,[12] or the posterior bladder wall-uterine interface,[13] the presence of a focal exophytic mass with the same echogenicity as placenta beyond the uterine serosa,[12] placental lacunae,[12–14] myometrial thickness of <1 mm,[14] placental-uterine wall interface-disruption,[15] placental lacuna flow,[16,17] prominent subplacental venous complex,[17] bladder-uterine serosa interface hypervascularity,[17] vessels extending from placenta to bladder,[18] vessels bridging from placenta to margin of uterus,[18] and vessels crossing interface-disruption sites.[15]

A diagnosis with ultrasound (+/– Doppler) has been reported to have a sensitivity ranging from 33 to 100% and a specificity of 79 to 100% using various sonographic diagnostic criteria in combination.[12–19] The sensitivity of individual criterion (placenta lacunae, absence of the retroplacental clear zone and interruption of posterior bladder wall-uterine interface) varies from 7% to 93% in one report.[13]

The diagnosis on MRI relies on evidence of placental invasion into the myometrium.[20] The use of MRI has a variable sensitivity ranging from 38 to 88%[19,21] and specificity of up to 100% when it is applied as a secondary diagnostic tool.[18,21] However, ultrasound is used more widely and the cost is lower compared with MRI.

The variable sensitivity and specificity of ultrasound suggests the need for the identification of more specific sonographic criteria for antenatal diagnosis of placenta accreta[15] and the possible incorporation of screening for this condition in high-risk patients.[13,15,18]

Often placenta accreta is not known before delivery (as noted in 9 out of the 16 cases in this series) and placental separation has already been attempted before placenta accreta is recognised. The management options are to withhold further separation followed by treatment with other conservative measures or to continue with placental separation until the uterine cavity is "empty."

Withholding repeated attempts at placental separation appears a feasible option from previous reports and may result in conservation of the uterus and subsequent fertility in this situation.[7,8]

Although separation of the placenta in our study was shown to be associated with an increased amount of blood loss and risk of emergency hysterectomy, separation of placenta was attempted successfully in Woman F with an antenatally diagnosed partial placenta accreta and no hysterectomy was required. There are situations where placental separation may be the preferred option of management, for instance, when the facilities for monitoring or resuscitation in case of severe haemorrhage are not readily available for geographical reasons.

Risks of conservative management have been reported, including recurrent haemorrhage,[22] DIC,[22,23] infection,[7,24] need for curettage,[22] and ultimately hysterectomy.[22–24]

The reliability of the exact incidence of these complications and the success rate with conservative management are difficult to assess because of the lack of confirmation of the diagnosis in cases managed conservatively. For this reason it is difficult to compare the pregnancy outcome between surgically managed and conservatively managed placenta accreta. We have chosen to avoid this by limiting only to confirmed cases in this analysis, giving us just a small number of cases.

Despite the limitations by the small number of total and conservatively managed cases, the relationship between improved maternal outcome with antenatal diagnosis of placenta accreta and non-separation of placenta was clearly shown.

The assessment of the site and extent of placenta accreta antenatally has been demonstrated to be possible with the use of MRI[20] and ultrasound.[10,25,26] If screening for placenta accreta in high-risk patients and accurate antenatal diagnosis and assessment could be effected reliably, this could allow a management strategy to be planned, and placental separation possibly avoided in indicated cases. Such management may be associated with less blood loss, less need for blood transfusion and a decreased risk of emergency hysterectomy.

Conclusion

Antenatal diagnosis of placenta accreta allows planned management and is associated with an improved maternal outcome in terms of decreased blood loss at delivery and decreased emergency/unplanned hysterectomy. These effects are more marked when

placental separation is not attempted in the presence of an antenatal diagnosis, resulting in less need for blood transfusion as well.

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Changes in cause of neonatal death over a decade

Annie Wong, Dawn Elder, Jane Zuccollo

Abstract

Aims To classify neonatal deaths at Wellington Hospital (Wellington, New Zealand) over a 10-year period and assess changes in cause of death over time.

Methods Retrospective audit from 1995–2004 of live-born infants ≥20 weeks gestation dying before 28 days of age. Deaths were classified according to the PSANZ-NDC Classification guideline. The years 1995–1999 and 2000–2004 were compared to analyse for changes in cause of death.

Results There were 219 neonatal deaths: 67(31%) of these were term infants and 154 preterm; 109 infants from 1995–1999 and 110 from 2000–2004. The autopsy rate was 62% and highest in term infants (76%). Deaths due to congenital anomaly and extreme prematurity decreased over time and deaths due to infection increased.

Conclusions Use of the PSANZ-NDC death classification system enables an accurate cause of death to be established for most neonatal deaths and allows monitoring of mortality rates over time.

Accurate documentation of cause of fetal and neonatal deaths enables analysis of change in perinatal death rates over time and assessment of their preventability. It is recommended that such audit should occur both regionally and nationally.[1]

Several classification systems have been designed to facilitate systematic documentation of the reasons for perinatal deaths.[2–5] These systems divide the main causes of perinatal death into subgroups but not all clearly differentiate the reason for neonatal death from the maternal factors contributing to the cause of death. This means that for some classifications, stillbirths and neonatal deaths are classified by the same diagnostic criteria, which is not always appropriate.

In Australasia, the Perinatal Society of Australia and New Zealand (PSANZ) has developed a system to classify the causes of fetal and neonatal deaths.[6] This system includes classification of obstetric factors by the PSANZ perinatal death classification (PSANZ-PDC), used for both fetal and neonatal deaths, and classification of neonatal diagnoses using the PSANZ neonatal death classification (PSANZ-NDC) for liveborn infants.

The PSANZ-PDC has 11 diagnostic categories each with a number of subgroups and the PSANZ-NDC 7 diagnostic categories also with further subgroup classifications. A secondary diagnosis can be classified if it is thought to be a significant contributor to the death, but not the main cause. However, the main purpose of classification remains the identification of the single most important fetal, maternal or neonatal factor that resulted in the stillbirth or neonatal death.[7]

It is expected that the PSANZ classification system will be used nationally to classify all perinatal deaths in both Australia and New Zealand. The aim of this study was to

use the PSANZ-NDC to retrospectively classify neonatal deaths in our institution over a ten-year period to determine as exact a cause of death as possible and to identify changes in the cause of neonatal death over time.

By doing this we hoped to create a database of cause of neonatal death in our institution with which to compare future prospectively collected data. Because this was a retrospective review from a neonatal rather than an obstetric perspective we were not able to accurately classify maternal antecedent factors.

Methods

Cases were sourced from the newborn and maternal health services database. The database analyst collates fetal and neonatal deaths for Wellington Hospital on a monthly basis and this constitutes the most accurate local record for hospital perinatal deaths. Although some cases each month were selected for discussion at the monthly perinatal education meeting, there was no formal review and classification process for all deaths during the study period.

Wellington Hospital provides tertiary care for the Capital and Coast District Health Board (CCDHB) and for the southern half of the North Island and northern part of the South Island of New Zealand.

The median number of neonatal unit admissions per year during the study period was 762 (range 649–830). Infants born in the CCDHB were classed as Wellington-born (around 3500 deliveries per year).

Eligible infants were liveborn at ≥20 weeks gestation from 1 January 1995–31 December 2004, died before 28 completed days of life, and were either born in Wellington and died in Wellington or elsewhere (or born elsewhere and died in Wellington) after transfer for tertiary care.

Neonatal deaths occurring in the community without a recognised antecedent illness in the neonatal period were not included. Infants were included in the time period according to date of birth rather than date of death. Fetal deaths were not included.

Maternal and neonatal medical records were reviewed including autopsy findings. Assignment of the PSANZ-NDC classification was by author DE (a neonatal paediatrician) in consultation with author JZ (a perinatal pathologist).

All autopsies were done by one experienced perinatal pathologist (JZ). Although obstetric factors were assessed to facilitate the neonatal diagnosis, the (PSANZ-PDC) was not used to formally classify these factors. Although this limits the utility of the study we did not have obstetric representation on the review panel and so did not feel that classification of maternal antecedents would be accurate enough. Also secondary factors were not routinely reported.

The study was reviewed by the Central Region Ethics Committee who determined that it fell under the definition of audit as per the local Operational Standard for Ethics Committees. Chi-squared tests were used to assess change in cause of death over time. A p value <0.05 was considered significant. Mortality rates were calculated for Wellington-born infants only.

Results

Medical records were available for all but one infant. For this infant the notes of the infant's twin and the maternal notes enabled an appropriate classification to be completed.

Demographic factors—There were 219 eligible neonatal deaths, 109 in the first 5 years of the decade and 110 in the second 5 years. Five infants, all in the first time period, were liveborn late terminations of pregnancy for congenital anomaly.

There were 111 female and 107 male infants; for 1 infant with a genitourinary anomaly, gender was not determined. The median gestation was 28 weeks (range 20–46 weeks) and median birthweight 1060 g (range 180–4475 g). The infant at 46 weeks gestation was an infant with a fatal congenital anomaly whose parents declined induction of labour.

Overall 152 (69%) infants were preterm (<37 weeks gestation) and 67 were term. Of the preterm infants, 25.6% were <24 weeks gestation, 26.5% 24–28 weeks, 5.9% 29–31 weeks and 11.4% 32–36 weeks gestation. The majority of infants were born at Wellington Hospital (73%). A further 5 (2.3%) infants were born at other CCDHB facilities. Two (0.9%) infants were born in the Wellington Hospital ICU for maternal reasons, 2 (0.9%) infants were born at home, 3 (1.4%) infants were born on the way to hospital, and 47 (21.5%) infant were born at other Level 1 or 2 hospitals in the region and transferred for neonatal intensive care.

With regard to ethnicity, 138 (63.0%) were New Zealand (or other) European, 48 (29.9%) Māori, 23 (10.5%) Pacific, and 10 (4.6%) of Other ethnicity. Death occurred in the delivery suite in 60 (27.4%) cases and all other deaths were after transfer for neonatal intensive care. Four of the delivery suite deaths were term infants and 39 (60%) were <24 weeks gestation.

Autopsy rates—Overall, 136 (62%) infants had autopsies; 85 term (rate 76%) and 51 preterm infants (rate 56%). Although rates were similar between the two time periods (61% in 1995–1999 and 64% in 2000–2004) there was an apparent increase in rates for term infants (68% in 1995–1999 versus 83% in 2000–2004) associated with only a slight decrease in rates for preterm infants (58% in 1995-1999 versus 54% in 2000–2004).

Autopsy rates for NZ or other European were 70%, for Māori 50%, for Pacific 34.8%, and those of Other ethnicity 70%. Māori were more likely to consent for autopsy for more mature infants with consent given for 8/11 term infant deaths but only 3/14 deaths <24 weeks gestation.

Causes of death—Causes of death according to the PSANZ-NDC group categories are listed in Table 1 for all infants. The commonest group cause of death was congenital anomaly followed by neurological causes and extreme prematurity with no or failed resuscitation. The commonest specific diagnostic categories were hypoxic ischaemic encephalopathy/perinatal asphyxia (16.9%), extreme prematurity—not resuscitated (16.0%), hyaline membrane disease (6.9%), cardiovascular congenital anomaly (6.4%), and congenital bacterial infection (5%). All cardiovascular anomaly deaths were in the first 5-year period.

Table 1. Group categories of cause of death for all infants for the first and second 5-year periods and complete 10-year period

PSANZ-NDC classification	Number of infants (%) 1995–1999 (n=109)	Number of infants (%) 2000–2004 (n=110)	Total infants (%) 1995–2004 (n=219)
Congenital abnormality	42 (38.5%)	23 (20.9%)	65 (29.6%)
Extreme prematurity	25 (22.9%)	19 (17.3%)	44 (20.1%)
Cardio respiratory	12 (11.0%)	16 (14.6%)	28 (12.8%)
Infection	5 (4.6%)	16 (14.6%)	21 (9.6%)
Neurological	17 (15.6%)	27 (24.6%)	44 (20.1%)
Gastrointestinal	3 (2.8%)	2 (1.8%)	5 (2.3%)
Other	5 (4.6%)	7 (6.4%)	12 (5.5%)

Changes in cause of death over the 10-year period—Table 1 describes changes in diagnosis for the whole group over the 10-year period. Apparent increases were seen in deaths due to both infection and neurological causes. The increased infection deaths were all because of bacterial infections, both congenital and acquired. The increase in neurological deaths was predominantly due to an increase in death due to perinatal asphyxia.

Mortality rates per thousand live births calculated for Wellington-born infants for the first and second periods are illustrated in Table 2. Mortality rates for term and preterm infants <37 weeks gestation were stable but there was a significant decrease in the mortality rate for infants ≤24 weeks gestation (p=0.003). This may reflect the fact that there was an increase in total births at 23 weeks gestation over the time period and these infants were likely to be offered resuscitation at our institution.

For all infants there was a decrease in death due to congenital anomaly (p=0.024) and an increase in death due to infection (p=0.032). When considered on a population basis the increase in deaths due to perinatal asphyxia was not significant.

Table 2. Changes in mortality rates for Wellington-born infants over the first and second 5-year time periods

Death classification for Wellington-born infants	1995–1999			2000–2004			P value
	All live births	Deaths <28 days	Rate per 1000 live births	All live births	Deaths <28 days	Rate per 1000 live births	
All deaths	15,222	87	5.7	16,735	84	5.0	0.39
Deaths ≥37 weeks gestation	13,391	16	1.2	14,761	16	1.1	0.78
Deaths <37 weeks gestation	1832	71	38.8	1978	68	34.4	0.47
Deaths ≤24 weeks gestation	48	25	520	75	19	253	0.003
Perinatal asphyxia	15,222	9	0.59	16,735	9	0.54	0.84
Term asphyxia	13,391	4	0.30	14,761	8	0.54	0.32
Congenital anomaly	15,222	29	1.9	16,735	16	0.95	0.024
Extreme prematurity*	15,222	25	1.6	16,735	19	1.1	0.22
Cardiorespiratory disorders	15,222	16	0.72	16,735	14	0.84	0.53
Infection	15,222	2	0.13	16,735	10	0.6	0.032

* Includes only those infants not resuscitated or not successfully resuscitated.

Discussion

The PSANZ neonatal death classification system proved to be a useful tool for documenting cause of the death for infants dying in the first month of life. This is the first time such a detailed system has been used to classify infant deaths in our institution and it provides useful information about the main cause of neonatal death to allow comparison with changes that may occur over time. High autopsy rates meant that autopsy results could be considered prior to classification for 62% of cases.

In Australia, the Victorian State Perinatal Mortality Report for the year 2003 includes cases of neonatal death classified by the PSANZ-NDC.[8] Congenital anomalies were the cause of 35% of neonatal deaths, extreme prematurity 38.4% of deaths, cardiorespiratory disorders 12.2%, infection 2.5%, neurological disorders 8.0%, gastrointestinal disorders 0.8%, and the other group 3.0% of deaths.

Compared to our findings, the differences with respect to extreme prematurity and neurological disorders most likely reflect the fact that our data come from a single institution (Wellington Hospital) rather than from a geographical region (Victoria in Australia).

A congenital anomaly classification was used when the anomaly was either the main cause of death or main reason for death, such as with termination of pregnancy. The decrease in congenital anomaly deaths seen has been reported by others and attributed to increased antenatal screening and subsequent terminations of pregnancies with major congenital anomalies.[9]

Improved survival of infants may also be a contributor although the current study reflects early survival only. Also these findings may reflect improved early antenatal diagnosis with termination of pregnancy before the 20-week cut-off that applies to this study.

Cardiovascular anomalies were the commonest fatal anomaly (21.5% of all anomaly deaths) with all deaths occurring in the first 5-year period. Differences were not seen for other malformations although numbers were small.

There was a significant decrease in mortality for infants at the borderline of viability. The second commonest group cause of death in our study was spontaneous preterm delivery of infants that either failed resuscitation or were not resuscitated. Although there were fewer deaths in this group in the second 5 years, the difference was not significant. At the same time in that gestational age range more infants died with a diagnosis of cardiorespiratory disorders, particularly hyaline membrane disease, and infection. Just under half the infection deaths were in this group even though the extremely preterm group comprised only 25% of all deaths. Four of six deaths due to bacterial infection in the second time period were congenital.

Our findings for immature infants are different from those of the Australian Victorian 2003 report and may reflect a more aggressive approach to resuscitation of infants at the borderline of viability in our unit. As there was an increase in births at 23 weeks gestation over the second 5-year time period and a significant proportion of these infants were likely to be offered treatment, it is not surprising that there would be increases in deaths due to complications of extreme prematurity such as infection and cardiorespiratory disorders.

The most frequent single classified cause of death in this study was perinatal asphyxia, accounting for 16.9% of all neonatal deaths compared with 7.6% in the Victorian 2003 state data. This most likely reflects a bias due to referrals for term infants requiring intensive care.

When deaths due to perinatal asphyxia were counted for Wellington-born infants only, they were 10% of the total local deaths, which is more compatible with

Australian figures and figures from National Women's Hospital in 2000 at the midpoint of our study period.[8,10,11]

Expert perinatal pathology is a critical component of perinatal death review. Our autopsy rate compares very favourably with rates <50% reported for two Australian studies reporting on deaths from neonatal intensive care.[12,13] Consent was given for autopsy in 65% of the neonatal deaths transferred for neonatal intensive care in our study.

As expected, autopsy rates were lower for very preterm infants than for term infants. This may reflect the fact that parents feel that being born very premature is itself enough of an explanation as to why their infant has died. This seems to be true for Māori parents.

Local studies have confirmed the utility of autopsy in our local New Zealand perinatal population. In a review of 56 neonatal deaths over a 2-year period 73% had an autopsy and new information was found in 59%.[14] A review of infants who died with a clinical diagnosis of Grade III hypoxic ischaemic encephalopathy indicated that the autopsy provided new information in 62.5% of cases.[15]

When autopsy reports for 29 very preterm infants dying at <28 days of age were reviewed, new findings were discovered in 79.3% and resulted in a significant change in diagnoses in 27.6%.[16] We are fortunate to have the services of an experienced perinatal pathologist but most other tertiary and secondary perinatal units in New Zealand need to transport infants to Wellington for autopsy if they are to receive the same service.

For Māori and Pacific people, in particular, it is critical that this service is available 7 days a week and if possible throughout the day. A study from Wales found that a decreasing autopsy rate over a 10-year period was due to parental refusal rather than failure of clinicians to seek consent.[17] It was felt that centralisation of expert perinatal pathology services with the need for the infant to travel for a post mortem was a possible contributor to parental failure to consent.

Concern about organ retention appears also to be a significant contributor to decreasing autopsy rates in the UK and Australia.[18] In our experience, careful discussion with parents during the consent process, avoidance of delay in the examination and provision of continuity of care through clinician attendance at the autopsy help to ensure an optimal service for families.

The PSANZ-NDC and the PSANZ-PDC are the classification systems being used for the national data collection initiated by the Perinatal and Maternal Mortality Review Committee (PMMRC), which commenced in New Zealand from July 2006. By using the PSANZ-NDC to classify our local data, we have been able to document changes in the cause of neonatal death in the first month of life, over a decade from 1995-2004, particularly with respect to death because of congenital anomalies.

This study also highlighted what appears to be an increase in successful early active treatment of extremely preterm infants some of whom succumb to the expected later complications of infection and hyaline membrane disease. This database now provides a base from which to monitor further changes in perinatal mortality in our region over time. In the future in line with the national perinatal mortality data

collection, classification of obstetric antecedents will be included as perinatal mortality review without consideration of maternal factors significantly limits the conclusions that can be drawn from the data.

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Unusual primary manifestations of multiple sclerosis

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Abstract

Objectives The aim of this study is to describe patients with unusual symptoms that were primary manifestations of multiple sclerosis (MS).

Patients and methods We report 21 multiple sclerosis patients who presented unusual initial pictures (acute brachial pain n=4, headache n=6, ptosis n=1, oculomotor nerve palsy n=1, peripheral facial palsy n=1, throat pain n=1, hypoglossal nerve palsy n=1, visual field defect n=2, epilepsia n=2, and coma n=2) as the first manifestations in the absence of other obvious symptoms or signs.

Results Investigations demonstrated changes highly suggestive of multiple sclerosis on magnetic resonance imaging, cerebrospinal fluid analysis and electrophysiological tests. All cases completely or partially recovered after high-dose corticosteroid therapy. These patients have been followed up for 5 years.

Conclusion In this study, we discuss possible correlations between clinical disturbances and neuroradiological abnormalities and show some rare or previously undescribed manifestations in multiple sclerosis.

In multiple sclerosis (MS), weakness or numbness, sometimes both in one or more limbs is the initial symptom in about half the patients. Other common modes of onset are optic neuritis, transverse myelitis, cerebellar ataxia, brainstem symptoms (vertigo, facial pain or numbness, dysarthria, diplopia), motor weakness, paresthesias, and disorders of micturition.[1] The rare manifestations have also been reported in the literature. The purpose of the present study is to describe the patients with unusual symptoms as primary manifestation of MS, something that has not been reported elsewhere in medical literature.

Patients and methods

The study population consisted of MS patients followed between 2001 and 2006 in our neurology department. They were selected among 141 MS patients because of unusual symptoms as primary manifestation. All cases fulfilled recently revised diagnostic criteria of MS.[2] Information about education, occupation, risk factors for other white matter diseases (such as vasulitis), other medical history, drug history, and family history were collected. A detailed neurological examination was undertaken.

To exclude other causes of white matter disease, a comprehensive series of investigations were carried out. Blood tests included urea and electrolytes, erythrocyte sedimentation rate, full blood count, C-reactive protein, and antibody screen (ANA, ANCA, anti-ds DNA, antiphospholipid, antithyroid antibodies).

Cerebrospinal fluid (CSF) examination consisted of cell, protein, glucose, electrolytes, viral and microbiological studies, immunoglobulin-G index, and oligoclonal band (OCB).

Radiological examination included chest X-ray as well as brain and spinal magnetic resonance imaging (MRI). In all cases a gadolinium-enhanced MRI was performed on a 1.5 Tesla machine within 7 days after the onset of the reported symptoms. Patients also had electroencephalography (EEG) and visual

evoked potential (VEP) examinations. Clinical evaluation of MS disability was performed with the Expanded Disability Status Scale. The patients were followed up for 3 and 5 years thereafter.

Results

We present 21 cases, (14 female, 7 male), aged 17 to 32 years at the time of presentation. None of the cases had the initial sensory, motor, cerebellar or optic symptoms typically seen in MS at the time of referral. Details of each patient's demographic, clinical presentations, VEP and OCB results, and their follow up periods are shown in Table 1. All patients were treated by high dose intravenous methylprednisone (IVMP) infusion (1 g/day for 5 days).

Table 1. Demographic, clinical, MRI, VEP, CSF, and follow-up data

n	Sex	Age	Initial manifestations	Neurological sign/symptoms	VEP	CSF (OCB)
1	F	27	Acute radicular pain	Pain, paralysis hypoesthesia, hyporeflexia C5-C6-left arm	+	+
2	F	21	Acute radicular pain	Pain, paralysis hypoesthesia, hyporeflexia C5-C6-left arm	+	–
3	M	29	Acute radicular pain	Pain, paralysis hypoesthesia, hyporeflexia C5-C6-right arm Lhermitte's sign	+	–
4	M	32	Acute radicular pain	Pain, paralysis hypoesthesia, hyporeflexia C6-C7-T1-left arm	+	+
5	F	31	Episodic tension headache	Babinski sign+	–	+
6	F	27	Migraine-like headache	Normal	+	-
7	F	23	Migraine-like headache	Brisk tendon reflexes, Babinki sign+	+	+
8	F	29	Migraine-like headache	Normal	+	+
9	M	30	Migraine-like headache	Normal	+	+
10	M	31	Migraine-like headache	Normal	+	+
11	M	30	Throat pain	Babinski sign+	+	+
12	F	27	Ptosis	Right ptosis	+	+
13	M	28	3. nerve paralysis	Left external ocular paralysis, ptosis	+	+
14	F	17	7.nerve paralysis	Left peripheral facial palsy	+	+
15	M	27	12. nerve paralysis	Paralysis in the left half of the tongue	+	+
16	F	21	Homonymous hemianopsia	Right homonymous hemianopsia	+	–
17	F	22	Altitudinal hemianopsia		+	+
18	F	30	Epilepsia	Babinski sign+	+	+
19	F	32	Epilepsia	Brisk tendon reflexes	–	+
20	F	31	Coma	Loss of conscious, quadriparesia, no brainstem reflexes	+	+
21	F	32	Coma	Loss of conscious, decerebrated, no brainstem reflexes	+	+

VEP: visual evoked potentials, +: bilaterally delayed, –: no delay.
CSF: cerebrospinal fluid.
OCB: oligoclonal band, +: present, –: absent.

According to their initial manifestations, patients were classified into the following groups: pain syndromes, cranial nerve disturbances, visual field defects, epilepsy, coma.

Pain syndromes

Acute radicular pain—Four patients (2 female, 2 male) described acute-onset sharp, burning and poorly localized radicular pain and weakness in the arm. Patients 1, 2, and 3 had weakness and paresthesis in the C5 and C6 distribution.

Affected muscles include the supraspinati, infraspinati, biceps, brachialis, deltoid, and brachioradialis, so the patients were unable to abduct the arm at the shoulder or flex at the elbow. The biceps and brachioradialis reflexes were diminished, and sensory loss is found over the lateral aspect of the arm, forearm, and thumb.

Patient 4 produced weakness, sensory loss, and areflexia in the C8 and T1 distribution. Weakness was present in both median- and ulnar-supplied intrinsic hand muscles and in the medial finger and wrist flexors. The finger flexion reflex was absent and there was sensory loss over the medial two fingers, the medial aspect of the hand, and the forearm.

Patients 1, 2, and 4 had active multiple periventricular, pontin (patient 1), and cerebellar (patient 2). T2-weighted hyperintense lesions on MRI. T2-weighted spinal MRI demonstrated a hyperintense lesion within the dorsal aspect of spinal cord extending from C5 to C7 level. Cranial MRI of patient 4 revealed multiple hyperintense T2-weighted lesions throughout the cerebral white matter, including corpus callosum. There was a T2-weighted hyperintense lesion between C6-C7 to the T1 level.

Following the administration of gadolinium, the spinal cord lesions and few of the cerebral lesions demonstrated enhancement in all 4 patients. Brachial plexus MRIs of all patients were normal. Three patients developed relapsing remitting MS and 1 patient had relapsing progressive pattern during the 5 years of follow-up.

Headache—Four female and 2 male patients presented newly onset headache without any abnormal neurological findings. These patients were referred from our headache outpatient clinic because of hyperintense lesions on a cranial MRI and no response to analgesic therapy.

Of these patients, 5 met criteria for migraine-like headache and 1 female patient met criteria for episodic tension-type headache.[3] The T2-weighted images showed multiple hyperintense lesions in the periventricular area (all patients), corpus callosum (all except patient 7), pons (all patients), and midbrain (patients 6, 8) (Figure 1). MRI findings of the cervical spine were normal in all patients. During the follow-up period, all patients had relapses (optic neuritis, sensorimotor, brainstem, or cerebellar).

Figure 1. Brain MRI, T2-weighted sequences showing multiple hypersignals in the pons, midbrain. and corpus callosum

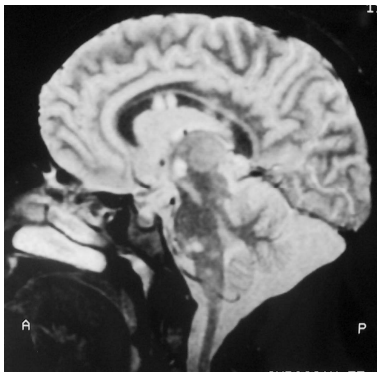
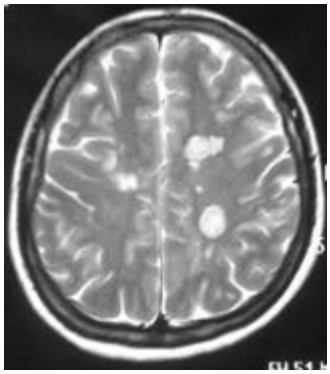


Figure 2. Brain MRI, T2-weighted sequences showing multiple hypersignals in centrum semiovale and cortex



Throat pain—A 30-year-old male (patient 11) was referred to us with the complaint of undefined throat pain and dysphagia of 3-month duration. This patient had been investigated by several otolaryngologists and psychiatrists. Physical, neurological, and psychiatric examinations did not reveal any abnormality.

A brain MRI study showed multiple T2-hyperintense lesions consistent with demyelination in the centrum semiovale, cortex (Figure 2), periventricular white matter, cerebellum, and pons.

A spinal MRI demonstrated an area of increased signal on T2-weighted images in the cervical spinal cord, with enhancement on T1-weighted images after intravenous gadolinium. Paraclinical findings supported the diagnosis of MS. Symptoms totally recovered within 2 weeks after IVMP infusion. He had 3 relapses (sensorimotor, spastic paraparesis) during the 5 years of follow-up.

Cranial nerve disturbances

Ptosis—A 27-year-old female (patient 12) was evaluated by us for a complaint of ptosis. Neurological examination was normal except upper right eyelid ptosis. Orbital electromyography, magnetic resonance angiographic imaging, carotid and vertebral Doppler ultrasonography were normal.

MRI revealed a T2-weighted hyperintense lesion in pontomesencephalic junction with enhancement on T1-weighted images after intravenous gadolinium and inactive lesions in periventricular area and corpus callosum. Ptosis rapidly recovered in 5 days after IVMP infusion. She had 3 other relapses (brainstem symptoms, hemiparesis) during the follow-up.

Third cranial nerve palsy—A 28-year-old male (patient 13) was admitted due to diplopia of 5-days duration. On clinical examination, there was limitation of elevation, depression, and adduction of the left eye with upper eyelid ptosis. The neurological examination was otherwise normal.

A cranial MRI demonstrated focal area of high signal intensity in the left ventral mesencephalon extending to the cerebral peduncle. Findings at cerebral angiography

were negative. Symptoms totally recovered within 3 months. Follow-up cranial MRI 6 months later showed multiple hyperintense T2-weighted lesions throughout the corpus callosum and centrum semiovale.

He later developed relapsing-progressive MS with brainstem (internuclear ophthalmologia) and spinal cord (spastic paraparesis) involvement.

Facial nerve paralysis—A 17-year-old female (patient 14) presented with an acute facial palsy, ipsilateral loss of taste, and peri-aural pain. Since the patient was young, a cranial MRI was planned.

MRI revealed a single, >5 cm hyperintense lesion in the pontine tegmentum ipsilateral to the facial weakness and multiple supratentorial hyperintense lesions, with enhancement. She had no previous neurologic symptoms. She had bilateral plantar reflex and the neurological examination was otherwise normal.

Three weeks after corticosteroid therapy, she dramatically recovered from her facial palsy. At age 20 and 21, she was again hospitalised due to hemiparesis attacks.

Hyoglossal nerve paralysis—A 27-year-old man (patient 15) noticed that he had difficulty in phonation and manipulating food in the mouth for 2 days. On examination, the left half of his tongue was paretic without atrophy or signs of denervation. No other cranial nerve deficits were noted. Results of a neurologic examination were normal, with no evidence of long-tract signs.

A cranial MRI demonstrated multiple focal area of increased signal on T2-weighted images in the centrum semiovale and periventricular white matter, with enhancement on T1-weighted images after intravenous gadolinium (Figure 4). The sign of hypoglossal paralysis totally recovered approximately in 2 weeks.

Two years later, on the basis of new signs and symptoms (optic neuritis, hemiparesis), the diagnosis of relapsing remitting MS was made.

Visual field defects

Homonymous hemianopsia—A 21-year-old female (patient 16) with no previous neurologic or ophthalmoscopic abnormalities developed right homonymous hemianopsia. MRI demonstrated bilateral high-signal suprageniculate lesions. The lesion located in the left parieto-occipital area was compatible with the field defect observed. VEP showed dysfunction of the visual pathways and CSF included OCB.

The visual fields, as determined by automated static perimetry, recovered completely in 2 weeks. Follow-up MR imaging at 1 month showed no change compared to baseline. One year after the initial attack she suffered sensorimotor paralysis, which resolved spontaneously within 1 week.

Figure 3. Brain MRI, T2-weighted sequences showing a hypersignal in the pons

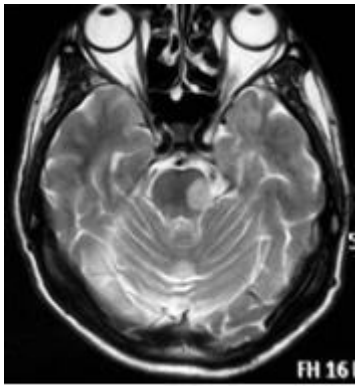
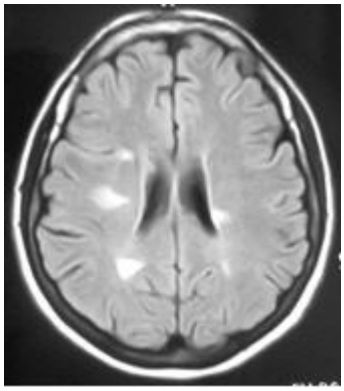


Figure 4. Brain MRI, T2-weighted sequences showing multiple hypersignals in the periventricular white matter



Monocular altitudinal defect—A 22-year-old female (patient 17) complained of a sudden vision loss in the upper half of the visual field of the right eye. She had no previous neurological and systemic disease. Visual acuity was 20/30 in both eyes. There was a right afferent pupillary defect. Funduscopic examinations showed bilateral temporal pallor. The visual field studied by automated static perimetry revealed a right superior altitudinal defect (Figure 5).

MRI of the brain demonstrated high signal abnormality in the periventricular white matter, parietal and parieto-occipital area. Monocular altitudinal defect was recovered in 2 weeks. Seven months later she developed internuclear ophthalmoplegia.

Epilepsia

Two female patients developed late onset seizures. They both had no known disease at the time and no history of trauma, intoxication, and previous convulsions. Patients were evaluated extensively for the other causes of seizure but no reason was found.

A 30-year-old female (patient 18) was admitted to the hospital due to the following seizures. She had experienced 3 episodes of generalized tonic-clonic seizure and had not regained consciousness between seizures. No findings suggesting a focal onset of seizures were observed. The seizures were resolved after the intravenous phenytoin administration.

On neurological examination, after regaining consciousness, she had no pathological findings except extensor plantar reflex on the left. EEGs that were obtained 1 day and 1 week after were normal. Cranial MRI scanning demonstrated multiple demyelinating lesions in the periventricular white matter and corpus callosum. With carbamezapine treatment she remained seizure-free. She had multiple relapses and then a progressive course developed.

A 32-year-old female (patient 19) had two late-onset tonic-clonic convulsions with a focal onset in one month. Her neurological examination was normal except brisk tendon reflexes. EEG revealed nonspecific findings. Cranial MRI showed multiple hyperintense lesions on T2-weighted images in the centrum semiovale and

periventricular area, with enhancement on T1-weighted images after intravenous gadolinium. CSF.

Epileptic seizures responded well to carbamezapine treatment and did not recur. She had retrobulbar neuritis 4 years later.

Coma—Two female patients presented with altered conscious level as the first manifestations of MS. None of the cases had previous medical or neurological disorders. The cases became quadriparetic with absent pupillary and brainstem reflexes approximately in 2 days. T2-weighted MRIs demonstrated multiple new and old plaques in the periventricular white matter (Figure 6), corpus callosum, pons, and cervical spinal cord without mass effect.

Following the administration of gadolinium, few of the cerebral lesions demonstrated enhancement in all patients. High dose of IVMP (1000 mg/d) and intravenous immune globulin (IVIG) (400 mg/kg) were administrated for 5 days.

Despite the poor prognostic signs, clinical recovery occurred within 2 to 4 weeks. Patient 20 had relapsing progressive course during the last 5 years. Patient 21 had another attack with recurrent stupor for a few days, accompanied by brainstem and cerebellar involvement and these symptoms remained stable over 5 years.

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Figure 5. Perimetry, showing a superior altitudinal defect of the right eye

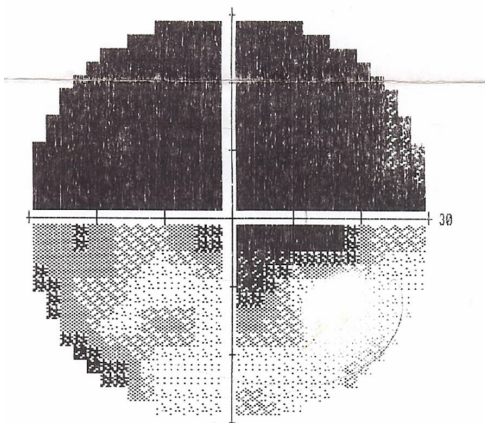
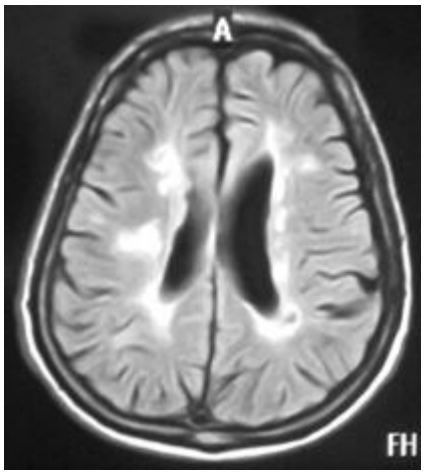


Figure 6. Brain MRI, T2-weighted sequences showing multiple hypersignals in the periventricular white matter



Discussion

MS lesions in the brain and spinal cord can damage every function of the central nervous system (CNS). The symptoms and signs of MS are notoriously variable but in general reflect the involvement of those parts of the CNS that are most heavily demyelinated.[1] The clinical presentation varies from mild to aggressive symptoms and from relapsing-remitting to progressive disease.

The initial manifestations of MS have been analysed in many series. McAlpine et al,[4] in a review of all previous published reports, found that the incidence of initial

symptoms was weakness in one or more limbs 40%, optic neuritis 22%, paraesthesiae 21%, diplopia 12%, vertigo 5%, and disturbance of micturition 5%.

The protean symptoms included fatigue as well as disturbed function in sensory, motor, bladder, bowel, sexual, cerebellar, brainstem, optic nerve, and cognitive realms in other series.[1]

Since MS can produce lesions anywhere in the CNS, including the cerebral cortex and deep grey nuclei or anterior horn cells, there are very few neurological symptoms and signs which have not occasionally been seen. In recent times, many of these symptoms have been shown to be associated with appropriately placed MRI abnormalities, leaving little doubt as to their casual relationship.[4]

Several interesting initial manifestations of MS have come to our attention over the years and have given rise to difficulties in diagnosis. It is evident that with increasing knowledge and experience, the proportion of patients in whom unusual symptoms were recognised as initial symptoms notably increased.

Our study describes some rare first manifestations in 21 MS patients in the absence of previous symptoms or signs. Four patients presented with acute radicular limb pain had radicular compression ruled out by MRI techniques. There was limb weakness with sensory loss and areflexia.

MRI showed demyelinating plaques at the cervical levels of the spinal cord with a characteristic T2 weighted images an area of abnormally high signal intensity. Eventually, MS was diagnosed and judged to be responsible for the acute radiculopathy. A direct relationship between the plaques and the clinical findings was established in all cases.

Treatment with corticosteroids was helpful, and other treatments for neuropathic pain (carbamazepine) were not necessary. Pain is frequently listed amongst the initial symptoms of MS or as occurring in the course of the disease. Trigeminal neuralgia, optic neuritis, painful tonic spasm, pain related to abnormal posture, spasm of the spinal musculature or osteoporosis linked to immobility are the common causes of pain in MS.[5–7]

Radicular pain is less common. Such pain has been reported as a presenting symptom of MS in 11 patients.[8] The distribution was lumbar or lumbosacral in 6, thoracic in 2, and cervical in 3 patients. Uldry et al presented 4 patients with established MS who developed pain and abnormal sensations in the distribution of cervical nerve roots.[9]

The mechanisms of radicular pain in MS are unknown but might be caused by focal demyelination involving the root entry zones, emphatic transmission, or inflammation or swelling. A plaque in the dorsal column may generate ectopic bidirectional sensory discharges with abnormal central and antidromic conduction to peripheral endings.[10]

Some evidence shows that antidromic impulses cause the release of substance P at the peripheral terminals of primary afferents; substance P in turn has been shown to cause release of histamine from mast cells.[11]

Headaches are more common in MS (27%) than in matched controls (12%).[12] They can herald exacerbations.[13] Although there have been numerous reports[14] of an

increased risk of migraine among patients with MS, there is scant evidence for an association in controlled studies.

One recent case-control study of risk factors for MS found that migraine was both associated with MS, and that migraine was an independent risk factor for the development of MS.[15] However, headache as a first symptom in MS is not well known.

We followed 6 patients who presented newly onset headache without history of previous headache and abnormal neurological findings but MRI and VEP, CSF abnormalities. None of the patients had optic neuritis and mass lesions of the cerebral hemispheres that both result in headache.

Of these patients, 5 met criteria for migraine-like headache and 1 female patient met criteria for episodic tension-type headache. The T2-weighted images showed multiple hyperintense lesions in the periventricular area and pons in these patients with headache. Large demyelinating lesions mimicking a tumor were not observed in the MRIs. All the patients had relapses during 5 years follow-up. The lesions on specific parts of the brain (pons) may result in headache in patients with MS.

Evidence shows that several brainstem areas are involved in the pathophysiology of migraine. Studies in animals and humans indicate that the trigeminocervical complex, the rostral brainstem and periaqueductal grey matter have primary roles in the complex mechanisms underlying migraine attacks.[16–19]

The repeated demyelinisation of brainstem structures can cause migraine-like headaches in MS.[13,20,21] It is also well known that vasoactive amines, prostaglandins, and kinins released by inflammatory cells may magnify the pain.

The onset of the disease was manifested in one case with a non-typical symptom; undefined throat pain and dysphagia. MRI studies demonstrated multiple T2-hyperintense lesions consistent with demyelination in the centrum semiovale, periventricular white matter, cerebellum, pons, and spinal cord. VEP results and presence of OCB supported the diagnosis of MS.

This patient developed 2 other relapses during the follow-up. Such rare symptoms are a source of puzzlement in patients until additional lesions or clinical findings developed. In recent times, many of these unusual symptoms have been shown to be associated with appropriately placed MRI abnormalities, leaving little doubt as to their casual relationship.

Apart from the optic nerve, several cranial nerves may be affected by MS, giving rise to characteristic symptoms. Isolated cranial nerve palsies were described in patients with definite MS.[22] Five of our patients presented with isolated cranial nerve palsies as an initial manifestation of MS. Although brain stem involvement commonly occurs during the course of illness in patients with MS, isolated cranial nerve palsies are uncommon.[23]

Combining three large retrospective studies investigating the causes of oculomotor nerve paralysis, only 1.7 of patients were noted to have MS. Clinical presentation varied in terms of degree of ophthalmologia, and ptosis.[24,25]

It is common for ocular palsies in MS to be accompanied by other abnormalities of eye movement. Oculomotor nerve lesions are often partial and complete ptosis is rare.[26] One patient presented with ptosis as a first symptom of MS. The CSF analysis was normal except for OCB. Furthermore, cerebral MRI was typical for MS and the patient had 3 other relapses during the follow-up.

Ptosis has multiple aetiologies, including supranuclear lesions, lesions of oculomotor complex, oculosympathetic lesions, lesions of the neuromuscular junction, diseases of the muscle, and the local mechanical lid abnormalities.[27] Supranuclear ptosis may be unilateral or bilateral.[28] Unilateral supranuclear ptosis is usually due to a lesion of the opposite cerebral hemisphere, especially ischemic lesions, tumor or vascular malformations.

We describe a patient with supranuclear ptosis due to MS lesions in the periventricular area and corpus callosum that has been rarely reported. One patient had isolated oculomotor nerve palsy as a first symptom of MS. A cranial MRI demonstrated focal area of high signal intensity in the left ventral mesencephalon extending to the cerebral peduncle. Isolated third nerve involvement is rare and may be due to nuclear (generally nuclear) or fascicular lesions. It is observed in several pathologies such as diabetes mellitus, intra-cavernous aneurysm and Tolosa-Hunt syndrome but has been reported in only a few cases of MS.[29]

Our data show that ptosis or isolated oculomotor nerve palsy can be the initial manifestation of MS. Although optic neuritis is the most frequent finding, we must emphasise the possibility of other ocular manifestations to be either preceding or occurring at the same time as this disease.

Facial nerve palsy is listed in virtually every account of the clinical features of MS but is hardly ever described in detail. There is reasonable agreement on the frequency of facial weakness at onset, varying from 1% to 4%.[4] Whether facial palsy, indistinguishable from idiopathic Bell's palsy, can be a symptom of MS is uncertain. A young female presented an acute facial weakness, ipsilateral loss of taste and peri-aural pain. In our case, the facial palsy was typical, suggesting a lesion limited to the pons, as demonstrated by MRI.

In a study of 100 cases of hypoglossal palsy, one-third of the patients showed bilateral involvement. Tumors produced nearly half of the cases and trauma (e.g. gunshot wounds) was the second most common cause. Stroke, hysteria, MS, surgery, Guillain-Barre neuropathy, and infection accounted for about one-third of the patients.[31]

The left and right hypoglossal nuclei are closely located together within the paramedian medulla and beneath the hypoglossal trigone of the fourth ventricle. Therefore, medullary lesions such as multiple sclerosis, syringobulbia, amyotrophic lateral sclerosis, and bulbar poliomyelitis often result in bilateral lower motor neuron palsy of the tongue. A young male presented with hypoglossal nerve palsy as the sole neurological manifestation, without simultaneous involvement of other cranial nerves or long-tract signs.

Lesions of the corticobulbar tract anywhere in its course from the lower precentral gyrus to the hypoglossal nuclei may result in tongue paralysis. Because supranuclear control of the genioglossus muscle originates mainly from the contrlateral cortex, a

lesion of the corticobulbar fibers above their decussation may result in weakness of the contrlateral half of the tongue.

A central monoparesis of the tongue seems probable in our case because a supranuclear lesion is unaccompanied by atrophy or fibrillations of the tongue. MRI showed the new T2-weighted lesion(s) with gadolinium enhancement in the right periventricular area. Any brainstem lesion was not observed on MRI.

Central monoparesis of the tongue may occur with lacunar infarcts affecting contrlateral corona radiata or internal capsule that interrupt in isolation the corticolingual pathways to the tongue.[27,31,32] Hypoglossal nerve paralysis due to medullary lesion in patients with MS have been rarely reported.

To our knowledge this is the first report of central monoparesis of the tongue in MS, which has essentially been described in infarcts.

A visual field defect presentation of MS appears to be rare. Two patients presented with visual field defects in the absence of other obvious symptoms or signs. Based on the clinical and radiologic findings, the final diagnosis was made as clinically definite MS. One patient developed right homonymous hemianopsia.

MRI demonstrated a high-signal lesion in the left parieto-occipital area. Symptomatic suprageniculate lesions in MS expressed as a visual field defect are infrequent. A higher incidence might be found with a higher index of suspicion and careful visual field testing with qualitative confrontation technique.[33,34]

We describe a patient with complete monocular superior altitudinal defect as the initial and unique symptom of MS. This altitudinal visual field defect involved both nasal and adjacent temporal quadrants of the right eye and respected the horizontal meridian. An altitudinal defect is one that is confined to the upper or lower half of the visual field but crosses the vertical meridian. The most common cause of a monocular altitudinal defect is ischemic optic neuropathy.

Other causes of a monocular altitudinal defect include choroiditis, choroidal coloboma, retinal detachment, glaucoma, optic nerve hypoplasia, chronic atrophic papiloedema, drusen, optic neuritis, optic nerve trauma, and masses affecting the optic nerve or chiasm.[1,27,35,36] Although monocular altitudinal defects are rare field defects and usually secondary to ischaemia of optic nerve we emphasise that MS should be suspected when a young person develops visual field defects.

Two patients developed late onset seizure as a first sign of MS. Epilepsy responded well to treatment and did not recur in our patients. When epilepsy presents before the onset of overt symptoms of MS, the casual connection may well be in doubt but epilepsy has been reported as the sole presenting symptom.[37]

Epilepsy coinciding with the onset of the disease, or developing later, as in the majority of reported cases is more convincing.[38] Demyelinating lesions have been proposed to act as an irritative focus.[39]

Oedema, which causes a size change over a 4–6 week period in new lesions, may play a part in seizure production in critically located lesions.[40–42] Other factors, some of which are still not clearly understood such as the fiber, electrolytic changes, size of

the plaque, and reactive gliozis seem also to play a part in the production mechanisms.[38]

We suggest that MS should be remembered in the aetiology of epilepsy before reaching a final diagnosis of idiopathic epilepsy.

The remaining two cases had acute coma before the manifestation of MS-specific symptoms. It is rare for the level of consciousness to be disturbed in MS, except as part of terminal coma.[4] Massive demyelination of the brainstem or a mass demyelinating lesion of the cerebral hemisphere can provide reasonable explanations for the effect on conscious level. Persistent or recurrent hypohermia with confusion and stupor has been also described in severely quadriplegic patients.[43]

MS lesions were scattered in the periventricular white matter and brainstem without mass effect in both patients. Despite the poor clinic findings recovery occurred in a short time in the patients.

Twenty-one patients who presented with unusual pictures in the absence of other symptoms signs are reported in this study. Investigations demonstrated changes highly suggestive of MS on MRI, CSF analysis, and electrophysiological tests.

Most physicians consider a diagnosis of MS only in the presence of usual symptoms or signs and this may reflect underdiagnosis. Physicians should consider symptoms outlined here as possible first manifestations of MS.

Competing interests: None known.

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Cystic lesions of the liver: 6 years of surgical management in New Zealand

Jonathan B Koea

Abstract

Introduction Cysts are a common radiological finding in the liver. Many affected patients do no require treatment. However a minority require further investigation and treatment for symptoms or risk of underlying malignancy.

Methods A computerised database of patients presenting to Auckland Hospital for the management of liver lesions was established in 2000. Details of demographics, presentation, investigations, management, and follow-up are entered prospectively.

Results Forty-seven patients (36 female, median age 61, range 37–86 years) requiring surgical treatment of cystic liver lesions were identified from a total of over 800 patients enrolled in the database. Twenty-five patients presented with simple cysts, of whom 12 had radiological evidence of polycystic liver and kidney disease. All 25 patients were symptomatic and all were managed successfully with laparoscopic fenestration. Nine patients presented with complex cysts which were treated with liver resection. Of these patients, four had benign cysts, three had underlying biliary cystadenomas, and two had biliary cystadenocarcinomas. One patient with a biliary cystadenocarcinoma is dead of disease. The median follow-up for all 47 patients was 26 months.

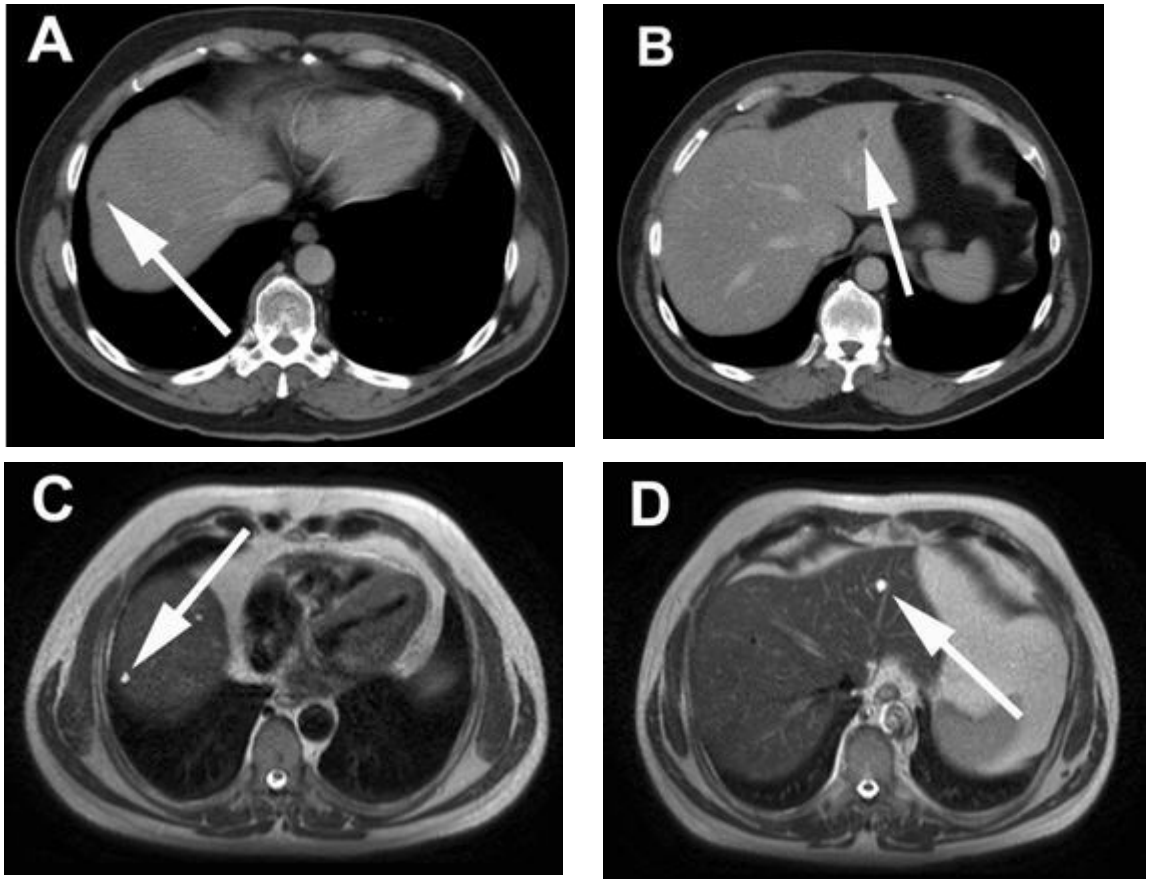
Conclusions Cystic liver lesions can represent a spectrum of underlying conditions. All cysts require investigation and complex cysts or symptomatic simple cysts require further treatment.

Cystic lesions of the liver are common and usually present as an incidental finding in patients undergoing radiological evaluation of the abdomen. The exact prevalence of simple hepatic cysts is unknown but at least 3% of patients undergoing ultrasonography or computed tomography of the liver are found to have asymptomatic simple cysts,[1] although other investigators have found cysts in up to 18% of asymptomatic patients.[2]

Consequently patients with the finding of cystic liver lesions will present for medical assessment and, with the increased utilisation of diagnostic imaging to assess abdominal symptoms, this may become more common. Most cysts are simple and asymptomatic and require no further management other than documentation of their presence (Figure 1). However symptomatic cysts, radiologically complex cysts and parasitic liver cysts require further investigation and evaluation for possible surgical management.

This investigation describes the management of 47 patients referred for surgical assessment of hepatic cysts to the Upper Gastrointestinal and Hepatobiliary Unit at Auckland Hospital.

Figure 1. A 76-year-old male presents with a locally advanced rectal cancer and a staging CT scan that appears to show multiple, small hypodense metastases (arrows in figure 1A & B) raising the question whether any active treatment should be undertaken. Subsequent MRI scan shows these lesions to be bright on T2-weighted images and simple cysts (arrows in figure 1C & D)



Methods

A prospective computerised database of patients managed by the Upper Gastrointestinal and Hepatobiliary Unit at Auckland Hospital was established in the year 2000. Demographic, clinical, pathological, management and follow-up data are recorded prospectively on all patients managed. Review of the database identified 47 patients who had undergone treatment for cystic liver lesions between January 2000 and December 2006.

All cysts were initially detected with ultrasound and were further investigated with computed tomography (CT scan) and/or magnestic resonance imaging (MRI scan: Figure 1). Unilocular cysts without internal septations or associated soft tissue mass were classified as radiologically simple cysts, while radiologically complex cysts were defined as multiloculated cysts and cysts with an associated soft tissue mass.

Results

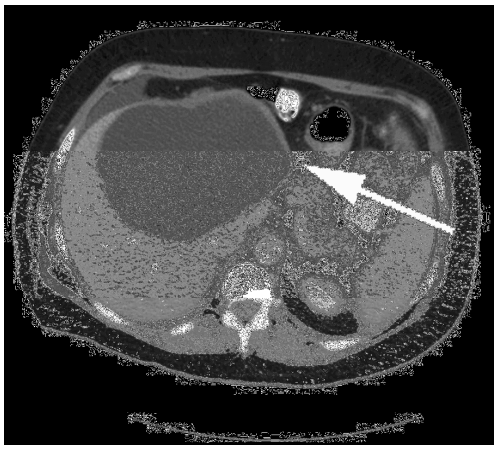
Overall, 47 patients (11 male, 36 females) with a median age of 61 (range 37–86 years) underwent surgical treatment for cystic liver lesions. In the same time period,

approximately 800 patients with a variety of hepatic and biliary lesions were managed surgically. Two further patients with multiple asymptomatic hepatic cysts were referred and have not been managed surgically but remain under clinical follow-up. All patients had been investigated with trans-abdominal ultrasound and CT scan. On the basis of these investigations they were classified as having either simple or complex cysts.

Simple cysts

Solitary—13 patients presented with large cysts (median maximal diameter 18 cm, range 11–52 cm) that were symptomatic (Figure 2). Overall, 11 of these patients were female with a median age of 62 (range 45–73) years. All patients were symptomatic with pain and abdominal distension. Tumour markers were within the normal range (median CEA = 1.4 , µg/L range 0–3 µg/L; median Ca 19–9 = 5 U/ml, range 0–17 U/ml).

Figure 2. Large simple cyst (arrow) replacing the left side of the liver in an 83-year-old female



On imaging, all patients had simple cysts with no associated septations or soft tissue mass (see Figure 2). All patients were treated with laparoscopic fenestration (median operating time 50 minutes, range 27–67 minutes) with a median hospital stay of 1 night. The operative findings were of solitary cysts containing clear fluid in 13 patients.

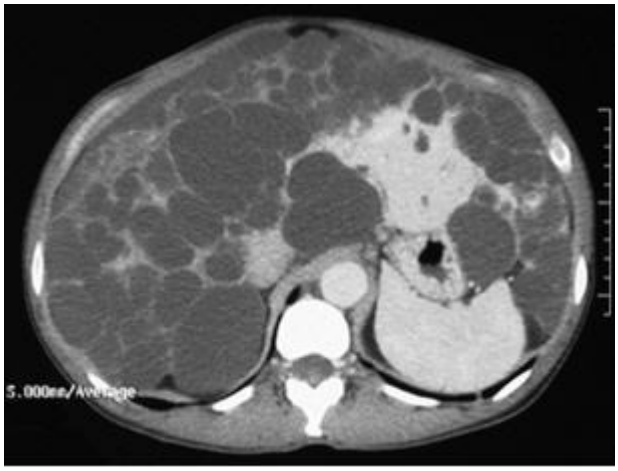
In one patient the cyst contained grey, turbid fluid. On inspection of the resected cyst membrane small papillary projections were apparent. This patient made a satisfactory recovery but developed a recurrent cyst within 4 months and then underwent left hepatectomy for a biliary cystadenoma. The median follow-up in these patients is 20 months. All patients remain well with no signs of further cyst development.

Multiple—Twelve patients presented with multiple hepatic cysts (Figure 3) and all were female with a median age of 62 (range 37–80) years. All patients presented with symptomatic disease with abdominal distension, and one patient complaining of early satiety.

Pain was present in two patients but was not the primary presenting symptom. Eleven patients were treated with laparoscopic fenestration (median operating time 87 minutes, range 63–130 minutes) and had a median hospital stay of 2 nights (range 2–7 nights). These patients were also investigated with trans-abdominal ultrasound and CT scan with the finding of multiple simple hepatic cysts. One patient was found to have a complex cyst in association with multiple simple cysts and this was resected.

Tumour markers were also within the normal range (median CEA = 3 µg/L, range 0–3 µg/L, median Ca 19–9 = 7 U/ml, range 3–15 U/ml). At a median of 26 months follow-up all patients are alive and well. Two patients have undergone a second fenestration for recurrent symptoms at a median of 42 months following their original procedure. Histological examination of resected cyst wall was benign.

Figure 3. Multiple simple cysts involving the liver in a patient with polycystic liver disease.



Complex cysts

Neoplastic—8 patients presented with solitary complex cysts of the liver. In addition, one patient with multiple simple hepatic cysts was found to have a single complex cyst in segment 5. In total, six of these patients were female with a median age of 54 (range 45–78) years. Five patients presented with symptoms related to upper abdominal pain or discomfort, while in four patients the lesions were noted as incidental findings on radiological investigations carried out for other indications.

The diagnosis of a complex cyst was based on the presence of an associated mass in two cases and both of these patients were subsequently shown to have a biliary cystadenoma (Figure 4). In addition, a further patient initially treated with laparoscopic fenestration for a radiologically simple cyst was found to have papillary projections on the cysts membrane and also had a biliary cystadenoma.

In six cases the diagnosis of a complex cyst was based on the presence of multiple septations. Two of these patients were found to have biliary cystadenocarcinomas,

two had benign complex cysts and two biliary cystadenomas. CEA was within the normal range in all patients (median 2 µg/L, range 0–5 µg/L). Ca 19-9 was also within the normal range in all three patients with biliary cystadenomas (median 7 U/ml, range 5–12 U/ml) but elevated in two patients with biliary cystadenocarcinomas at 1012 U/ml and 1800 U/ml respectively.

All patients with complex cysts were treated with hepatic resection (4 segmental resections, 2 right hepatectomies, 2 left hepatectomies) with a median blood loss of 200 cc (range 100–800 cc) and a median day stay of 7 days (range 3–14 days).

Three patients developed postoperative complications of an ascitic leak in one patient, and two patients developed bilomas which were managed with percutaneous drainage. One patient with a biliary cystadenocarcinoma represented with pseudomyxoma peritoneii at 20 months post-resection and died of disease 18 months later. The other patient with a cystadenocarcinoma remains alive and well 20 months after resection. The remaining seven patients, including four patients with biliary cystadenomata are alive and free of disease at a median follow-up of 24 months.

Hydatid disease—13 patients (7 female, median age 64 years, range 52–86 years) were referred with a diagnosis of hydatid disease. Of these patients 9 were of Caucasian descent, 3 were Māori, and 1 Middle Eastern. In 5 patients there was a documented past history of hydatid disease requiring treatment; 9 patients presented with symptoms (abdominal pain in 8, fevers and jaundice in 1 patient related to a biliary obstruction) while in 4 patients the presence of a cyst was noted incidentally.

Four patients had complex disease with extrahepatic abdominal disease present in 2 patients, pulmonary disease in 1 patient and a biliary fistula in 1 patient. Hydatid serology was positive in all patients and imaging with ultrasound and CT scan showed appearances typical for hydatid disease with laminated cyst membrane and the presence of daughter cysts (Figure 5).

Figure 4A. Post-contrast CT scan of a patient with a complex, multi-loculated cyst (arrow) involving segment 4

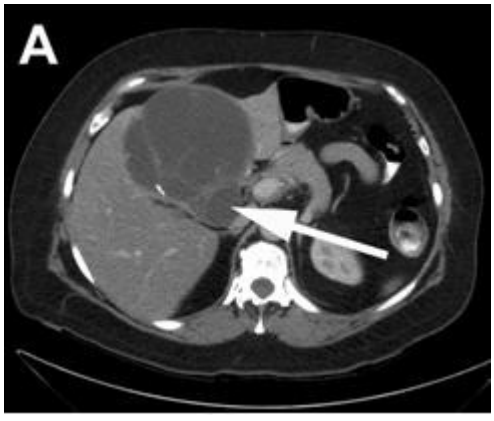


Figure 4B. Pathological examination shows multiloculated structure containing mucin with histopathology confirming a biliary cystadenoma

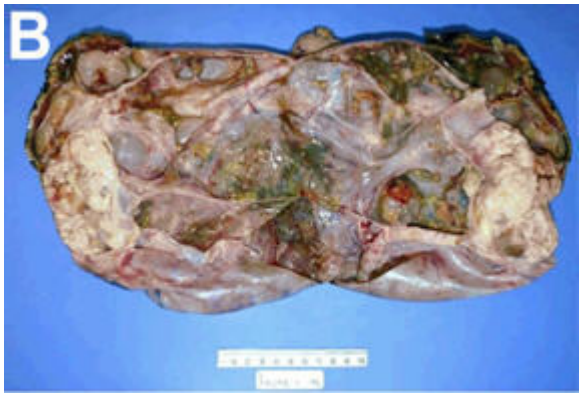
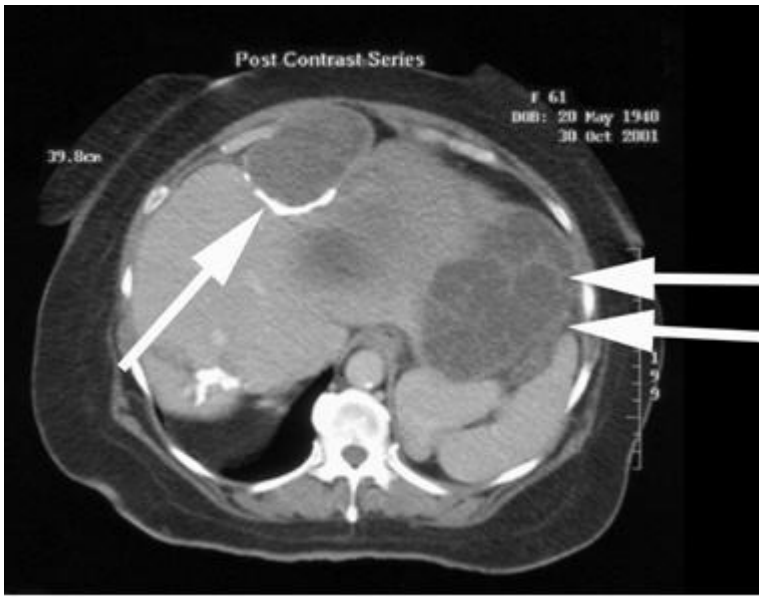


Figure 5. Post contrast CT scan showing hydatid disease with a calcified cyst in segment 4 (single arrow) and a large cyst hanging from segment 3 containing multiple daughter cysts (double arrow)



All patients were treated with an initial course of albendazole for 6 weeks although the treatment was discontinued in 2 patients because of thrombocytopenia. All patients were treated surgically with either cystectomy (10 patients) or hepatic resection (3 patients). These procedures were combined with a pulmonary resection in one patient and resection of abdominal disease in two patients.

The median blood loss for these procedures was 200 cc (range 50–500cc) and 4 patients developed postoperative complications (wound infection 2 patients, biloma treated with percutaneous drainage 1 patient, incisional hernia and wound pain 1 patient). All 13 patients are alive and free of disease at a median follow-up of 19 months.

Discussion

Cystic lesions are common radiological findings in the liver.[2] Most are no more than incidental findings and require no further treatment or follow-up. However all cystic lesions do require some form of radiological assessment and a minority will require treatment. These lesions are often noted on trans-abdominal ultrasound carried out to investigate abdominal or pelvic pain. Further assessments can be carried out with CT scan or MRI.

Asymptomatic simple cysts require no further intervention other than their documentation. Multiple asymptomatic simple cysts may indicate the presence of polycystic disease, particularly if bilateral renal cysts are present.

Based on the results of this small series, simple cysts of the liver that require treatment appear to be more common in women and tended to present in the sixth decade of life. This finding may reflect a selection bias with females more likely to be

investigated with ultrasound to define the presence of gallstones or pelvic disease. However other investigators have also noted this finding.[3]

Solitary simple cysts may reach great size and contain a significant amount of fluid. The largest cyst in this series was present in a 62-year-old man and measured 30 cm × 15 cm and contained 2.8 litres of fluid. These cysts tend to present with abdominal distension, poorly localised pain and occasionally early satiety. Rarely, acute, severe abdominal pain can result from a haemorrhage into the cyst.

In our hands laparoscopic fenestration was a safe and effective treatment. No patient required conversion to an open procedure and lasting symptomatic relief was obtained.

Patients with polycystic liver disease also present with symptoms related to the presence of intra-abdominal space-occupying lesions, principally abdominal distension and discomfort. This condition is also more prevalent in women[3] and most present in middle age.

Laparoscopic fenestration in these patients also provides good symptom relief without significant morbidity. However, unlike patients with solitary cysts these patients have numerous cysts which are often deeply placed within the liver. The aim of fenestration in this setting is to drain as many cysts as possible. The majority of these will be surface lesions but with intra-operative ultrasound it is possible to drain deeper cysts which may abut superficial cysts that have already been drained.

Consequently, recurrence of symptoms is common as residual cysts increase in size and multiple fenestration procedures may be necessary over the course of a patients lifetime. In this respect the application of laparoscopic surgical principles to this condition has greatly improved patient outcomes.

Previously, laparotomy was necessary, causing increased hospital stay and morbidity.[4] In addition, open fenestration made repeated procedures technically difficult and increased the risks of perioperative morbidity.[4]

In contrast, repeat laparoscopic fenestration is technically straightforward and can be carried out with a 1-–2 night hospital stay.[5] The primary aim of this procedure is to decrease symptoms related to the presence of the cysts and improve quality of life. In this respect, laparoscopic fenestration has been shown to be effective and is accompanied by minimal morbidity.[5]

Since cysts expand slowly they cause atrophy of the surrounding hepatic parenchyma causing crowding of the intra-parenchymal bile ducts and blood vessels at the edge of the cyst. Technically this is an important point since fenestration must remove a significant portion of the cyst wall to prevent recurrence. However, if the fenestration extends into adjacent compressed hepatic tissue edge, bleeding and bile leakage are more common.[5]

Cystic liver tumours are rare and generally present as complex cysts. In this series, one patient presented with a simple cyst which on fenestration was shown to be complex with the finding of intra-cystic papillary lesions that were not shown on imaging. In addition, this cyst contained brownish fluid indicative of a secretory biliary epithelium.

In contrast, simple cysts contain clear or straw-coloured fluid. Overall we have treated three patients over 5 years with biliary cystadenomas. This tumour is rare and other investigators have found a similar incidence with 18 patients presenting to Vanderbilt in Nashville, Tennessee over a 15-year timeframe.[6]

The risk of malignant change in cystadenomas is unclear. However in the largest pathological review to date 18 of 70 cystadenomas (25%) contained cystadenocarcinomas.[7,8] In most of these cases malignancy was an incidental finding on pathological examination with very few preoperative investigations able to predict the presence of a cystadenocarcinoma although a raised Ca19-9 is a useful indicator of malignant transformation.

For this reason we have used hepatic resection to treat all complex cystic lesions, based on the high frequency of neoplastic lesions presenting as complex cysts. However we have also found that four of our nine patients had a diagnosis of benign, complex cysts. Surgical resection also provides the opportunity for complete pathological examination of the tumour and, for cystadenomata, is curative.

In addition there is frequently a communication between the cystadenoma and the biliary system which must be formally closed in order to avoid postoperative bile leak. However other investigators have treated cystadenomas with enucleation or fulgeration and obtained good longterm results with no mortality and minimal morbidity.[6,9]

Hydatid cysts were once a common cause of liver disease in New Zealand.[10] However, with a dedicated public health campaign, this disease has become rare. The 13 patients reported all presented with liver disease and 9 were complex with the presence of extrahepatic disease in abdomen or lung a common finding. In addition 5 patients had previously had at least one surgical procedure for hydatids.

In all patients the diagnosis of hydatid disease was made based on the typical radiological appearances of the cyst (Figure 5). With the finding of active disease on hydatid serology patients were treated with either albendazole or mebendazole for up to six weeks.

Surgical treatment focused on decompression of the cysts and destruction of the geminal lining membrane. Hypertonic saline was utilised as a scolicidal agent as this is the least toxic to biliary epithelium if a biliary communication exists. Most patients with complex cysts were treated with cystectomy although four patients were treated with hepatic resection, with both procedures yielding satisfactory results.

Assessment of cystic liver lesions remains a small but significant role for the general surgeon. With increased use of radiological investigations to investigate abdominal complaints, both simple and complex cystic lesions will be encountered regularly.

Ironically, hydatid disease which was once common and managed surgically in many New Zealand hospitals has become rare and many recent surgical graduates have seen few, if any, cases. Simple cysts which are symptomatic can be treated with laparoscopic fenestration in the expectation that this will be curative in solitary cysts but further procedures may be required in patients with polycystic liver disease.

Neoplastic cysts are rare. They are usually benign cystadenomas and should be treated with hepatic resection.

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Risk and severity of injury in a population of BASE jumpers

Erik Monasterio, Omer Mei-Dan

Abstract

Aim To determine the frequency and severity of accidents in a population of BASE jumpers (people who jump with parachute from a fixed object such as from a cliff).

Methods To determine the frequency and characteristics of BASE jumping accidents, a cross-sectional survey of experienced BASE jumpers was completed.

Results 35 BASE jumpers enrolled in the study. Findings revealed that there were approximately 9914 jumps made and the estimated rate of injury was 0.4%. 39 accidents involving 21 (60%) BASE jumpers were found. 28 accidents (72%) predominantly involved the lower limbs, 12 (31%) involved the back/spine, 7 (18%) the upper limbs, and 1 (3%) was a head injury.

Conclusion BASE jumping is associated with a high risk of serious injury and appears to be significantly more dangerous than skydiving.

New Zealand has attracted an international reputation as an adventure sport destination. Worldwide adventure tourism and adventure sports are important leisure activities, of growing popularity. In this context, commercial adventure tourism has become increasingly important to the New Zealand economy. Adventure sports encompass a number of outdoor activities including rock climbing, mountaineering, skydiving, white-water rafting, mountain biking, and BASE jumping.

Recent reports in the literature have highlighted significant risk of injury and death associated with mountaineering, skydiving, white-water rafting, and mountain biking.[1–5]

BASE jumping is a sport that developed out of skydiving and uses specially adapted parachutes to jump from fixed objects. "BASE" is an acronym that stands for the four categories of fixed objects that one can jump off. These are: **B**uilding, **A**ntenna, **S**pan (a bridge, arch, or dome) and **E**arth (a cliff or other natural formation).

BASE jumping is an “extreme sport” and is ranked as being amongst the most dangerous adventure sports in the world (Figure 1).[6] As such, BASE jumping has been banned from many popular launch sites such as the Eiffel Tower in Paris and in Yosemite National Park (e.g. from El Capitan cliff where there has been fatalities) in California.

BASE jumping is considered to be significantly more dangerous than skydiving. As BASE jumps are made from lower altitudes than skydives (often less than 500 feet above ground level), BASE jumpers generally fall at lower speeds, have far less aerodynamic control, and may lose flying stability.

If the parachute is deployed while the jumper is unstable there is a high risk of entanglement or malfunction. The single canopy used may also be facing the wrong

direction. Such an off-heading opening is not problematic in skydiving, but off-heading opening that results in object strike is the leading cause of serious injury and death in BASE jumping. Also as BASE jumping takes place in close proximity to a cliff or tower which provides the jump platform, the BASE jumper may collide with the object.

Figure 1. BASE jumping examples

Jumper: Dr OM-D. Photo: R Topelberg.
Location: Israel

Jumper: Dr OM-D. Photo: Red Bull Archive.
Location: Austria

The only published study on morbidity and mortality associated with this sport examined the frequency of injuries and death associated with BASE jumping from a cliff in Norway and determined that BASE jumping is associated with a five- to eightfold risk for death or injury, compared with data on regular skydiving.[7] Interpretation and application of this data is limited by the absence of information on demographic characteristics or BASE jumper level of experience. Furthermore the report findings relate to the outcome of jumps from a single cliff, rather than the broad range of objects from which jumpers may launch.

The purpose of this paper is to report the demographic characteristics and morbidity findings in an international group of BASE jumpers. The degree of risk has been estimated utilising accident rates as denominator data and frequency of BASE jumps as numerator data. The data is taken from a study that has also examined the

psychological characteristics in this population (Monasterio, Mei-Dan, and Mulder in preparation).

Method

Volunteers were recruited from BASE jump group meetings, adventure website forums, and from personal communication among the BASE jumping community. All volunteers who expressed an interest and contacted the authors were recruited into the study.

After giving written consent, participants completed several questionnaires providing demographic information and BASE jump information (estimated number of base jumps per year, how long they had been involved in the sport, whether they had had "near misses", and whether they had suffered base jumping accidents).

The Cloninger Temperament and Character Inventory was also completed.[8]

Severity of accidents was rated as either:

- **Mild—**if injury required medical help, but did not lead to hospital admission and convalescence was less than 1 week;
- **Moderate—**if injury required hospital admission and/or convalescence was more than 1 week, but less than 3 months; or
- **Severe—**if injury led to risk of death, protracted convalescence (more than 3 months) and/or long-term health problems.[2]

Results

Demographics—A total of 35 volunteers completed the questionnaires. Only one volunteer who requested inclusion into the study failed to return completed questionnaires. Thirty-four subjects (97%) were male and the median age was 34 (range 21 to 55 years.). Nineteen subjects (54%) were single/unmarried and most (27; 77%) did not have children. Fourteen participants (40%) were from the North American continent, 13 (37%) from Europe, 6 (17%) from Oceania, and 2 (6%) from Israel.

Thirty-five (100%) of the participants were involved in other adventure sports—the most common was skydiving involving all participants (35; 100%) and rock climbing/alpinism (16; 41%) participants.

BASE jumper characteristics are summarised in Table 1.

Table 1. BASE jumper characteristics

Years BASE jumping		Total number of BASE jumps		Estimated frequency of "near misses"		Estimated accident frequency		Witnessed others dying from BASE jumping accidents	
Med	Range	Med	Range	Med	Range	Med	Range	Yes	No
4	(0.25–17)	274	(7–1600)	3%	(<1%–10%)	0.5%	(0.01%–30%)	26	9

Med=Median.

The median time of participation in BASE jumping was 4 years (0.25–17 years.), and the median number of jumps was 275 (7–1600). All 4 objects were used as launching platforms, without any particular object preference.

Participants estimated that the frequency of "near misses" from jumping was 3% and injury was 0.5%. Interestingly, 26 subjects (74%) had witnessed the death of at least one jumper from BASE jumping.

Accident findings are summarised in Table 2.

Table 2. Accident characteristics of study participants

Mild injuries (N=10)	Moderate injuries (N=17)	Severe injuries (N=12)
• Tendon strain/soft tissue injury to ankle ×3 • Contusion/soft tissue injury to lumbar spine ×2 • Ligament damage to knee ×2 • Laceration to arm requiring sutures • Contusion/soft tissue injury to lower limb ×2	• Fractured talus, 1st Metatarsal and ligament tear ×2 • Fractured talus ×2 • Multiple contusions/abrasions/soft tissue injury of lower limbs ×2 • 1st metacarpal and carpal fracture ×2 • Fracture to ankle and tear of Achilles tendon. • Fractured tibia and fibula ×2 • Fractured radius and ulna—right and left side • Dislocation/ soft tissue injury to ankle • Concussion, loss of consciousness and sutures to skull • Fractured ankle ×2 • Soft tissue injury to spine	• Fracture of femur • Fractured vertebrae (2) • Open fracture of tibia and fibula • ICU admission with fracture vertebrae (2), compression of vertebrae (4), fractured ribs (5), fractured cochix and scapula, pneumothorax and haemothorax. • Spinal compression with fracture of multiple spinous processes • Multiple fractures to tibia/fibula with 180-degree dislocation of ankle. • Fracture of elbow, skull, multiple ribs with sprained ankle and pelvis • Multiple spinal and rib fractures with fractured tibia/fibula ×2 • Spinal fracture with fractured tibia/fibula • Fractured L5 vertebra • Severe fracture to ankle

An estimated 9914 jumps were made; 39 accidents were reported, involving 21 (60%) of the participants. There was therefore 1 accident for every 254 jumps—a 0.4% injury rate. There were 12 severe, 17 moderate, and 10 mild accidents.

Of those who had more than one accident, nine participants were involved in two separate accidents; one each had three, four, and five accidents respectively. Twenty-eight accidents (72%) predominantly involved the lower limbs, 12 (31%) involved the back/spine, 7 (18%) the upper limbs, and 1 (3%) was a head injury.

Discussion

To the authors' knowledge this is the first cross-sectional survey that examines the demographic, BASE jumping, and morbidity characteristics in a population of BASE jumpers. The study has captured a population of experienced BASE jumpers, who have been involved in the sport for many years.

The findings suggest that the sport attracts predominantly male participants in their mid-30s (participants become involved in the sport in their mid-20s, when they gain sufficient skydiving experience and the required maturity, and continue with the sport into their 30s), who are actively involved in a number of other adventure sport activities.

The participants generally BASE jumped from all four categories of fixed objects, without indentifying any specific object preference. Sufficient data was not collected

to determine whether accident frequency was related to particular jumping sites or objects.

The accident rate of 0.4% is exactly the same as that of a recent report by Soreide et al which examined injury rates from BASE jumping from a single site (Kjerag Massif) in Norway.[7] However, in contrast to the findings by Soreide et al (who found that most BASE jumping injuries were minor), 75% of injuries recorded in our study were moderate or severe.

Possible explanations for this difference include: (a) the Kjerag Massif is considered among the BASE jumping community to be a "safe" object to jump from. This is because the cliff is high (1000m) and therefore allows greater speed before parachute deployment and control by jumpers, (b) it has a clear landing area, (c) it is a legal launch site and therefore more dangerous, rushed, or night time jumps (to avoid authorities) are unlikely to occur, and (d) the site is known to attract beginner as well as experienced jumpers.

The inclusion of a high number of beginners may paradoxically decrease the risk of injury severity as they do not generally attempt "complex manoeuvres" that are more commonly associated with severe injuries.

The overall risk of non-fatal injury associated with modern skydiving has been estimated to be between 48 and 174 per 100,000 jumps.[4,9] Risk of injury from BASE jumping in this study is three to eight times higher (394 per 100,000 jumps). Moreover the rate of injuries requiring hospitalisation in our study was 294 per 100,000 jumps and 16 times higher than that found by Burrows et al (18 per 100,000 jumps) in their study freefall skydiving injuries.[4]

The BASE jumpers in this study appear to have a reasonable understanding of the rate of injury associated with the sport, as they "estimated" that the accident frequency from BASE jumping is 0.5% which is very similar to the accident frequency found in the study (0.4%).

The majority of accidents (80%) involved significant injuries to the lower limbs and spine, and the overall severity of these suggests that BASE jumping injuries are likely to present a significant burden to health services, particularly hospital accident and emergency, trauma, and rehabilitation departments. They are also likely to contribute to persisting chronic disabilities and significant loss of productivity.

Several methodological limitations need to be considered in interpreting the results of this study. The population was not a random sample. All participants who volunteered were included and the sample size was relatively small. This may have lead to selection bias as those jumpers who had experienced prior accidents may have been more motivated to share their experience and therefore more likely to participate in the study.

As the study included only active jumpers, cautious BASE jumpers, who had given up the sport following an injury or a "near-miss" experience, may have been excluded. The sample may therefore represent those with a particularly high risk-taking propensity. Alternatively the sampling process may have excluded particularly high-risk groups; as less experienced, more impulsive and higher risk-taking jumpers may

have been involved in fatal accidents at earlier stages of their BASE jumping careers and therefore were unavailable for inclusion in the study.

Of concern, Soreide et al found the death rate associated with BASE jumping from the "safe" Kjerag Massif to be 0.04%.[7] Given the greater severity of injuries found in our sample we are concerned that our population presents an even higher risk of mortality, and intend to undertake 2- and 5-year follow-ups of this population to determine whether this is the case.

Competing interests: In the past EM has worked as a mountain and jungle guide (12 years ago) and mountain cycle guide (6 years ago). OM-D is an active BASE jumper and has worked as a promotional stuntman.

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THE NEW ZEALAND MEDICAL JOURNAL
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Accessory breast tissue presenting as a large pendulous mass in the axilla: a diagnostic dilemma

Rashesh Solanki, Dilip B Choksi, Dipesh D Duttaroy

Abstract

Accessory breasts are an uncommon entity. They may present as asymptomatic masses or cause symptoms such as pain or restriction of arm movements. They may prove to be a diagnostic challenge if found in locations along or outside the mammary line. We report a case of an ectopic accessory breast presenting as a large pendulous mass in the axilla which proved to be a diagnostic dilemma. Excision biopsy was diagnostic.

Ectopic mammary tissue appears in humans owing to an incomplete embryologic regression of the mammary ridges. They are thus located most frequently along the mammary line extending from axilla to pubic region. The same pathology that affects normally positioned breasts, including carcinoma, can occur in ectopic mammary tissue.

Enlargement of ectopic accessory breast tissue occurs commonly during hormonal stimulation as in pregnancy or lactation and they can then prove to be a diagnostic challenge.

Case report

A 30-year-old Asian Indian female presented with a large pendulous swelling in the left axilla (Figure 1) of 3 years duration; 2 weeks after delivering a stillborn child in her third pregnancy.. It had appeared during the first trimester of her second pregnancy but remained static in size until her third confinement, when the swelling grew to its present dimensions. During her second pregnancy the swelling decreased after each breastfeeding session.

Examination revealed a large pendulous swelling in the left axilla ,15×10 cm in size, that was firm, mobile, pigmented with skin free from the underlying tissue. Clinically, a diagnosis of an enlarged accessory breast was arrived at with an intent to rule out other pathologies of the normal breast.

Differential diagnosis included neurofibroma and galactocoele. The swelling was excised under general anaesthesia. Histopathology revealed accessory breast tissue with lactational changes. The postoperative course remained uneventful.

Figure 1. Accessory breast tissue: mass in the axilla

Discussion

Accessory breasts occur in 0.4–6% of women.[1] They may present as asymptomatic masses or cause pain, restriction of arm movement, cosmetic problems, or anxiety.[1] Commonly accessory breasts are bilateral. Aberrant breast tissue is usually present along the milk line above or below the normal breast location and result due to incomplete embryologic regression of mammary ridges. Occasionally, they are found in unusual locations, such as the axilla, scapula, thigh, and labia majora.[2] Ectopic breast tissue usually becomes noticeable only after hormonal stimulation, usually during puberty, pregnancy, or lactation.

Accessory breast tissue, presenting as palpable thickenings in the axilla, can undergo monthly premenstrual changes, such as tenderness and swelling and irritation from clothing. Accessory tissue may range from a subcutaneous focus of breast tissue to a full accessory breast complete with areola and nipple. When nipple and areola are absent, the diagnosis becomes exceedingly challenging. It may also be a diagnostic

challenge, as other benign and malignant lesions occur in this area.[3] Interestingly, soft tissue sarcoma (malignant fibrous histiocytoma) have also been reported.[4]

Mammographic and sonographic findings include masslike density that is identical to that of the normal breast parenchyma in the axilla.[5] Fine needle aspiration is a useful tool.

Ectopic breast tissue is subject to the same pathologic events that occur in normally positioned breasts. Indeed, there have been reports of fibroadenomas[6] and even cancer developing in the accessory breast.[7,8] Excision of ectopic axillary breast tissue may be required for diagnosis, treatment of symptoms, or cosmesis[2] and is the definitive treatment for the above mentioned indications. However, according to a report, complications after removal of accessory breast are not uncommon. These include incomplete removal of the accessory breast, poor scar, and intercostobrachial nerve injury. Hence conservative treatment may be considered especially for asymptomatic cases.[1] Liposuction may be a feasible alternative in selected cases.[1]

Conclusion

Accessory breast in the axilla may prove to be a diagnostic dilemma and this entity must be kept in mind while dealing with swellings in the axilla. The former enlarge upon hormonal stimulation during puberty, pregnancy or lactation. Excision is usually required for symptomatic cases but liposuction may be an alternative mode of therapy.

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THE NEW ZEALAND MEDICAL JOURNAL
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Aorto-enteric fistula: recurrence of a fistula to the sigmoid stump following Hartmann's procedure

Marianne Lill, Gavin Wilton, Rene Van Den Bosch

Aorto-enteric fistula (AEF) is an uncommon and potentially fatal complication of open abdominal aortic aneurysm (AAA) repair; it is associated with infection of the graft, and leads to serious morbidity or death.

We report an unusual case of recurrence of an AEF. This is the first reported example of aortic fistulation to the blind sigmoid stump following Hartmann's procedure. The Hartmann's procedure was originally performed due to complications of an aorto-jejunal fistula repair.

Case report

The patient presented in 2000 aged 72 for elective repair of an infrarenal AAA, with a 20 mm Microvel double velour knitted vascular graft. The straight tube graft was covered with aneurysm wall. An omental patch was used for additional covering of the proximal anastomosis.

In 2004, the patient returned to hospital with a gastrointestinal (GI) bleed and shock. At laparotomy, a fistula was found between small bowel and the distal aortic anastomosis. The small bowel segment was resected and the defect in the aortic anastomosis closed. The remainder of the graft was well incorporated without evidence of infection.

Ten days postoperatively the patient developed faecal peritonitis secondary to ischaemic sigmoid perforation. We suspect that the hypotensive episode secondary to the bleed from the aorto-jejunal fistula rendered the sigmoid ischaemic. The sigmoid colon had been made more susceptible to ischaemia by ligation of the inferior mesenteric artery at the initial aneurysm repair. This is routinely done to prevent backbleeding into the aneurysm sac.

At laparotomy the ischaemic sigmoid was resected and an end colostomy was brought out. The distal sigmoid stump was oversewn. He had a long postoperative course, but ultimately made a good recovery.

During 2006 the patient was readmitted three times with rectal bleeding. CT angiography and gastrografin enema were negative for a fistula.

In January 2007 he returned (age 79), with further PR bleeding. This had recurred suddenly, with an estimated loss of 600 ml of fresh blood. Abdominal CT showed the rectal stump adherent to the base of the aortic graft (Figure 1).

Sigmoidoscopy showed no definite bleeding point, but a small granuloma at the top of the stump (Figure 2). At laparotomy the rectal stump was adherent to the aorta at the distal anastomosis of the graft. The rectal stump was taken off the suture line and the defect was closed. Again, the remainder of the graft was well incorporated.

Gentamycin beads were placed around the area of the defect. The rectal stump was shortened and closed. The patient was treated with prophylactic antibiotics and did not develop sepsis. He made an uneventful recovery and remains well.

Figure 1. CT scan showing sigmoid stump adjacent to the distal anastomosis. The arrow indicates a blush of contrast entering the adherent sigmoid stump

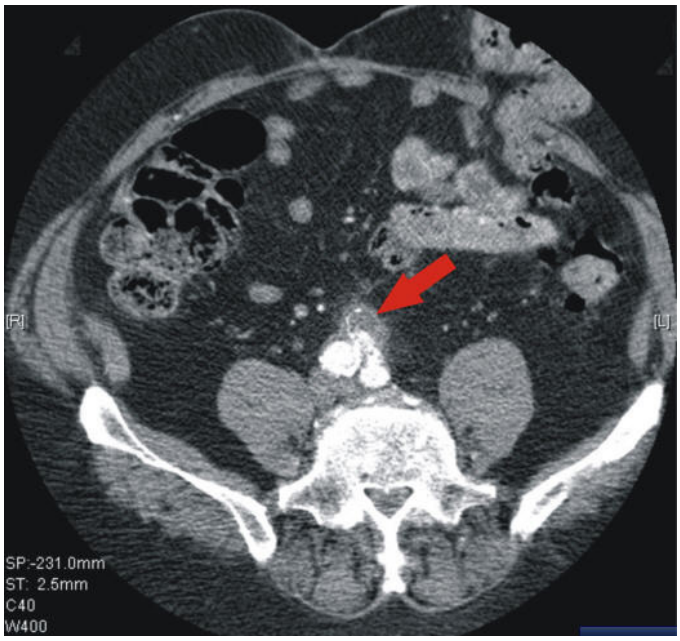
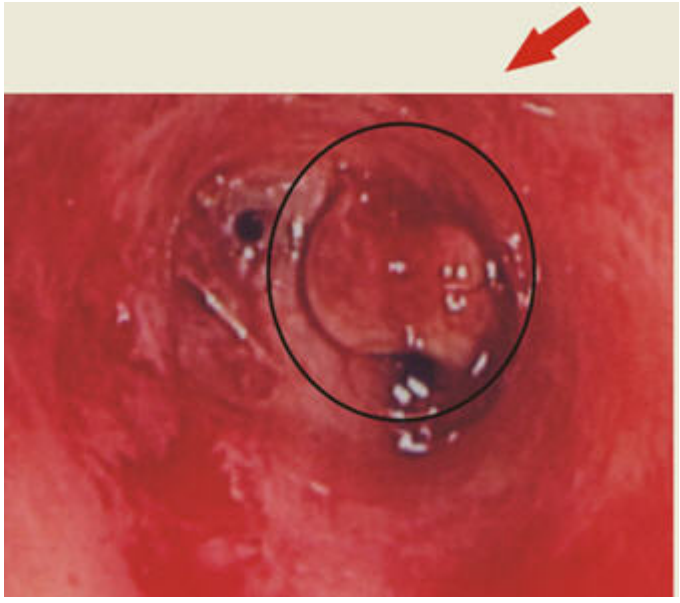


Figure 2. Image at sigmoidoscopy with the area of granulation tissue at the opening of the fistula indicated by the black circle



Discussion

Secondary aorto-enteric fistula formation occurs in 0.36–1.6% of patients post AAA and iliac aneurysm repair.[1,2]The rate of mortality is high, with reports ranging from 24% to 85%[2–6] although the prognosis has improved over the past few decades.[7]

The duodenum is the most common site of fistulation, accounting for 60–88% of cases. The small bowel is the next most frequently involved site (19%); the colon or other sites[4,7] are seldom involved.

GI bleeding is the most common presenting symptom, which occurs in 80% of cases. Other presentations may include sepsis (44%), abdominal pain (30%), a pulsatile abdominal mass (56%), back pain (15%), and groin pain (12%)[4]. Fistulation usually affects the proximal end of the graft,[2,5,7,] although in this case the distal end was involved.

Earlier studies have recommended that in the presence of infection the best treatment is to remove the infected graft and either replace it in situ or with an extra-anatomical bypass.[1,2] Local repair of the defect has also been described, particularly in the absence of gross infection.[5]

Recurrence of aorto-enteric fistulae is rare, with few reports in the literature.[3] A fistula to a sigmoid stump following Hartmann's procedure has never before been reported, and this case demonstrates the unexpected ways in which this problem can manifest. Although in the absence of obvious infection, a good result can be achieved with local repair, there is a risk of recurrence, as this case illustrates.

The importance of covering an aortic graft at the proximal anastomosis is clear; this case re-emphasises the need to cover the distal anastomosis with aneurysm wall, peritoneum, and/or omentum.

We recommend that where a rectal stump is present it be placed in the pelvis, well away from the graft to prevent this unusual complication.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Hyaline vascular-type Castleman's disease of the retroperitoneum

Chien-Ming Liao, Ying-Chun Chiu, Wei-Chou Chang, Chang-Hsien Liu, Ching-Jiunn Wu, Guo-Shu Huang

Castleman's disease is a rare lymphoproliferative disorder characterised by masses of lymphoid tissue. The most common site of the disease is the mediastinum.

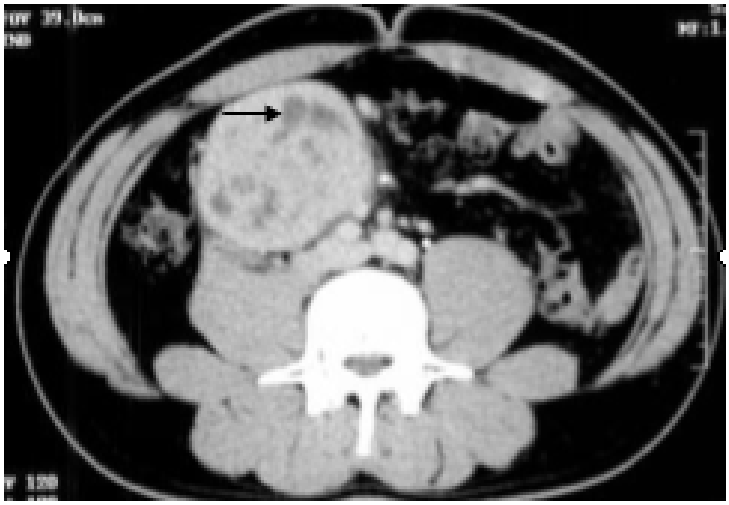
We report the rare case of a 36-year-old Chinese man with a Castleman's tumour in the retroperitoneal cavity located below the level of the right kidney—and mimicking a sarcoma, neural tumour, metastasis, or lymphoma.

Case report

A 36-year-old man presented with a self-detected mass in the right lower abdominal quadrant. He had no medical history or past surgical history. Physical examinations were generally normal, except for the palpable mass over the right lower quadrant of the abdomen. The results of a routine complete blood count and his serum biological profile were unremarkable.

A heterogeneously enhanced lesion with multiple low-attenuation areas was present on post-contrast computed tomography (CT; Figure 1). The mass was in the right retroperitoneal cavity, adjacent to the right psoas muscle. The fat plane between the retroperitoneal mass, right psoas muscle, common iliac vessels, and right ureter was clear. The encapsulated mass was completely removed.

Figure 1. Axial post-contrast CT scan shows a heterogeneously enhanced right retroperitoneal mass with multiple low-attenuation areas (black arrow)



Its gross pathology revealed an encapsulated tumour measuring about 8 cm, located in the right retroperitoneal cavity, grey in colour, with an ovoid-shaped contour and with haemorrhage. Microscopically, the specimen showed the proliferation of numerous lymphoid follicles with collagenous germinal centres and hyaline vascular proliferation, the appearance typical of hyaline vascular-type Castleman's disease. There were no surgical complications and the patient recovered well.

A CT scan after 3 months was normal, with no evidence of recurrence.

Discussion

Castleman's disease is a poorly understood proliferative disease of the lymphoid tissue that occurs mainly in young, healthy patients in the age range of 8–66 years, with no sex predominance.[1] Most (70%) Castleman's disease occurs in the mediastinum, with 20% in the neck, shoulder, and inguinal regions, and 7% in the retroperitoneum.[2]

Castleman's disease is classified into two pathological subtypes: a localised and a multicentric subtype.[3] Localised Castleman's disease presents as a solitary mass, which may be well circumscribed and usually has a benign course. In contrast, multicentric Castleman's disease usually has a worse clinical course, which can include malignancy, infection, and death.[4]

Abdominal Castleman's disease has been described in the radiology literature as an enhanced mass over the mesentery, retroperitoneum, porta hepatis, and pancreas.[5] Meador and McLarney reported that an enhanced pattern on abdominal CT and a Castleman's disease tumour of less than 5 cm usually presents with homogeneous enhancement, whereas tumours greater than 5 cm usually present with heterogeneous enhancement with areas of low attenuation.[5] These radiological features are not sufficiently specific to differentiate Castleman's disease from retroperitoneal masses such as sarcoma, metastasis, lymphoma, or neural tumour.

To the best of our knowledge, retroperitoneal sarcoma is usually a large unilateral mass, displacing the retroperitoneal organs or viscera. It is usually heterogeneously enhanced on contrast-enhanced CT.

Retroperitoneal lymphoma tends to surround the adjacent vessels, presenting with a "floating" aorta[5] and low attenuation, without significant enhancement on contrast-enhanced CT.[6]

Although radiological images can help us differentiate the possible diagnoses of a retroperitoneal mass, surgical resection and histological evaluation allow an absolute diagnosis of Castleman's disease. The use of haematoxylin-eosin (H&E) staining for Castleman's disease was important in this case and led to the correct diagnosis.

In conclusion, we have reported a large retroperitoneal mass (>5 cm) with a heterogeneously enhanced pattern and areas of low attenuation. Radiological imaging studies are not sufficiently specific to identify Castleman's disease and a histopathological examination is necessary for a final diagnosis.

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THE NEW ZEALAND MEDICAL JOURNAL
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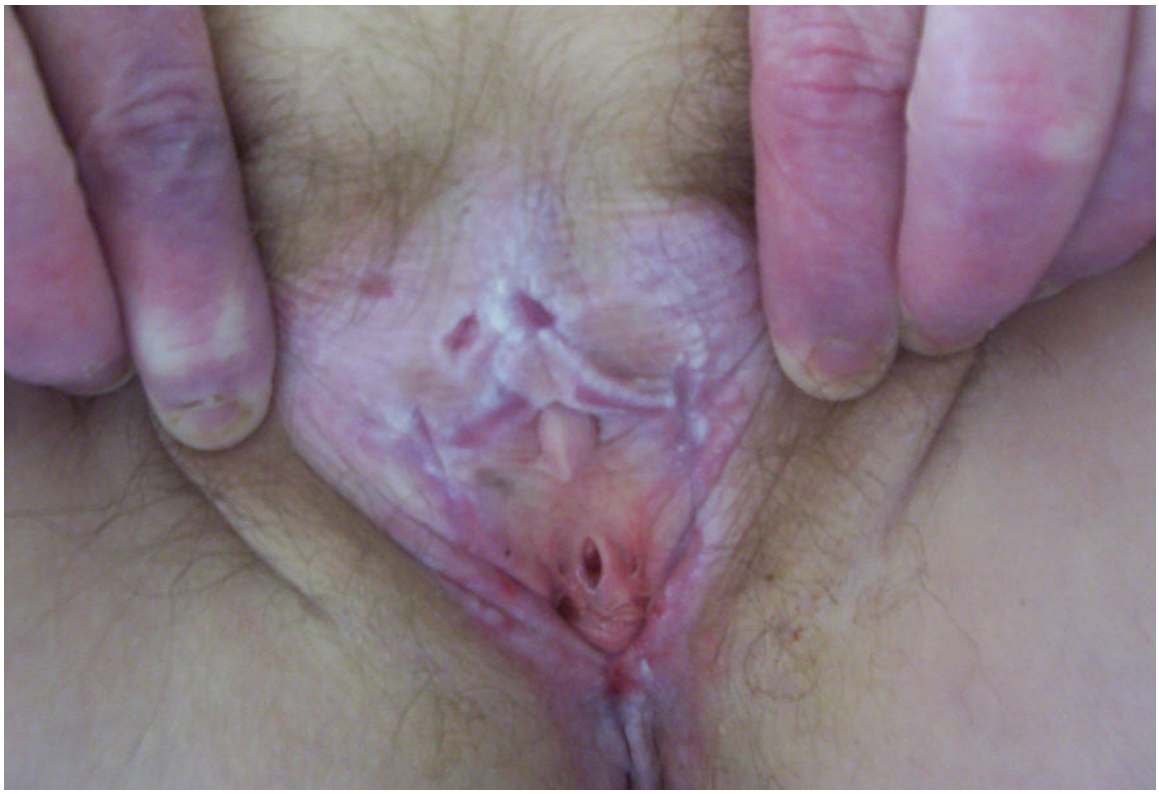
Genital lupus

Tarek Darwish

A 54-year-old Caucasian woman, who had a history of systemic lupus erythematosus (SLE) and CREST syndrome, presented with worsening pruritic vulvar and vaginal lesions, associated with burning urination and painful defecation.

Physical examination showed white type lesions with ulcerations from top of clitoris to anus confined to the inside of labia minora; erythematous patches were also noted (Figure 1).

Figure 1



Laboratory studies revealed positive antinuclear antibodies (1:640 titre; speckled pattern), and elevated sedimentation rate (ESR) 77 mm/hr with normal double-stranded DNA and complement levels. Genital herpes and syphilis were ruled out. Skin biopsy from the genital lesions showed hypertrophic dystrophy with chronic inflammatory infiltrate.

Clinical picture, laboratory findings, and skin biopsy were attributed to genital lupus—a high potency corticosteroid cream (clobetasol propionate 0.05%) was applied twice daily with remarkable improvement.

Discussion

Genital lupus is uncommon manifestation of SLE; moreover, the data is very limited regarding its prevalence. Burge SM et al[1] did review the mucosal involvement in 121 patients with lupus erythematosus (LE); vulvar lesions were found in 5% of patients with chronic cutaneous LE.

Although skin biopsy can help to establish the diagnosis in most cases, extra-genital involvement is the mainstay.[2,3] Due to the unfavourable result of untreated lesions, physician awareness has to be increased of this unusual manifestation.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

A sweaty lady with large digits

Thattungal M Anoop, Soman Simi, Puthiyaveettil K Jabbar, Paramu Sujathan

A 50-year-old female presented with one-year history of increased perspiration, disfigurement of face and extremities, frequent change of her slipper size, and mild visual impairment.

A photograph of the hands (Fig A), X-ray of the skull (Fig B), and magnetic resonance imaging (Fig C) are shown.

Fig A

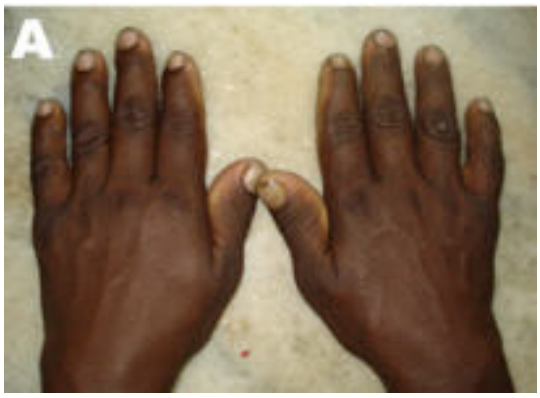


Fig B

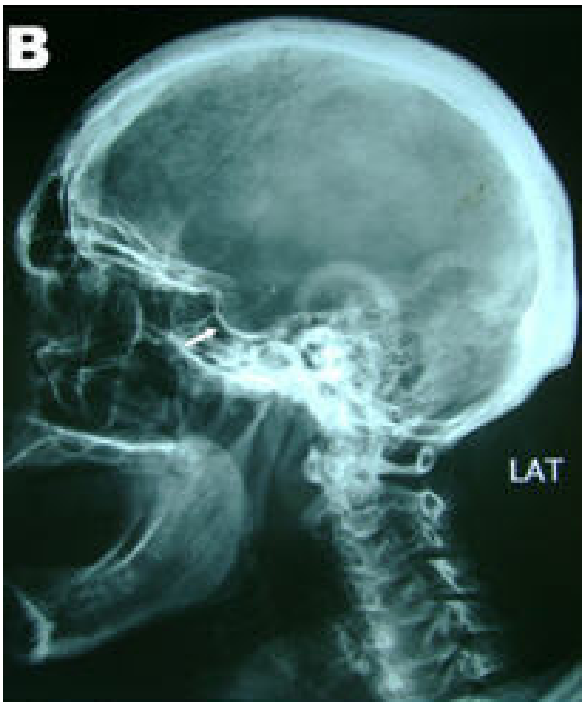
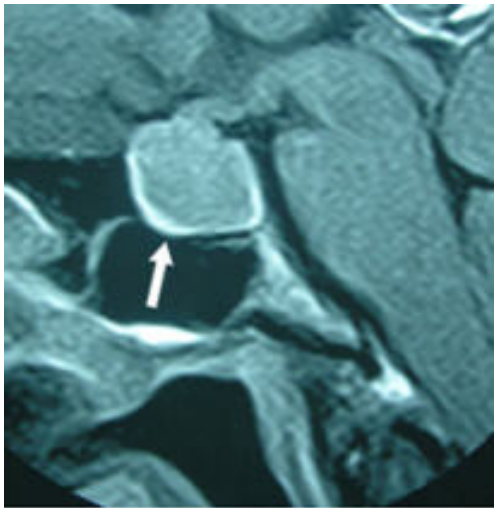


Fig C



What is the diagnosis and what is the management?

Answer

The diagnosis is *acromegaly with pituitary macroadenoma*.

- Physical examination shows enlarged extremities (Fig A).
- Radiograph of skull shows enlarged pituitary fossa with thinning of the posterior clinoids (Fig B; small white arrow).
- The T1-weighted sagittal magnetic resonance imaging of pituitary after contrast showing an enlarged pituitary with large extra-axial mass lesion of 2.2 × 1.8 × 1.2 cm with suprasellar and parasellar extension (Fig C, arrow).

The prolactin and thyroid function test were normal. The serum levels of post glucose challenge growth hormone and IGF (insulin-like growth factor) were elevated 65.5 and 1037 respectively.

Pituitary macroadenoms account for 10% of all primary intracranial tumours. Macroadenomas are >10 mm diameter while microadenomas are <10 mm diameter. They are benign and slow-growing tumours. Clinically 75% of macroadenomas are hormonally active. Most pituitary adenomas are microadenomas.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Dr Truby King and a scheme for the prevention of cruelty to infants

Editorial published in NZMJ 1908;6(26):41–2.

GRADUALLY the idea which has been floating more or less vaguely through the minds of all to whom the welfare of the race is a matter of any moment the idea that there has been, and still is, a terrible waste of human life in the high rate of infant mortality, and that the waste is largely preventable, gradually has this partially submerged idea come to the surface, until now throughout the civilised world the necessity for doing something to conserve infant life has become a subject of first importance. Many things have contributed to bring this question into prominence of late years; First, there is the instinct of humanity which is undoubtedly growing, as proved by the increasing horror at the thoughts of war and its attendant misery; while those of us who have any feelings of honour or patriotism know that there are worse things than war, we yet insist that if war is to come our soldiers, whether sick or wounded, shall have the best medical and surgical skill, and the best nursing possible.

The horrors of the Crimea will never again be repeated. We value life too highly; moreover, our more sensitive natures shrink from the very idea of anything living enduring any unnecessary pain. Hence, innumerable societies for the prevention of cruelty to animals, and at last it has occurred to this 20th century to start a scheme for the prevention of cruelty to infants, and to Dr Truby King all honour is due for his efforts to start on a sound basis in New Zealand what is practically a society for the prevention of cruelty to infants, although the modest beginning in which the idea, which had been for many years floating in his brain, at last crystalised was called the "Karitane Home for Sick Babies."

That movement initiated by him has now spread throughout New Zealand, and promises to be a valuable agent in checking the rate of infant mortality. Her Excellency Lady Plunket, having taken a great interest in the scheme, there has, largely through her energy, been formed a guild of district nurses, whose work is confined to the care of infants and the instruction and helping of mothers in the care of their young.

It is a remarkable fact that whereas the lower animals seem to have by instinct the necessary knowledge for rearing and guarding their young, the human mother, in our highly civilised condition, probably because she is highly civilised, seems to have entirely lost the instinct, and, we say it with shame and sorrow, when she turns to the doctor as the proper counsellor she gets advice far too often worse than useless.

We hear still of cases where ignorant foolish mothers, living in dirty, untidy surroundings with an ailing, puny, whining baby consult a doctor and get this valuable advice, "give the infant peptonised milk," there in these surroundings with a dirty bottle, with 18 inches of foul india-rubber tubing, is a mother giving her baby "peptonised milk!" Under a doctor's advice and believing and ready to state at the inquest, only too imminent, that everything possible had been done.

What a grim farce! If Dr. King's movement has no other result than in abolishing for ever this fetish of "peptonised milk," it will have done at any rate a vast amount of good. But it will do and has done much more. It has set doctors thinking and mothers thinking. Doctors for very shame will have to come down from the heights from which in the past they have surveyed infantile suffering and death, and will have to give their minds seriously to the question, and mothers will have to learn and are beginning to learn that it is their duty to know at any rate some few elementary facts about the babies they are responsible for, and to Dr. Truby King must always be ascribed the credit for having focussed attention on the waste of life that is going on, and for having set going a workable scheme for preventing it.

He has made no new discovery, and he would be the last to wish it to be thought that he laid any claim to a monopoly of knowledge on the subject, but he saw more clearly perhaps than others that the time was ripe for a crusade, and he threw himself into it with characteristic energy.

NZMJ Note: Read about Sir F Truby King at http://www.teara.govt.nz/1966/K/KingSirFredericTrubyCmg/KingSirFredericTrubyCmg/en and http://www.historic.org.nz/Register/ListingDetail.asp?RID=4430

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Does it matter that medical graduates don't get jobs as doctors?

The *BMJ* has regular debates on topical matters and this is one of them. The starting point is the problem of too many graduates in the UK because of European Union migration and overexpansion of UK medical schools in the last decade.

A senior doctor says "as a nation we invest in medical training because we want the services of doctors, not to produce management consultants or playwrights." And…"it is surely just as important that we keep faith with our own medical students and graduates, whose recruitment and training has been on the explicit understanding that they are needed to work as doctors. The present situation does not just matter; it is a scandal."

The opposing view put forward by Alan Maynard, celebrated health economist, appears to be, hard luck—"medical graduates like all other graduates, gamble when they invest in their training. Their success brings riches, but if they fail due to lack of skills in making career choices and because of their inadequacy as doctors, they are no more eligible than other graduates for compensation in terms of job guarantees." I won't tell you which viewpoint I favour; you can probably guess.

BMJ 2008;336:990–1

Counterfeit drugs

We knew that this was a problem in Asia. But we are shocked to find the size of the problem. Apparently the Center for Medicine and the Public Interest in the US estimates the sales of counterfeit drugs will reach US$75 billion in 2010.

And the US Food and Drug Administration (FDA) has seen an 800% increase in the number of new counterfeit cases between 2000 and 2006. In developing countries, where drug regulatory systems can be weak or non-existent, around 10–30% of medicines might be counterfeit. Antimalarials have been a particular target for counterfeiters, and fakes have flooded the market in many Asian countries.

How to cope with this problem is the subject of this editorial. Relevant factors—poor reporting, poor regulation, no specific laws against counterfeiting. Perhaps the reputable pharmaceutical industry should become interested.

Lancet 2008;371:1551

Antibiotic therapy in the demented elderly population

Persons with advanced dementia are frequently exposed to antimicrobials, especially during the 2 weeks before death.

In this paper and in the accompanying editorial this problem is reviewed. The basic data in the study is that 42% of their subjects received antimicrobials during the 2 weeks before their death; over 40% of them by the parenteral route.

As the paper arises from Boston, USA it is unsurprising that quinolones and third generation cephalosporins were commonly used. The issues debated include therapeutic futility, cost, promotion of bacterial resistance and of course ethics.

The editorial concludes that the data in the paper "require us to consider whether we are overusing antibiotics in the severely demented elderly population, especially at the end of life, without paying adequate attention to the ramifications of their use."

Arch Intern Med 2008;164(4):357–62 & 349–50

Hypertension in patients 80 years of age or older

There is debate about the utility of treating hypertension in the elderly. In this study 3845 patients who were 80 years of age or older and had sustained systolic blood pressure of 160 mmHg or more were randomised to receive either the diuretic indapamide (sustained release, 1.5 mg) or matching placebo.

The angiotensin-converting-enzyme inhibitor perindopril (2 or 4 mg), or matching placebo, was added if necessary to achieve the target blood pressure of 150/80 mmHg. The primary end point was fatal or nonfatal stroke. At 2 years the mean blood pressure was 15/6 mmHg lower in the treatment cohort and there was a 30% reduction in strokes compared with the placebo cohort. Very good. However, the subjects in the study were healthier than normal for their age. This study and its authors received support from Servier.

Could it be a coincidence that Servier produces indapamide and perindopril? I suspect the good results could have been achieved by other antihypertensives as well.

N Engl J Med 2008;358:1887–98 & 1958–9

Spirometry in screening for chronic obstructive pulmonary disease (COPD)

Spirometry the gold standard? Perhaps not. The authors of the systematic review of the literature concluded that screening would predominantly capture people with mild to moderate airflow obstruction, who would not benefit from being diagnosed with COPD.

So what's the harm in that? Well, it's a waste of time and resources and probably results in unnecessary treatments—years of unnecessary steroid and β-agonist inhalers.

The review also found no evidence that spirometry improved cessation rates in people who smoke tobacco.

Ann Intern Med 2008;148:529–34 & 535–43

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Pharmaceutical industry spending

Dear Editor,

I refer to the editorial by Des Gorman and John Kolbe (*Just how safe is the New Zealand health system?*; http://www.nzma.org.nz/journal/121-1270/2946) published in the 14 March 2008 issue of *NZMJ*. I note that this article was re-published in the June issue of the *NZMJ Digest*.

Of considerable concern is the third to final paragraph which seems to be out of context with the thrust of the article and is not supported by the references that are cited. The offending paragraph states:

> "This has to be seen against a background of the pharmaceutical industry in the USA alone spending more money on direct to doctor propaganda than the combined budgets of all the medical schools"

It is hard to see the relevance of industry spend in the US on an editorial regarding the safety of the NZ health system and this seems to reflect an unfortunate yet irresistible urge by many in medical academia to unfairly criticise the pharmaceutical industry at every opportunity.

The claim referred to above is factually incorrect and inadequately referenced.

In neither of the two references cited can we find any information that could lead the authors to be able to substantiate the above claim. The first reference has cited the authors incorrectly (or the subject incorrectly) and in neither of the Breen et al correspondence nor the article entitled *On the need for probity when physicians interact with industry* by Scott could any reference be found that would support the claim that industry in the US spends more money on "direct to doctor propaganda" than the combined budgets of all the medical schools?

In the second reference (Hoffman et al) there is a comment made about direct to doctor expenditure in the US being "about as much" as is spent for all medical schools and residency training combined however the source referenced in this article from 16 years ago (*Chest* 1992:102;270–3) makes no such claim at all in the paper?

The pharmaceutical industry is the most heavily regulated industry. The discovery and development of medicines is both a high risk and extremely costly process, and drugs that are produced by industry make a real difference to the lives of many New Zealanders. Importantly, interactions with health care professionals are heavily regulated by industry codes of conduct that set out rigorous standards of conduct for the activities of companies when engaged in the marketing or selling of prescription medicines. While self regulation may be viewed with scepticism by some, the fines are very real as is the threat of litigation. There is a requirement to report any breaches of the local code to company senior management.

Ironically, if we had to apply the standards of the local industry RMI code to the claim above, the authors would be found to be in breach of section 4.3.1 where all claims "must be current, accurate, capable of substantiation and must not be

misleading either directly, by implication or by omission" and potentially they would need to pay a fine of up to $80,000.

Perhaps you could draw our concerns to the attention of the editorial writers and in the interests of accuracy and fairness publish our response.

Dr Pippa MacKay
Chairman
Researched Medicines Industry Association

Gorman and Kolbe's response

At the outset, we would like to thank Dr MacKay for bringing a citation error to our attention; we had intended to quote both the original paper by Dr Ian Scott,[1] and the consequent correspondence. Unfortunately, the two references became compressed.

However, in her spirited justification of the activities of the pharmaceutical industry, Dr MacKay has somewhat missed our point. Based on the report of the Government Health Quality Improvement Committee, and given the milieu in which local health providers currently work, we are surprised that the New Zealand health system is functioning so well!

The point of the sentence that caused Dr MacKay such offence, was to draw attention to the fact that there is a relative paucity of funding to institutions and organisations with the responsibilities of delivering unbiased and evidence-based medical education that is free of external influence, including that of the pharmaceutical industry.

There is ample evidence that doctors are substantially influenced by information provided by the health-disease industry—this has been well reviewed recently by Drs Scott (*Internal Medicine Journal*) and Moynihan (*BMJ*) and those who are interested are certainly encouraged to read them both.[1,2]

We strongly believe that the continuing professional development of New Zealand doctors should not be so heavily dependant on material supplied by pharmaceutical companies. Further, the continuing professional development curricula of New Zealand doctors need to include material from domains traditionally neglected by the narrow focus of pharmaceutical companies.

Such broad areas of medical education include communication, professionalism, ethics, advocacy—and particularly relevant to the focus of our article, Quality and Safety.

Professor Des Gorman
Head of the School of Medicine

Associate Professor John Kolbe
Head of the Department of Medicine,
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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

The frequency of medicines advertising on New Zealand television

Dear Editor,

I am writing in connection with a letter published in the June *NZMJ Digest* regarding the advertising of medicines on New Zealand television since 2001 (Wijesinghe PR, Norris P. *Increased advertising of medicines on New Zealand television since 2001*. http://www.nzma.org.nz/journal/121-1271/2992).

In this letter the authors conclude that **"medicines advertising is pervasive and television watchers are exposed to a considerable number of medicines advertisements"**.

From the evidence presented in the letter it is difficult to see how the authors could draw these conclusions and it is more likely that this represents an inherent bias against direct to consumer advertising of medicines as opposed to an objective conclusion consistent with the evidence from the study.

We understand the authors are looking at all medicine advertising, both general sale and prescription, and claim that the increase in advertising in this area is 58%. In absolute terms, however, this is really an increase of **0.42** advertisements per hour (from 0.72–1.14).

It is important to note that on each day on one free-to-air channel across 4 hours of prime time it is estimated that close to 100 advertisements may be run and therefore across six channels close to 600 advertisements may be run per day over the 4 hour prime time period. More detail on the study methodology is needed to understand just how relevant the 1.14 medicines advertisements per hour is. One thing is certain though, it is hard to see how the authors could draw the conclusion that the 1.14 medicines adverts per hour means that in NZ we are "exposed to a considerable number of medicines advertisements"

Whilst the authors raise the important issue of advertising general sale medicines, the real debate has centred on the advertising of prescription medicines. The authors conclude that advertisements for prescription only medicines has declined as a proportion of medicine advertising from 28% in 2001 to 17% in 2006. If we use the relative reduction (which the authors use) this represents a **39%** reduction. It is important to highlight the proportion of prescription-only advertising in the context of all advertisements on television during the study period.

As cited by the authors, prescription-only advertisements accounted for 17% of medicine advertising, however medicine advertising was a mere 5.3% of all advertisements on television during the study period. In absolute terms, prescription-only advertisements were a paltry **0.9%** of all television advertisements during the study period.

We would question whether this number or even the "5.3% of all advertising" could lead the authors to conclude that medicines advertising is pervasive.

From the evidence presented in the letter, a more objective and logical conclusion would be that overall, medicines advertising has increased marginally in 5 years but that as a percentage of overall television advertising it remains low. Importantly, the advertising of prescription medicines has decreased by almost 40% compared to the level that it was at in 2001.

Finally, we believe it is misleading to broaden the definition of medicines in the research to include herbal medicines, homeopathic medicines, and dietary supplements. The debate in New Zealand has been primarily focussed on the advertising of prescription only medicines and whilst the authors acknowledge that they have defined medicines more broadly than the legal definition the conclusions of the research still have the potential to mislead and bias the direct to consumer advertising of medicines debate. In the original research published in 2005 only 18% of advertisements for "medicines" were for prescription only medications.

In the interests of accuracy and fairness we would ask that you publish our response.

David West
Business Manager
Pfizer New Zealand

Response from Norris

David West from Pfizer New Zealand claims that our conclusions represent "an inherent bias against direct to consumer advertising of medicines".

While we question the idea that opposing DTCA represents an "inherent bias" rather than a reasoned position, our letter was not primarily about DTCA. In debates about DTCA, concerns are often raised about its potential to medicalise problems (that is, for problems previously seen as non medical to be defined and treated as medical problems), and to encourage the idea of "a pill for every ill". However in the 2005 paper (http://www.nzma.org.nz/journal/118-1215/1462) and this 2008 letter we wish to broaden out this debate: advertisements for non-prescription medicines, both orthodox and alternative, are also likely to contribute to this process.

We suggest that 1.14 medicines advertisements per hour is a considerable number, considering that in the 1998/9 Time Use survey New Zealanders watched almost 20 hours of television a week. We disagree that a 58% increase could be described as "marginal".

Although the advertising of prescription medicines has decreased as a proportion of medicines advertisements, it increased slightly in real terms. The definition of medicines in this study was the same as that used in our earlier study, and is consistent with the concern over medicalisation.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Psychotropic medicines in residential care facilities

Tucker and Hosford's[1] (http://www.nzma.org.nz/journal/121-1274/3063) article regarding the use of psychotropic medicines in residential care facilities raises a number of interesting points regarding the current prescription of these agents.

Unfortunately the term 'audit' is used loosely here and your readers could be forgiven for thinking that an audit is just a 'survey' from this article.

Clinical audit is a quality improvement process that aims to improve patient care and outcomes by carrying out a systematic review and implementing change[2] (http://www.rcpsych.ac.uk/pdf/clinauditChap1.pdf). An audit consists of an initial evaluation of a practice area against an agreed standard. Results are then fed back and a further survey is performed to see if changes in practice have resulted in the standards being met (audit cycle). This study therefore represents a service evaluation rather than a clinical audit. The only exception would be if the initial evaluation showed 100% concordance with best practice standards and therefore no change would be necessary.

Practitioners need to be aware that audit usually involves a change in practice rather than just reporting practice.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Screening of Cushing's syndrome in patients with Type 2 diabetes

Cushing's syndrome (CS) has been considered an unusual disorder with a reported incidence of 2–2.5 cases per million inhabitants per year.[1]

Although the syndrome is clinically unmistakable when full-blown, the spectrum of clinical presentation is broad and the diagnosis can be difficult in mild cases. Almost no features of CS are unique, instead most features caused by cortisol overproduction are also common in the metabolic syndrome such as central obesity, hypertension, dyslipidaemia, impaired glucose tolerance, and Type 2 diabetes (T2DM).

In CS, the prevalence of diabetes varies between 20% and 50% which is probably an underestimation as an oral glucose tolerance test is usually not performed in the presence of an apparently normal fasting glycose.[2] Epidemiological studies have shown that cardiovascular complications in patients with CS is elevated leading to a markedly increased mortality.[2] Moreover, CS is potentially curable by surgery, making it important to diagnose as early as possible.

Several studies have been published in the last 12 years addressing the issue of screening of CS in the setting of mainly T2DM.

Five different studies have found unknown CS in a diabetes population:

- In a cross-sectional study of 90 overweight patients (BMI >25 kg/m^2) with poorly controlled diabetes (HbA1c >9%), 3 female patients (3.3%) were diagnosed with CS who all improved their glycaemic control markedly after surgical removal of the pituitary (2) or adrenal (1) tumour.[3]
- In a study with 48 ambulatory overweight patients with T2DM, one female patient (2.1%) was proven to have CS with normalisation of glycaemic control after pituitary surgery.[4]
- In a prospective study on 200 overweight patients with T2DM with poor metabolic control (HbA1c >8%), 4 patients (2%) with proven CS were found (3 pituitary, all females, and 1 adrenal cause), all responding well on surgical/radiotherapy/ketoconazole treatment alone or in combination.[5] The average reduction was 5.5% in body weight and 2.5% in HbA1c in 6 months. Seven additional patients (3.5%, 4 females) were also found with mild CS and unilateral adrenal tumour of 10–29 mm in size showing uptake on iodocholesterol scintigraphy. However, these did not receive any further treatment, so the definitive diagnosis was not established. In total this study demonstrated a 5.5% frequency of CS among patients with poorly controlled T2DM.
- In a prospective case-control study of 294 hospitalised poorly controlled overweight patients with diabetes, 27 patients (9.2%) demonstrated biochemical evidence of CS together with a radiological cause (21 adrenal, 4 pituitary, and 2 pulmonary cause).[6] Three additional patients had biochemical

evidence of CS but no imaging findings. Seventeen were females. Follow-up after surgical treatment is only available for 3 patients (1.0%) and all markedly improved their metabolic control. One hundred and eighty-nine consecutive age- and BMI-matched non-diabetic inpatients admitted for severe obesity or multinodular goitre with normal thyroid function were selected as controls. Four of these (2.1%) revealed biochemical evidence of CS together with a radiological cause (3 adrenal and 1 pituitary cause). No results after surgery are available.

- In a prospective study, 99 consecutive patients newly (<30 days) diagnosed as having diabetes (seven were diagnosed with Type 1 diabetes) were evaluated biochemically.[7] One woman (1%) had a definitive diagnosis of CS and her metabolic situation improved after surgical removal of a pituitary adenoma.

Two studies have failed to demonstrate any undiagnosed CS in a diabetes population:

- In a prospective study, 154 male veterans (mean age 61.8 years) with T2DM were evaluated biochemically and no case of CS was revealed.[8]
- In the most recent study published 2008, 171 consecutive overweight patients with T2DM were screened and none were found to have CS.[9]

Thus, the majority of studies have suggested an increased frequency of CS in a setting of patients with T2DM.[3–7] The reason for the contradictory experience in the two last studies is unclear.[8,9] However, Cushing's disease (ACTH-producing pituitary tumour) is far more common in females than males which may in part explain the negative result in one study.[8] Moreover, the frequency is still quite low in the positive studies, sometimes with only one patient proven to have CS, so it could be a chance finding that no patient was screened as positive in the two negative studies. The patients characteristics were also very variable from poorly controlled hospitalised to well-controlled ambulatory.

In all studies except one, the screening method was overnight 1-mg dexamethasone suppression test with variable cut-off limits for serum/plasma cortisol (50–140 nmol/L); in the remaining late-night salivary cortisol was measured. The false positive rate was up to 63.8% requiring many additional investigations which may be unacceptable. No health economic analysis has been done.

In conclusion, the frequency of Cushing's syndrome seems increased in patients with Type 2 diabetes, especially females. However, it is not clear if screening is economically and practically defensible.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Deaths caused by diabetes mellitus

In reply to Ellis and Hamer's editorial published in the 15 February 2008 issue of the *NZMJ* and April *NZMJ Digest* (*Cardiovascular health in New Zealand: areas of concern and targets for improvement in 2008 and beyond*; http://www.nzma.org.nz/journal/121-1269/2927), it should be noted that diabetes is now known to be the primary initiating cause of death in New Zealand as a result of two good peer-reviewed case note audits both in Christchurch and in Dunedin. The audits showed it caused at least 17% of deaths. This percentage has now risen to 20% in a very careful analysis from Counties Manukau District Health Board's Health Group.

There are also now some 40 or more internationally published papers showing dysglycaemia or abnormal blood glucose values (i.e. over 5.5 mmol/L) at any time in a person's life to be the primary initiating cause of death and the best single indicator for earlier mortality.

In 2008 the death rate for diabetes is expected to be between 4000 and 5000, or 10 times all road deaths.

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Ciprofloxacin-induced seizures in a healthy patient

Fluoroquinolones-induced seizures have been noted on high-risk patients with underlying renal or neurological disease. To our knowledge, no cases have been reported of ciprofloxacin-induced seizures in healthy patients following the first dose. We present one such case in this letter.

A previously healthy 25-year-old African American female was brought to our emergency department by ambulance with recurrent seizures. On history taking, the husband stated that she had had two episodes of generalised jerky movements which lasted a couple seconds each, with no loss of consciousness. There was no bladder or bowel incontinence. No history of trauma or fall was reported.

Approximately 6 hours earlier, she had taken the first dose (500 mg) of oral ciprofloxacin which was prescribed for a urinary tract infection (UTI). Her past medical, surgical, and social histories were non-contributory including alcohol and polysubstance drugs abuse. Her routine medication was only a daily combination of ethinyl estradiol / norgestimate for contraception.

On physical examination, she was afebrile, fully oriented, with no focal weakness or neurological deficit. The rest of her examination was unremarkable. Laboratory studies were within normal limits, and a urine drug screen was negative. Head computed tomography (CT) and magnetic resonance imaging (MRI) didn't show any intracranial processes. Electroencephalography (EEG) was normal.

Ciprofloxacin was discontinued on admission and no antiepileptic drugs were given. Oral nitrofuratonin was initiated for a UTI. The patient remained seizure-free during hospitalisation. Her symptoms attributed to ciprofloxacin-induced seizures despite not having any of predisposing factors. Three months follow-up was uneventful with no recurrence of seizures.

The incidence of fluoroquinolones-induced central nervous system (CNS) adverse effects is almost rare; it accounts only 1% of the total adverse events.[1] A review of the literature revealed many cases of fluoroquinolones-induced seizures. However, renal dysfunction, history of epilepsy, and increased age account for the majority of these patients.[2]

It was believed that ciprofloxacin may lower seizure threshold by any route of administration.[3] However, the exact mechanism was not fully understandable, although it was attributed to the inhibition of γ-aminobutyric acid (GABA) to its receptors.[4]

Interestingly, coadministration of nonsteroidal anti-inflammatory drugs (NSAIDs) and theophylline has been found to enhance fluoroquinolones toxicity and to increase the risk of CNS adverse events, including seizures.[5]

This case highlights the fact that ciprofloxacin can produce seizures even after a single oral dose in an otherwise healthy person, and practicing physicians need to be aware of unusual reactions to otherwise commonly used medications.

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Having more knowledge of cervical cancer does not increase uptake of screening in Chinese women: findings from a New Zealand study

The New Zealand National Cervical Screening Programme (NCSP) reported a low coverage rate of about 45% among Asian women.[1] Little is known about the reasons for the low coverage. This pilot study examined the knowledge of risk factors of cervical cancer and its association with the uptake of cancer screening practices in Chinese women living in Auckland.

The survey was conducted between November 2006 and February 2007. Women were eligible if they (1) were born in Mainland China; (2) resided in Auckland New Zealand, and (3) were aged 20 to 69. A community-based survey was conducted with support from the Chinese New Settlers Services Trust (CNSST) who helped us to recruit participants via access to their database. Ethics approval was obtained from the AUT Ethics Committee. Details of the project design and recruitment have been reported elsewhere.[2]

Participants were asked to identify the risk factors of cervical cancer from 12 questions that were provided. A knowledge score was calculated by adding the total number of correct responses for each participant.

Of the 234 participants, 65% reported ever being screened in New Zealand and 56% reported they were recently screened in New Zealand. Less than two-thirds (62%) knew that the purpose of the cervical smear test was to detect abnormal cells that can develop into cervical cancer.

More than half of the respondents identified the risk factors of being older (75.2%), having a sexually transmitted disease (62.4%), having multiple sexual partners (59%), or having sexual activity with a man who has had multiple sexual partners (52.7%). However, only 42.3% identified the lack of 3-yearly smear tests. Approximately one-third of participants recognised the following as risk factors: human papillomavirus infection, smoking, or having intercourse at an early age. Only about one in five considered that giving birth to many children (20.9%) or using contraceptive pills (17.1%) put women at higher risk for cervical cancer.

The mean knowledge score of risk factors of cervical cancer was 4.9 (SD 2.8). Women with qualifications at tertiary level and above and those who could converse in English had more knowledge than those with secondary or lower levels of education or those who could not converse in English. One unit increase of knowledge score, the odds ratio (OR) of ever being screened was 1.05 (95%CI: 0.95–1.15). The adjusted OR remained non-significant after controlling for sociodemographic factors (adjusted OR 1.06; 95%CI: 0.96–1.16).

Our findings have significant implications for health promotion and prevention. While more than half the participants recognised some cervical cancer risk factors associated with sexual activities such as having a sexually transmitted disease, having multiple

sexual partners, and having sexual activity with a man who has had multiple sexual partners, it was of concern that the major risk factors (human papillomavirus infection and not having regular 3-yearly smear tests) were not widely known.

Studies in North America have shown that 72% to 84% Chinese immigrants recognised the importance of obtaining regular smear tests in reducing a women's risk of cervical cancer.[3–4]

This knowledge gap could be attributed to a number of factors such as the lack of a targeted programme for Chinese and other Asian groups in New Zealand and the previous lack of exposure to an organised population health programme in China for women from mainland China.

We also found that having more knowledge of cervical cancer did not lead to an increase in the uptake of cervical cancer screening. This contradicts the results of other studies in the US general population or Chinese women living in North America, where greater knowledge of cervical cancer has been associated with receiving adequate cervical smear testing compared to women with a lower knowledge of cervical cancer risk factors,[3–6] but is similar to a South African study.[7]

Yu and Rymer argue that women see the smear test as irrelevant in terms of their behaviour, therefore those who do not perceive themselves to be at risk will see no reason to go through with the test.[7] Our findings suggest that although women may be aware of some risk factors for cervical cancer, they may not fully comprehend the purpose or benefits of routine screening, thus highlighting the importance of educating Chinese women about the importance of routine smear tests.

A limitation of our study was that only women living in the Auckland regional area took part and our principal method of recruitment via CNSST networks could have caused a selection bias. There may also have been measurement error as a result of using a self-reported assessment of screening. In addition, as a pilot study, our sample size was small.

Despite these limitations, this study has identified a significant issue which is that the majority of Chinese women in this study did not recognise the importance of regular cervical screening to prevent cervical cancer.

Our findings suggest there is a need to educate Chinese women and their families in order to increase awareness and understanding of cervical cancer and the benefits of cervical screening as well as increasing the cultural competence of services and staff to enhance the uptake of cervical cancer screening among their clients.

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