Reversible diabetes insipidus in a patient with multiple myeloma

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ABSTRACT

We present a case of reversible diabetes insipidus in a 64-year-old man with multiple myeloma. Central diabetes insipidus developed in association with a myelomatous lesion of the clivus, but without evidence of macroscopic pituitary compression. Resolution of this patient's diabetes insipidus was observed following treatment of his myeloma.

A 64-year-old man presented with bone pain and weight loss. Blood tests revealed serum IgA 12.8 g/L (normal range 0.8–4.0), serum free lambda light chains 857 mg/L (6–26), beta-2 microglobulin 7.5 mg/L (0.0–3.2), corrected calcium 3.41 mmol/L (2.10–2.55), albumin 41 g/L (38–52) and creatinine 134 umol/L (60–105). X-rays demonstrated multiple long bone lytic lesions. A diagnosis of advanced IgA lambda multiple myeloma (MM) was made and the patient commenced chemotherapy with cyclophosphamide, dexamethasone and bortezomib.

On the day of his third weekly dose of the first cycle of chemotherapy, he required hospital admission with profound dehydration and hypotension. He reported that he had been passing six litres of urine per day and drinking copious fluids. In retrospect, he had noticed increased thirst and urine output for six months, but had not mentioned it previously. His regular medications at this time were aciclovir, trimethoprim/sulfamethoxazole, ezetimibe, allopurinol, aspirin, cilazapril and dexamethasone. Admitting blood tests showed a creatinine of 152 umol/L (60–105), corrected calcium of 2.22 mmol/L (2.10–2.55) and a sodium of 137 mmol/L (135–145). His anti-hypertensive agent (cilazapril) was discontinued and he was rehydrated with IV fluids.

An overnight water deprivation test was suggestive of diabetes insipidus (DI), with a urine osmolality of 288 mOsm/kg (normal >750) and a matched serum osmolality of 293 mOsm/kg (normal urine/serum osmolality >2.4).

He then underwent a formal 7-hour water deprivation test, as per the local protocol.[1] Despite being nil by mouth he continued to produce 75–200mL urine per hour. At the end of the test his urine osmolality was inappropriately low at 270 mOsm/kg with a serum anti-diuretic hormone (ADH) of only 0.8 pmol/L (normal >1.0). Following administration of 2mcg of IV desmopressin his urine osmolality increased to 359 mOsm/kg and urine volume reduced to 30mL/hour (Table 1).

A diagnosis of central DI was made[1] and nasal desmopressin prescribed. The patient reported resolution of his nocturia and return to a normal fluid intake. There was no evidence of anterior pituitary dysfunction and he had a morning serum cortisol of 430 nmol/litre (200–700). He had a normal plasma glucose and none of his medications were known to cause central DI.

An MRI pituitary was arranged (Figure 1). The pituitary gland was normal, apart from absence of the posterior pituitary bright spot. There were mottled changes of the skull base, in particular the clivus, confirmed as lytic lesions on a subsequent CT head scan (Figure 2). The bone lesions were consistent with myeloma. On the MRI scan there was also anomalous cerebral vasculature with a primitive trigeminal artery that caused distortion of the pituitary gland.

Table 1: Results of a formal 7-hour water deprivation test.

Hour	Urine Volume (mL)	Urine Osmolality (mOsm/kg)	Plasma Osmolality (mOsm/kg)
0	190	228	302
1	190	220	
2	200	224	
3	80	232	
4	160	250	
5	150	261	
6	110	270	294
Desmopressin given			
7	30	359	298

Figure 1: MRI pituitary demonstrating persistent primitive trigeminal artery (solid lines) and mottled changes of the clivus (broken line)

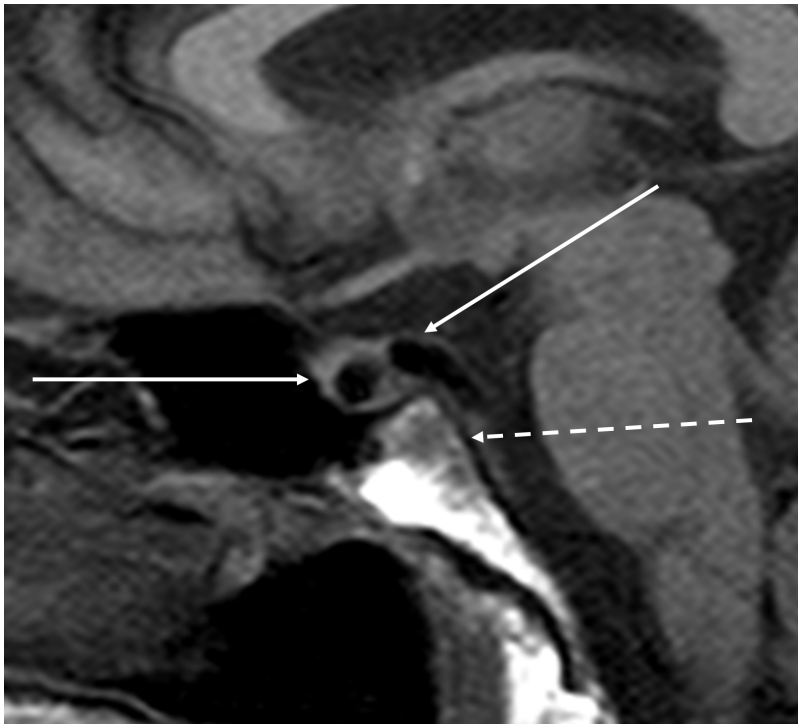
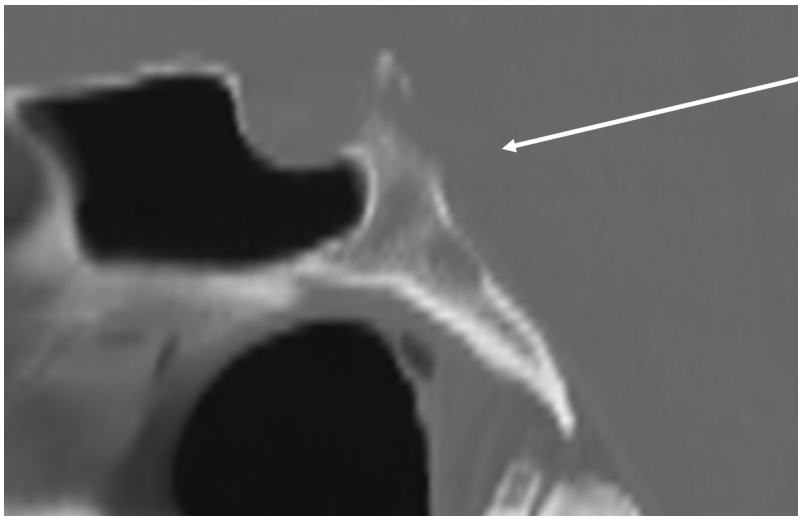


Figure 2: CT head demonstrating lytic lesions of the clivus (arrow)



Chemotherapy was continued with good effect associated with a rapid fall in serum free light chains after three cycles of four doses each. With this improvement the polydipsia and polyuria also decreased and the patient stopped his desmopressin nasal spray after 6 weeks without a recurrence of symptoms.

Discussion

This case demonstrates reversible central DI caused by MM with involvement of the skull base. The lytic lesions in the clivus presumably compromised posterior pituitary function. The mechanism is unclear; microscopic impingement seems most likely. With chemotherapy, our patient experienced a reduction in tumour burden and resolution of his DI symptoms. This patient also has a persistent primitive trigeminal artery that has been previously reported to cause compression of the pituitary gland and stalk.[2] His symptoms only developed around the time of his MM presentation so anomalous cerebral circulation alone is unlikely to be the cause of his DI, but may have contributed to its development. We did not test anti-vasopressin cell antibody but there was no personal or family history of auto-immune disease and his DI initially worsened with dexamethasone treatment. Cyclophosphamide has previously been linked to nephrogenic DI[3] but not central DI and is therefore unlikely to have been the cause of our patient's presentation.

Neurological sequelae of myeloma are well documented with diverse aetiology, including metabolic derangement, spinal cord compression, secondary amyloidosis and medication side effects.[4]

However, direct central nervous system (CNS) involvement is rare and is generally associated with widespread intracranial disease.[5] Pituitary dysfunction has been described in the context of sella plasmacytomas[6] but we could only find one case report in the English literature of a patient with MM complicated by central DI. This patient had a sella plasmacytoma and panhypopituitarism which did not improve with treatment of his myeloma.[7]

This case documents an unusual manifestation of multiple myeloma and contributes to our growing knowledge of the varied systemic effects of this disease.

Competing interests: Nil

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