From left to right: an unusual presentation of Tolosa-Hunt syndrome with bilateral eye involvement

Matthew Cowie, Roderick Duncan, Yassar Alamri

ABSTRACT

Here we discuss a presentation of Tolosa-Hunt syndrome (THS) in a 44-year-old female with new right-eye ptosis, ophthalmoplegia and headache. Four days prior, she had almost identical ptosis and ophthalmoplegia in her left eye, which resolved. Cavernous sinus inflammation and symptom improvement with glucocorticoid treatment indicated THS with bilateral eye involvement, a presentation which may be undervalued by the current THS classification.

Tolosa-Hunt syndrome (THS) is an uncommon clinical syndrome characterised by painful ophthalmoplegia caused by an idiopathic granulomatous inflammatory process of the cavernous sinus.[1–3] Diagnosis can be challenging and requires the exclusion of vascular, infective, malignant and other known inflammatory causes. Classically, optic or retro-orbital pain precedes ophthalmoplegia by up to 30 days.[4] Symptoms are mostly unilateral and commonly affect cranial nerves (CN) III (85–78% of cases), VI, IV and V, with a bilateral presentation in only 4–5% of cases.[4,5]

The diagnosis involves multiple investigations (including serial neuroimaging), and classification has changed over time. The current classification set by the International Classification of Headache Disorders Third Edition (ICHD-3) requires "unilateral orbital or periorbital headache" and "paresis of one or more of the ipsilateral CN III, IV and/or VI."[6] Visualisation of gadolinium contrast enhancement in the cavernous sinus (often extending into the superior orbital fissure) is suggestive of the diagnosis; obtaining histological confirmation of granulomatous inflammation is often abdicated due to the high-risk location of biopsy.

A hallmark feature of THS is the rapid resolution of headache with glucocorticoid treatment. It is still unclear whether the initial high-dose regime improves ophthalmoplegia, which can take several months to resolve.[7] Tapering of glucocorticoids with on-going follow-up is suggested and leads to a positive but often relapsing prognosis.[8]

Case presentation

This 44-year-old women was referred to our service with chronic daily headaches, four days of left-eye ptosis and right CN III and IV palsies. The current presentation was preceded by worsening of bilateral retro-orbital headaches for three months, which were initially attributed to an enlarging pituitary adenoma. The patient's case was discussed at our haematology/oncology multi-disciplinary meeting, and a primary CNS lymphoma was deemed highly unlikely. Given the new abnormalities of ocular movements, we suggested commencing parenteral glucocorticoid therapy and transferring the patient to our service (at a tertiary hospital). By the time of her arrival a day later (ie, after one dose of methylprednisolone 1,000mg), her left ocular symptoms had resolved, but she developed right-sided ptosis and CN III and IV ophthalmoplegia. Her previous medical history included diabetes, obstructive sleep apnoea, asthma/COPD overlap syndrome, obesity and current smoking.

Upon reviewing her history and neuroimaging, it was found that she had undergone a CT with angiography at the time of her headache onset (Figure 1A). This showed no abnormalities. A subsequent MRI was performed a week later and showed enlargement of the pituitary and cavernous sinus (Figure 1B). Blood tests, cerebro-spinal fluid analysis and chest x-ray did not identify any obvious inflammatory or malignant processes. Inflammatory markers including anti-neutrophil cytoplasmic autoantibodies (ANCA), angiotensin converting enzyme (ACE), IgG sub-class levels and pituitary hormones were all normal. A repeat MRI at our institution demonstrated progression of pituitary enlargement (Figure 1C).

After commencing steroid therapy, the patient's headache resolved within 24 hours, and both ptosis and ophthalmoplegia improved over the course of the treatment (Figure 2). A follow-up MRI demonstrated reduced enlargement, and prednisone was tapered over 12 weeks.

Discussion and conclusions

This was a highly unusual presentation of THS with dynamic and bilateral eye involvement. To the best of our knowledge, disappearing ophthalmoplegia and ptosis that re-presents in the contralateral eye has seldom been documented in the literature.[9] One simple explanation for this unusual presentation could be documentation error. But we think this is unlikely because the patient made it clear that her symptoms "switched eyes" and was told to specifically mention this was not documentation error. A more suitable explanation for this presentation would be the dynamic inflammatory nature of the underlying condition. What is known about the exact pathogenesis of THS is limited. However, it seems plausible that, given the location of the inflammation, a small change may cause rapid resolution or progression of symptoms. As mentioned, the diagnosis of THS can be challenging, and >75% of patients with painful ophthalmoplegia will not have THS.[10] It is important to consider other key differentials in the present case. A history of sub-optimal diabetic control could suggest diabetic CN palsy and vascular or malignant causes could also cause fluctuating CN palsies with headache. However, we find it unlikely that such dramatic and continued response to glucocorticoid treatment would be present with these aetiologies. a comprehensive range of inflammatory disorders were also investigated and normal, we make note that the sensitivity and specificity of these are varied.

This case may highlight limitations with the current classification of THS. Bilateral cranial nerve presentation is estimated to occur in 4–5% of cases,[4,5] yet the ICHD-3 criteria state "unilateral" headache with "ipsilateral" cranial nerve involvement, with no further mention of bilateral presentation.[6] Another abnormality in the present case was the length of time that headache existed before ophthalmoplegia. The ICHD-3 states headache should precede ophthalmoplegia by ≤2 weeks. Other literature suggests this may be up to several months.[4] In this case, it is possible that mild ophthalmoplegia went unnoticed for some time.

Figure 1: The initial CT scan revealed no abnormalities (A), but a subsequent MRI showed enlargement of the pituitary gland and cavernous sinus (B) which progressed on repeat MRI a few days later (C).

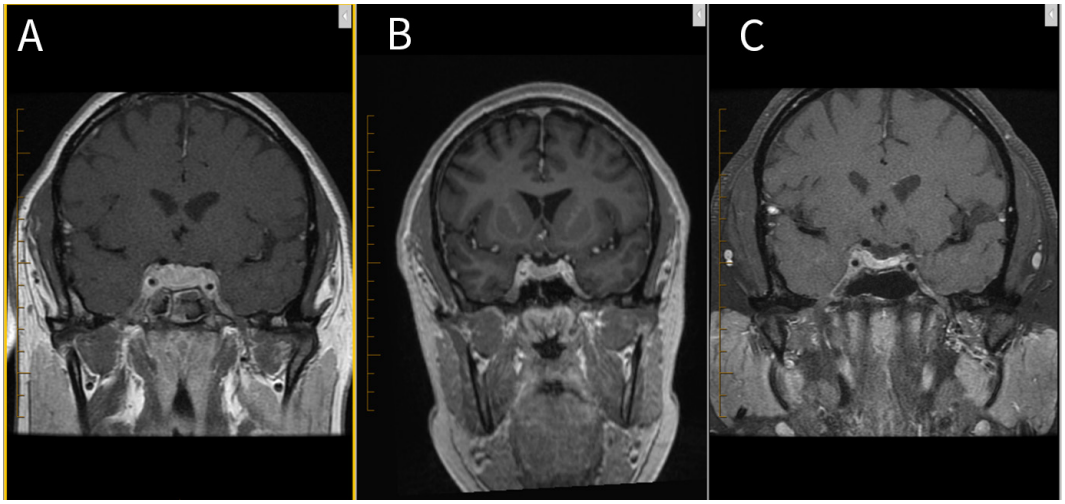
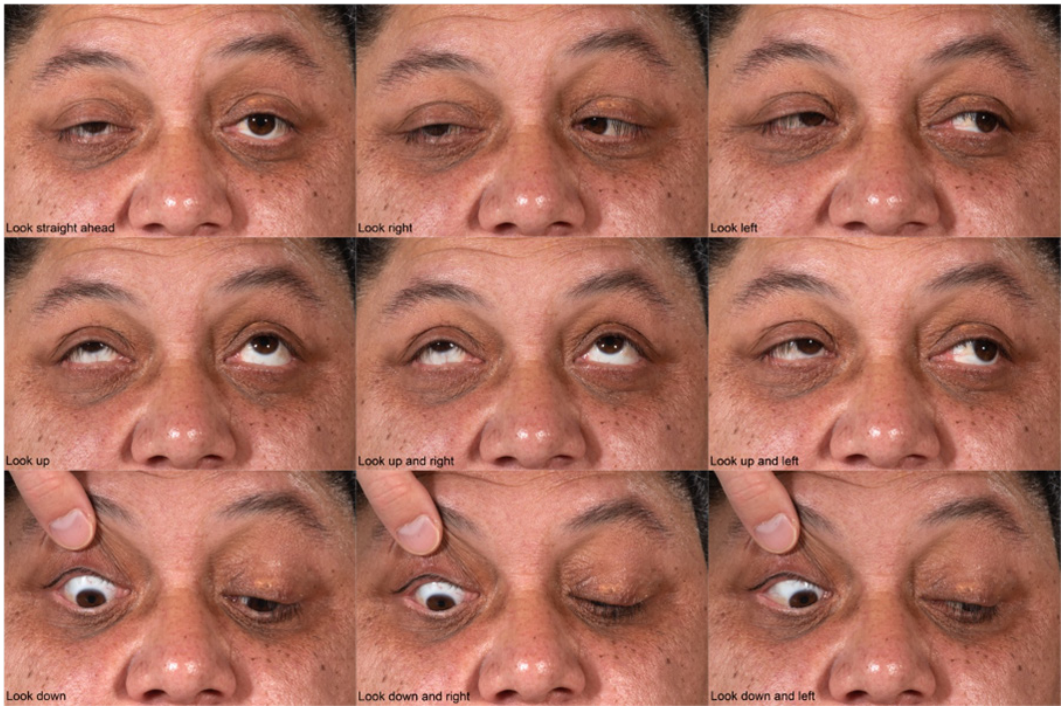


Figure 2: Gaze positions two days after commencing intravenous methylprednisolone. The images are consistent with moderate right-eye ptosis, best seen in neutral vertical gaze images (top left), and right abducens nerve palsy, best seen in right horizontal gaze images (bottom middle).



Competing interests:
Nil.

Author information:
Matthew Cowie: University of Otago, Christchurch, New Zealand.
Roderick Duncan: Department of Neurology,
Canterbury District Health Board, Christchurch, New Zealand.
Yassar Alamri: University of Otago, Christchurch, New Zealand;
Department of Neurology, Canterbury District Health Board, Christchurch, New Zealand.
Corresponding author:
Yassar Alamri, MBChB, PhD, Canterbury District Health Board, 2 Riccarton Avenue, Christchurch 8011, New Zealand; 006421750015 (phone); 006433786080 (fax)
yassar.alamri@nzbri.org

URL:
www.nzma.org.nz/journal-articles/from-left-to-right-an-unusual-presentation-of-tolosa-hunt-syndrome-with-bilateral-eye-involvement

REFERENCES

1. Smith JL, Taxdal DS. Painful ophthalmoplegia: the Tolosa-Hunt syndrome. American journal of ophthalmology. 1966;61(6):1466-72.
2. Tolosa E. Periarteritic lesions of the carotid siphon with the clinical features of a carotid infraclinoidal aneurysm. Journal of neurology, neurosurgery, and psychiatry. 1954;17(4):300.
3. Hunt WE, Meagher JN, LeFever HE, Zeman W. Painful ophthalmoplegia: its relation to indolent inflammation of the cavernous sinus. Neurology. 1961;11(1):56-.
4. Zhang X, Zhou Z, Steiner TJ, Zhang W, Liu R, Dong Z, et al. Validation of ICHD-3 beta diagnostic criteria for 13.7 Tolosa-Hunt syndrome: Analysis of 77 cases of painful ophthalmoplegia. Cephalalgia. 2014;34(8):624-32.
5. Tessitore E, Tessitore A. Tolosa□Hunt syndrome preceded by facial palsy. Headache: The Journal of Head and Face Pain. 2000;40(5):393-6.
6. Olesen J. Headache Classification Committee of the International Headache Society (IHS) the international classification of headache disorders, asbtracts. Cephalalgia. 2018;38(1):1-211.
7. Zhang X, Zhang W, Liu R, Dong Z, Yu S. Factors that influence Tolosa–Hunt syndrome and the short-term response to steroid pulse treatment. Journal of the neurological sciences. 2014;341(1-2):13-6.
8. Zurawski J, Akhondi H. Tolosa-Hunt syndrome—a rare cause of headache and ophthalmoplegia. The Lancet. 2013;382(9895):912.
9. Świątkowska-Stodulska R, Stodulski D, Babińska A, Piskunowicz M, Sworczak K. Bilateral Tolosa-Hunt syndrome mimicking pituitary adenoma. Endocrine. 2017;58(3):582-6.
10. Keane JR. Cavernous sinus syndrome: analysis of 151 cases. Archives of Neurology. 1996;53(10):967-71.