Tolosa-Hunt Syndrome

Synonyms: superior orbital fissure syndrome, cavernous sinus syndrome, cavernous sinus granulomatosis and Tolosa-Hunt ophthalmoplegia

The syndrome manifests as hemicranial or periorbital pain, ophthalmoplegia and sensory loss. Unilateral orbital or periorbital pain associated with paresis of one or more of the IIIrd, IVth and/or VIth cranial nerves, caused by a granulomatous inflammation in the cavernous sinus, superior orbital fissure or orbit. Some reported cases have additional involvement of the Vth nerve (commonly the first division) or optic, VIIth or VIIIth nerves. Sympathetic innervation of the pupil is occasionally affected.

Epidemiology

It is a rare condition and most of the literature is case reports rather than series. The estimated incidence of Tolosa Hunt syndrome (THS) is about one case per million per year. It is found worldwide without any geographical or racial preponderance. It is unusual to see THS in young people. The average age of onset is 41 years according to the National Organization for Rare Disorders.

Presentation

Hunt’s original description describes the following features as necessary to make the diagnosis:

- Persistent hemicranial or periorbital ‘gnawing’ pain, which may occur before or after other symptoms and signs.
- Cranial nerve involvement which may affect any or all of cranial nerves III, IV, V (V1/V2 division) and VI. Cranial nerves III and VI are the most commonly affected. The optic nerve and periarterial sympathetic nerves may also be involved.
- Diplopia is common, as would be expected. Diplopia and cranial nerve lesions are discussed elsewhere. It may precede the pain by several days.
- Involvement of the ophthalmic division of the trigeminal nerve can cause paraesthesia over the forehead. The corneal reflex may be lost on that side.
- The lesion is usually unilateral but bilateral cases have been described.
- Symptoms may last any length of time from days to weeks and may recur at intervals of months to years.
- If untreated, spontaneous remissions may occur, although may be associated with some residual neurological deficit.
- There is no evidence of other pathology.

Since this original description, other features have been added by subsequent case reports, and presentations of the syndrome have been known to include:

- Pain that is periorbital, retro-orbital, frontal or temporal. It is described as severe, ‘gnawing’ or ‘stabbing’ in nature.
- There may be a mild proptosis.
- Pupillary reactions may be normal, or there may be sympathetic involvement giving Horner’s syndrome or parasympathetic lesions associated with oculomotor nerve involvement.
- Optic disc may be normal, pale or swollen.
- Visual acuity can be normal or impaired. Loss of acuity may be (rarely) permanent.
- Other cranial nerves are sometimes involved, usually the maxillary and mandibular branch of the trigeminal nerve.
- Nausea and vomiting are reported.

Differential diagnosis

Several other conditions may present in a similar manner to THS and there is no single feature that is pathognomonic for this disease. Other considerations include:

- Trauma.
- Vascular lesions such as cavernous artery aneurysm or thrombosis or carotid cavernous fistula.
- Tumours, such as pituitary adenoma, meningioma, giant cell tumour, metastases.
- Infection - eg, sinusitis, herpes zoster, tuberculosis, fungal.
- Giant cell arteritis.
- Sarcoidosis.
- Granulomatosis with polyangiitis (Wegener’s granulomatosis).
- Eosinophilic granuloma.
- Diabetic ophthalmoplegia.
- Migraine.
Investigations

Investigations are largely aimed at excluding other causes of signs and symptoms. If THS is suspected, investigations may include:

- FBC.
- U&E, blood glucose, LFTs.
- CRP.
- *Syphilis* serology.
- Anti-nuclear antibody, anti-double stranded DNA and anti-smooth muscle antibodies.
- Serum protein electrophoresis.
- Lumbar puncture and examination of CSF.
- CT scan or MRI scan.
- Biopsy.

Careful follow-up is required for two years to exclude other causes of painful ophthalmoplegia, such as tumours, vasculitis, basal meningitis, sarcoid or diabetes mellitus.

Diagnosis

The clinical criteria for THS are not unique and their application alone does not assure a correct diagnosis. The requirements to make a diagnosis have changed significantly over a period of 10 years. Other criteria specifically highlighted by the International Classification of Headache Disorders (ICHD) are:

- A: unilateral orbital or periorbital headache fulfilling criterion C.
- B: both of the following:
  - Granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbit, demonstrated by MRI or biopsy. (It should be noted that MRI technology may not be able to identify the granulomatous inflammation reliably, and biopsy is not always appropriate.)
  - Paresis of one or more of the ipsilateral IIIrd, IVth, and/or VIth cranial nerves.
- C: evidence of causation demonstrated by both of the following:
  - Headache is ipsilateral to the granulomatous inflammation.
  - Headache has preceded paresis of the IIIrd, IVth and/or VIth cranial nerves by ≤2 weeks, or developed with it.
- D: not better accounted for by another ICHD-3 diagnosis.

In addition if left untreated, the painful episodes typically last eight weeks. Treated, the pain responds to steroids within 48 hours. Cranial nerve involvement coincides with the pain or occurs no more than two weeks after the onset of pain.

Management

- The treatment of THS is oral corticosteroids to which there is usually a dramatic response with alleviation of pain in 24-72 hours. High doses are used (in the order of 60 mg or more, daily) and then tapered off.
- Noticeable improvement is often evident within the first 24 hours of treatment but the ophthalmoplegia may take weeks or months to resolve.
- Failure to respond to steroids suggests an alternative diagnosis.
- Repeat imaging should be done every 1-2 months until there is resolution of the imaging abnormalities.

Prognosis

Up to half of patients experience recurrences even several months or years after the first episode; recurrences are usually ipsilateral. Long-term steroid treatment may be required.

Some patients may have residual cranial nerve damage (including the optic nerve, in which case sight is compromised). There may also be complications relating to long-term corticosteroid use.

Historical background

The disease is named after Eduardo Tolosa and William Hunt. They did not work together but independently described the condition. Eduardo Tolosa was a Spanish neurosurgeon who was born in 1900 and died in Barcelona in 1981. William Hunt was an American neurologist and neurosurgeon who was born in 1921 and died in Ohio in 1999. Tolosa first published in 1954 whilst Hunt et al published in 1961.
Further reading & references

- Tolosa-Hunt Syndrome; Whonamedit?

1. International Classification of Headache Disorder (version 3); International Headache Society. 2018
4. Amrutkar C, Burton EV; Tolosa-Hunt Syndrome
5. Tolosa-Hunt syndrome; National Organisation for Rare Disorders

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