Tolosa-Hunt Syndrome

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

Tolosa-Hunt syndrome (THS) describes a rare, granulomatous inflammatory process adjacent to the cavernous sinus or within the superior orbital fissure and/or orbital apex. The syndrome manifests as hemicranial or periorbital pain, ophthalmoplegia and sensory loss.

Several combinations of cranial nerve lesions have been described in the syndrome but all localise the site of the lesion to the cavernous sinus or superior orbital fissure. It is a syndrome which responds readily to treatment with steroids but which may recur months or years after the initial attack in up to 50% of cases. [1]

The aetiology is unknown, although it shares histopathological features with idiopathic orbital pseudotumour.

Epidemiology

It is a rare condition and most of the literature is case reports rather than series. Cases of THS have been documented worldwide and at all ages. Males and females appear to be equally affected. The age distribution is fairly uniform except for being rare before age 20 years. There are very few paediatric cases described in the literature. [2]

Presentation

Hunt's original description describes the following features as necessary to make the diagnosis. [3]

- 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 periorbital 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.

Classification

The International Classification of Headache Disorders classifies Tolosa-Hunt syndrome as: [4]

- Episodic orbital pain associated with paralysis of one or more of the third, fourth and/or sixth cranial nerves which usually resolves spontaneously but tends to relapse and remit. Diagnostic criteria:
  - One or more episodes of unilateral orbital pain persisting for weeks if untreated.
  - Paresis of one or more of the third, fourth and/or sixth cranial nerves and/or demonstration of granuloma by MRI or biopsy.
  - Paresis coincides with the onset of pain or follows it within 2 weeks.
  - Pain and paresis resolve within 72 hours when treated adequately with corticosteroids.
  - Other causes have been excluded by appropriate investigations.

- Other causes of painful ophthalmoplegia include tumours, vasculitis, basal meningitis, sarcoid, diabetes mellitus and ophthalmoplegic 'migraine'.
Some reported cases of Tolosa-Hunt syndrome had additional involvement of the trigeminal nerve (commonly the first division) or optic, facial or acoustic nerves. Sympathetic innervation of the pupil is occasionally affected. Careful follow-up is required to exclude other possible causes of painful ophthalmoplegia.

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:[5]

- 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.
- Wegener's granulomatosis.
- Eosinophilic granuloma.
- Diabetic ophthalmoplegia.
- Migraine.

Investigations

The diagnosis of THS is a diagnosis of exclusion.[5] Investigations are largely aimed at excluding other causes of signs and symptoms. If THS is suspected, investigations may include:[6]

- FBC.
- U&E, blood glucose, LFTs.
- CRP.
- Syphilis serology.
- Antinuclear antibody, anti-double stranded DNA and anti-smooth muscle antibodies.
- Serum protein electrophoresis.
- Lumbar puncture and examination of CSF.
- MRI scans or CT scan: MRI studies of the cavernous sinus and orbital apex show high sensitivity for the detection and follow-up of inflammatory mass lesions in THS.[7]
- Biopsy.

Diagnosis

In 2004, the International Headache Society (IHS) redefined the diagnostic criteria of THS, specifying that granuloma, demonstrated by MRI scan or biopsy, is required for diagnosis.

A review of the literature on THS from 1988 (when the first IHS criteria were published) to 2002, analysed individual cases in relation to the new IHS criteria.[8] They identified 124 cases. It appeared that clinical presentation was similar in all, but 44 (35%) were reported to have inflammation on MRI or biopsy evidence of granuloma, 41/124 (33%) had normal neuroimaging findings and 39 (31%) had a specific lesion, so the THS was secondary.

This confirms that clinical criteria for THS are not unique and their application alone does not assure a correct diagnosis. The requirement for inflammation on MRI will result in better classification of painful ophthalmoplegias. Other features specifically highlighted by the Society are:

- 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.
- Other conditions should be excluded by neuroimaging (± angiography).

The status of cases which fulfil the clinical criteria but have normal MRI remains to be clarified.

Management

- The treatment of THS is oral corticosteroids to which there is usually a dramatic response with alleviation of pain in 24 to 72 hours. High doses are used (in the order of 60 mg or more, daily) and then tapered off.[9]
- Noticeable improvement is often evident within the first 24 hours of treatment but the ophthalmoplegia may take weeks or months to resolve.[9]
- Failure to respond to steroids suggests an alternative diagnosis.[9]
- Repeat imaging should be done every 1-2 months until there is resolution of the imaging abnormalities.[9, 10]

Prognosis

THS usually responds rapidly to treatment with oral steroids. Relapses can occur and long-term steroid treatment may be required.[9]
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.

As THS is a diagnosis of exclusion, it is recommended that patients with a diagnosis of THS must be re-investigated at intervals for at least two years, even if the initial MRI scans were negative, to prevent the possibility of more sinister pathology being missed.

History

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

- The International Classification of Headache Disorders; International Headache Society
- Tolosa-Hunt Syndrome; Whonamedit?

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