Review Article

The Tolosa-Hunt syndrome

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Summary

The Tolosa-Hunt syndrome, or painful ophthalmoplegia, is a rare condition caused by a granulomatous nonspecific process at the level of anterior cavernous sinus, superior orbital fissure and orbital apex. The syndrome is characterized by pain behind, above or around the eye, involvement of the cranial nerves which pass through the cavernous sinus, spontaneous remissions and exacerbations, and a favourable response to steroid therapy. Recognition of this condition is important because administration of steroids may prevent residual damage.

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In 1954 Tolosa[1] published a report on a 47-year-old man with unilateral painful ophthalmoplegia who died 3 days after surgical exploration. Histological examination revealed a granulomatous peri-arteritic process of the internal carotid artery in the cavernous sinus region. In 1961 Hunt *et al.*[2] reported 6 cases of painful ophthalmoplegia that responded well to steroid therapy, while 5 years later Smith and Taxdal[3] described 5 similar cases and applied the eponym Tolosa-Hunt syndrome (THS) for the first time. These authors stressed the dramatic response, often occurring within hours, to systemic corticosteroid therapy.

Clinical features

The main clinical features of the syndrome are: (*i*) steady pain in the eye; (*ii*) involvement of the cranial nerves passing through the cavernous sinus: the 3rd, 4th, 6th, and first division of the 5th cranial nerve, with possible involvement of the peri-arterial sympathetic fibres and the optic nerve; (*iii*) spontaneous remissions and exacerbations; and (*iv*) extreme sensitivity to steroid therapy.

The steady pain in the eye is usually described as 'boring', and it may be behind, above or around the eye. It may occur either before or simultaneous with paralysis of the cranial nerves and usually subsides spontaneously within 2-3 weeks in untreated cases. A major feature is that the pain is usually the first symptom favourably influenced by steroid treatment.

Involvement of the cranial nerves passing through the cavernous sinus usually also includes the pericarotid oculosympathetic fibres; paresis or paralysis of both sympathetic and parasympathetic pupillomotor fibres may often be combined. The parasympathetic fibres are damaged as they are associated with the 3rd nerve, and the sympathetic fibres are interrupted at the level of the pericarotid plexus of the oculosympathetic pathway. The 3rd nerve is by far the most frequently affected cranial nerve. Partial or complete ptosis should therefore be considered a characteristic and constant clinical sign of THS.

The 6th and 4th cranial nerves are slightly less frequently affected, and a lesion of the 5th nerve is even less common. The optic nerve is rarely involved in THS, and one rarely finds primary optic atrophy after a recurrence of symptoms.

Remissions and exacerbations may be spontaneous or therapeutically induced. Residual neurological deficit is common and some patients are left with dilated, unresponsive pupils or other signs of cranial nerve involvement, such as diplopia or ptosis. Recurrences usually involve the same side.

Sensitivity to steroid therapy is one of the hallmarks of the condition. High-dose steroid therapy administered promptly causes significant improvement of the neurological deficit and may prevent residual damage. Steroid therapy should cause marked improvement in the patient's condition within 24-48 hours. Failure of response in this period requires further investigations to rule out other aetiological possibilities such as malignant lymphoma or parasellar tumours. Long-term steroid therapy does not appear to be beneficial.

Systemic manifestations are rare in THS, although some authors reported mild fever and malaise in some patients.[4] Peri-orbital oedema, bulbar conjunctivitis and proptosis are seldom found, and usually suggest other conditions.

THS is a relatively rare condition and only about 50 cases have so far been reported in the literature. Both sexes are equally affected and there is no geographical preference. Onset of the illness may occur at any age, but the 5th decade appears to be the most common period of onset. There have been reports of children affected before the age of 10.[5]

Pathological findings

THS is caused by a granulomatous process at the level of the anterior cavernous sinus, superior orbital fissure and orbital apex. Tolosa[1] found granulomatous tissue in the cavernous sinus around the carotid artery that infiltrated only the adventitia of the carotid artery and a granulomatous lesion around the 6th nerve. Lakke[6] found some necrosis and lined granulomatous tissue of the dura in the region of the superior orbital fissure.

The available pathological data indicate that THS is caused by an indolent nonspecific inflammation or granuloma at the level of the cavernous sinus or the adjacent superior orbital fissure.

Diagnosis

Diagnostic procedures in patients suspected of having THS should include arteriography and possibly orbital venography. Every patient who presents with an atypical clinical picture or course should undergo both investigations before receiving steroid treatment. Other diagnostic procedures such as a full laboratory work-up, radiography of the orbit, skull and sella and computed tomography (CT) are usually very helpful. Routine

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skull radiographs may reveal other causes for the ophthalmoplegia, such as meningioma of the sphenoid wing. A raised ESR is rare and is more typical of temporal arteritis. CT may demonstrate parasellar tumours and suprasellar extension of pituitary gland tumours. Arteriography is recommended to exclude internal carotid aneurysm and parasellar tumours. Segmental narrowing and slight irregularities of the intracavernous portion of the carotid artery have been reported in a few cases.[7] Orbital venography has been performed by Sondheimer and Knapp,[8] who demonstrated complete ipsilateral occlusion of the superior ophthalmic vein and partial obliteration of the cavernous sinus. However, these venographic findings are nonspecific and may be found in parasellar meningiomas and pituitary tumours. Lakke[6] reported the occurrence of pleocytosis in THS, and other authors[5] have suggested that it may reflect an aseptic inflammatory response in the cavernous sinus. However, the cerebrospinal fluid appears to be normal in the majority of cases of THS. Surgical exploration is not necessary if there is a good response to steroid therapy.

Differential diagnosis

Temporal arteritis may have features similar to those of THS. In the former the age of onset is usually later than in THS, and there is a clear predominance of females over males, which is not the case in THS. The ESR is rarely elevated in THS. Paralysis of the 3rd cranial nerve is the most common ocular finding in THS, whereas in temporal arteritis blindness is characteristic. Diabetic ophthalmoplegia, intracavernous carotid aneurysms, nasopharyngeal tumours, tumours of the orbit and ophthalmoplegic migraine are the most common entities to be considered in the differential diagnosis. Orbital myositis may easily be mistaken for THS, but the presence of chemosis of the bulbar conjunctiva and exophthalmos favours the former diagnosis.

Treatment

High doses of steroids evoke a good response in 24-48 hours. Long-term steroid therapy does not appear to be beneficial, but steroid therapy may be repeated if there are recurrences.

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