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CASE REPORTS

Tolosa-Hunt Syndrome: A Case Report and Review of the Literature

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Abstract:

Tolosa-Hunt Syndrome is a painful ophthalmoplegia which is characterized by periorbital or hemicranial pain, with ipsilateral ocular motor nerve palsies, oculosympathetic paralysis, sensory loss in the distribution of the ophthalmic and occasionally the maxillary division of the trigeminal nerve. Various combinations of these cranial nerve palsies may occur, localising the pathological process to the region of the cavernous sinus/superior orbital fissure. We report the case of a patient presented with severe pain in the right side of face which was periorbital with ipsilateral 3rd,4th, 6th cranial nerve palsies along with ophthalmic and maxillary division of trigeminal nerve involvement. MRI of orbit showed hypo-intense lesion in right cavernous sinus extending to right superior orbital fissure (suggestive of granulomatous infiltration). After taking oral steroid her pain was relieved quickly and cranial nerve palsies reversed within one week. Azathioprin was added and she was completely cured of within next three months.

Introduction:

Tolosa-Hunt Syndrome is caused by a non specific inflammatory process with occasional granulomatous features in the region of superior orbital fissure often extending into the cavernous sinus. It was first described by Tolosa in 1954[1] and by Hunt in 1961. It is a rare disorder characterized by painful ophthalmoplegia[2] with palsies of third, fourth ,sixth cranial nerves as well as first and second division of trigeminal nerve. In 2004, the International Headache Society included granuloma as one of its diagnostic criteria and now is a part of classification ICHD – II. ICD-10 for Tolosa Hunt Syndrome is G44.850[3]. With no sex predilection Tolosa-Hunt syndrome can affect people of any age from 1st to 8th decades of life. The characteristic findings are pain which may precede the ophthalmoplegia by several days, or may not appear until sometime later. Pain is steady, felt behind the eye often described as “gnawing” or “boring”. The neurological involvement is not confined to the third cranial nerve, but may include the fourth, sixth, and first division of the fifth cranial nerves. Periarterial sympathetic fibers and the optic nerve may also be involved. Symptoms last for days to weeks. Spontaneous remissions may occur and sometimes with residual neurological deficit. Attacks recur at intervals of months or years. Exhaustive studies, including angiography and surgical exploration have produced no evidence of involvement of structures outside of the cavernous sinus. There is no systemic reaction[4].

The etiology of Tolosa-Hunt syndrome remains unknown. A possible risk factor for Tolosa-Hunt syndrome is a recent viral infection. It seems that the syndrome falls within the range of idiopathic, sterile inflammation of the cavernous sinus. Its pathology is described as fibroblastic, lymphocytic, and plasmacytic infiltration of the cavernous sinus. Pathology may extend to involve the superior orbital fissure (sphenocavernous or parasellar syndrome)[5] or orbital apex and affect the nerve. Hunt et al [2]

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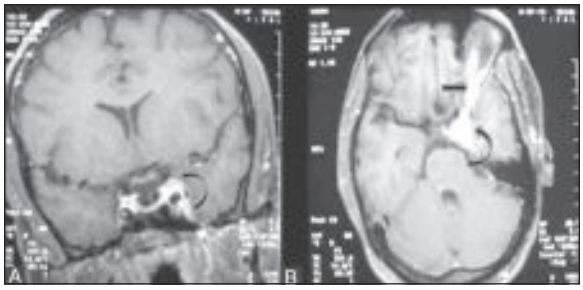
corroborated these findings,emphasizing the lack of necrosis and pointed out that "such inflammatory changes, in a tight connective tissue, may exert pressure upon the penetrating nerves". Subsequent reports have shown granulomatous inflammation, with epithelioid cells and occasional giant cells[6,7]. Necrosis may also be seen and no infectious organism was found.

MRI of brain may show evidence of inflammatory changes in the region of the anterior cavernous sinus, superior orbital fissure and/ or orbital apex[8] and signal changes shows:

- T1 : involved region is iso intense [9] to hyper intense[8] compared with muscle
- T2 : involved region is hyper intense
- C+ (Gd) : may show contrast enhancement during active phase with resolution of enhancement following treatment [10,11]

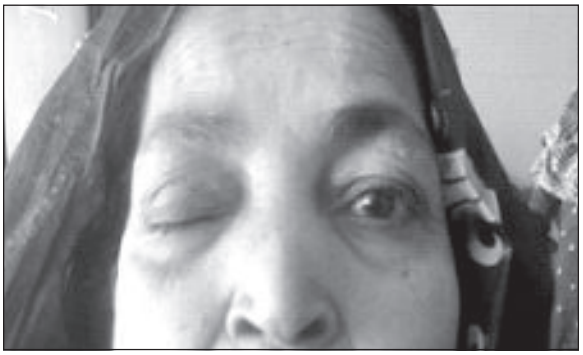


In fact, during the initial patient evaluation there are often no clues in the history or physical examination to distinguish Tolosa-Hunt syndrome from other causes of painful ophthalmoplegia. Therefore, the clinician should be aware of causes of parasellar syndrome and other entities producing painful ophthalmoplegia. To establish the diagnosis biopsy is required through neurosurgical approach which is rarely done[12-16.]

Tolosa-Hunt syndrome is not a fatal disorder, and can be treated with steroid.[2] This usually provides pain relief within 24-72 hours of starting the medication. The visual problems and numbness in frontal region may take weeks or months to resolve, and sometimes the symptoms never go away completely. It is clear that spontaneous remissions may occur, but there is no doubt that corticosteroids markedly reduce the periorbital pain. Although steroids are generally tapered over weeks to months, in some cases prolonged therapy may be necessary. Because of this fundamental limitation of initial imaging studies, some authorities would suggest that resolution of imaging abnormalities after a course of systemic corticosteroids should be considered "diagnostic" of Tolosa-Hunt syndrome[17,18] .As many as 30-40% of individuals may have a relapse of Tolosa-Hunt syndrome, usually on the same side.

Case report:

Our patient was a 70 yrs old lady who presented with a 3 weeks history of severe periocular headache which was sudden in onset, global, continuous, associated with vomiting for 2 times, this relieved the headache to some extent. The following morning when she woke up from sleep, found that she cannot open her right eye voluntarily but can do manually. Her left eye was normal as well as vision. Headache and right periorbital pain was present. She never had this kind of problem before.



On clinical examination, her vital signs were normal. She had complete ptosis on right sided, total paralysis of right extraocular muscles indicating right third, fourth, sixth nerve palsy. Pupil was dilated, non-reacting to light on right side. sensory loss of right sided ophthalmic and maxillary distribution over face. Fundoscopic examination was normal. Left eye findings were normal and no other neurological deficit was found. Routine blood tests and cerebral fluid study were within normal limit. Erythrocyte sedimentation rate (ESR) was significantly increased but ANA, p-ANCA, c-ANCA was within normal limit. An MRI was done before admission which was inconclusive. Magnetic resonance angiography

(MRA) and magnetic resonance venography (MRV) was done where MRA was normal and MRV showed non-visualization of left transverse sinus which could not be correlated with clinical findings. No evidence of cavernous sinus or superior ophthalmic vein (SOV) thrombosis was seen. Repeat MRI of orbit and cavernous sinus with contrast was done in multiple axial, coronal and sagittal sections which showed iso to hypo-intense lesion in right cavernous sinus extending upto right superior orbital fissure and left cavernous sinus also. The lesion was brilliantly contrast enhancing and causing significant compression of the neurovascular structure of right cavernous sinus. Both optic nerves were spared.ICA was also normal in diameter.

Patient was treated with oral steroid 1mg/kg body weight which started 3 weeks after onset of her illness. She got relief from headache and periorbital pain within 3 days but improvement of third, fourth, sixth or second division of trigeminal nerve palsy except ophthalmic division was noted after one week. Then oral Azathioprin was added. Patient was discharged from hospital and followed up in every fortnightly for next three months. She was completely cured of her ailments after three months.

Discussion:

Tolosa[1] first described the condition in 1954, in a patient with unilateral recurrent painful ophthalmoplegia involving cranial nerves III, IV, VI and V1. The patient was imaged using carotid angiography and segmental narrowing of the carotid siphon was seen. Hunt *et al*. described 6 patients with similar clinical findings in 1961, and proposed a low-grade non-specific inflammation of the cavernous sinus and its walls as the cause of the syndrome[2]. Pathologically, infiltration of lymphocytes and plasma cells as well as thickening of the dura mater was seen. In 1966 Smith and Taxdal termed this condition as Tolosa-Hunt syndrome[18]. The latter author stressed the importance of the dramatic rapid response to steroid therapy. Neuro-imaging, particularly MRI, is an essential part of the workup of any patient presenting with features of THS, as these features are non-specific and have a wide differential diagnosis, including meningioma, sarcoidosis, pituitary tumours, tuberculous meningitis (TBM) and lymphoma[19]. MRI findings classically demonstrate a soft-tissue mass lesion involving the superior orbital fissure or cavernous sinus. Signal characteristics are typically hypo intense to fat and isointense to muscle on short TR/TE sequences and isointense to fat on long TR/TE sequences[20]. Significant enhancement of the mass lesion is demonstrated on CE sequences. Of particular value is the post-contrast fat-saturated thin-slice coronal image through the orbital apex and cavernous sinus. THS essentially remains a diagnosis of exclusion. The role of the radiologist is to exclude other conditions causing similar clinical features. Some authors reported that using carotid angiography there was segmental narrowing of the carotid siphon was seen[21]. Distinctive MRI findings and rapid resolution of clinical symptoms with steroid therapy are characteristic. So,Tolosa Hunt syndrome is diagnosed by exclusion and which should be done by clinical and MRI finding and treatment response to steroid therapy which was very much characteristic to this case.

Conclusion:

Tolosa-Hunt syndrome is a rare disorder and the pathogenetic basis remains unknown, and on clinical stand point it can be regarded as a distinct entity which may be simulated by various other disorders. Tolosa-Hunt syndrome is not a fatal disorder, and can be treated with steroid medication such as prednisone. Though treatment response is good, relapse may occur. Hence careful evaluation, appropriate treatment, and scrupulous follow up are required. Because many disorders can have similar symptoms, individuals should report any new symptoms or side effects from treatment to their physicians.

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