Tolosa-Hunt Syndrome and Ocular Myasthenia: A Rare Coexistence or Real Association

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Abstract
Tolosa-Hunt syndrome is a rare steroid responsive disorder caused by granulation tissue involving the cavernous sinus or superior orbital fissure presenting as painful ophthalmoplegia and facial pain. In this report, we describe coexistence of Tolosa-Hunt syndrome with ocular myasthenia which may point towards an autoimmune etiological basis behind the cavernous sinus granulation tissue formation and also offered therapeutic challenge to ameliorate the symptoms.

Case Report
A 65 year old hypertensive, non-diabetic female was admitted with complaining of burning sensation over left side of the face along with left retro-orbital sharp stabbing pain and diminished sensation over left side of the face for last 20 days. The pain was initially intermittent in nature but gradually it became continuous. Ten days after onset of facial pain, the patient also developed diplopia. There was no history of headache, altered sensorium, convulsion or weakness of any limb. Complaints like difficulty in chewing, swallowing, nasal intonation of voice or nasal regurgitation of food, vertigo, deafness, tinnitus, slurring of speech or hoarseness of voice were absent. The patient complained of drooping of eyelids for last 1 year, noticed more in evening hours or after prolonged reading. There was no history of fever, significant loss of weight, cough, joint pain, rashes, photosensitivity, redness or dryness of eye, dryness of mouth, oral or genital ulcer or past history of tuberculosis. Dietary history and family history were non-contributory.

General survey was unremarkable. CNS examination revealed preserved higher mental function including speech. She had left sided LMN type of facial palsy (Figure 2). The patient had bilateral incomplete ptosis, more on the left side. There was restricted movement of multiple extra-ocular muscles including left sided lateral rectus, medial rectus, superior rectus and superior oblique with sparing of pupil bilaterally (Figure 1). All modalities of sensation were diminished over left side of the face in the distribution of first division of trigeminal nerve sparing the muscles of mastication. Other cranial nerves were intact. Motor, sensory and autonomic system revealed no abnormality. Gait was normal, cerebellar and meningeal signs were absent.

Investigations revealed a normal hemogram, liver and renal functions and blood sugars. Chest x-ray and USG of abdomen were normal.

MRI Brain was done and it revealed a granulation tissue in left cavernous sinus (Figure 3). Right side was normal. Serum ACE level was 23 U/L (normal-8-65U/L). ANA (Hep 2) was negative. Extractable nuclear antigen (ENA) profile showed borderline positive SSA with negative Anti dsDNA, p-ANCA and c-ANCA were negative. CSF study was done which showed 8 cells/cumm, sugar-63 mg/dl, protein-56 mg/dl, LDH-21 u/l and ADA-3.5 (normal<5).

Ach receptor antibody was 0.6 [>0.4-positive]. Repetitive nerve stimulation test suggested ocular myasthenia. CECT thorax was done and there was no evidence of thymoma.

A combined diagnosis of Tolosa Hunt syndrome and Myasthenia gravis was done. The patient was treated with oral pyridostigmine 60 mg thrice daily with incremental dosage of...
prednisolone, finally up to 50 mg daily. The patient responded gradually over the next few days. Facial pain diminished to a great extent and bilateral ptosis improved dramatically during her discharge from the hospital.

Discussion

In our case report we are describing a case with background history of bilateral ptosis aggravated in evening and prolonged reading which was non-disabling in nature, over which left sided painful external ophthalmoplegia, numbness of face and facial palsy developed and drew medical attention. MRI evidence of granuloma in the cavernous sinus with exclusion of all possible causes of granuloma namely tuberculosis, sarcoidosis and Wegener’s granulomatosis as well as dramatic response to steroid pointed towards the diagnosis of Tolosa Hunt syndrome. After being first described by Tolosa in 1954, in the year 1961 this syndrome was re-defined by Hunt. Hunt et al described six cases of painful ophthalmoplegia that responded well to steroid and also outlined six clinical criteria characterizing the syndrome—

- One or more episodes of unilateral orbital pain persisted for weeks if untreated
- Paresis of one or more of the third, fourth, and/or sixth cranial nerves and/or demonstration of granulomas 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

Note: Other causes of painful ophthalmoplegia include tumours, vasculitis, basal meningitis, sarcoid, diabetes mellitus and ophthalmoplegic migraine.

THS criteria was later provided by International Headache Society in 1988 and was revised in 2004 as shown in Table 1.

Our patient fulfilled all the criteria and diagnosis of THS was established. Dramatic response to steroid not only indicated the diagnosis of THS, but also indirectly excluded fungal or neoplastic origin of cavernous sinus mass. Diagnostic criteria clearly mentioned reported cases of THS with additional involvement of facial nerve. In previous reports involvement of facial nerve in THS has been described as a part of extended area of inflammation outside cavernous sinus.

On the background of myasthenia gravis, cranial nerve palsies created a confusing picture, but presence of facial numbness in the distribution of first division of trigeminal nerve pointed spontaneous remissions (5) recurrent attacks (6) prompt response to steroid therapy.

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On the background of myasthenia gravis, cranial nerve palsies created a confusing picture, but presence of facial numbness in the distribution of first division of trigeminal nerve pointed towards cranial nerve involvement in cavernous sinus as etiological factor of ophthalmoplegia rather than due to neuromuscular junction involvement.

To the best of our knowledge the co-existence of these two diseases has not yet been reported. As ANA, Anti ds-DNA, ANCA were negative, the possibility of SLE and Wegener’s granulomatosis as the causes of painful ophthalmoplegia were ruled out. Borderline positive SSA probably does not have any clinical relevance. However, the presence of ocular myasthenia in the same patient along with THS may indicate an obscure autoimmune background of THS yet to be described.

Another important issue is the management protocol chosen for this dual pathology. Usual mode of therapy for THS with high dose steroid could not be adopted in this patient due to co-existent myasthenia gravis to avoid possible myasthenic crisis. However initiation of therapy with low dose oral prednisolone with gradual up-titration along with concomitant use of pyridostigmine was able to produce the desired response.

### Table 1: Revised THS diagnostic criteria (2004)

Description: Episodic orbital pain associated with 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 persisted for weeks if untreated
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Comments: 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 pupils occasionally affected.
Conclusion

THS and ocular myasthenia are two uncommon disorders and their co-existence is a rare association. As external ophthalmoplegia is a common presentation of both the diseases, there may be a diagnostic dilemma and one of the disorders may be overlooked. An unknown autoimmune mechanism yet to be defined may be the aetiological factor. Compromised therapy for THS with incremental dose of steroid is needed to avoid subsequent myasthenic crisis.

References

5. Lance JW, Olesen J. The International Classification of Headache Disorders ICHD II. Cephalalgia 2004; 24:3