IDIOPATHIC TOLOSA–HUNT SYNDROME: FOUR ADDITIONAL CASES

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Idiopathic Tolosa–Hunt syndrome (ITHS) is a very rare cause of painful ophthalmoplegia characterized by unilateral orbital pain, ipsilateral oculomotor paralysis and prompt response to steroids. In this paper we report 4 additional cases of ITHS. This rare cause of painful ophthalmoplegia effects the cranial nerves due to a granulomatous lesion of unknown etiology in the cavernous sinus or superior orbital fissure. The International Headache Society redefined the diagnostic criteria for ITHS but it is still mostly a diagnosis of exclusion. Careful evaluation and follow-up is essential for diagnosis. Optimal therapy duration and dosage and prophylactic treatment in recurrent cases needs further research.

Keywords: idiopathic Tolosa–Hunt syndrome, painful ophthalmoplegia, diagnosis, exclusion

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I\textsuperscript{diopathic Tolosa Hunt Syndrome (ITHS) is a very rare cause of painful ophthalmoplegia characterized by unilateral orbital pain, ipsilateral oculomotor paralysis and prompt response to steroids\textsuperscript{1}. The syndrome is given the name after Tolosa fully described the clinical syndrome in 1954 and Hunt described prompt response to steroids in 1961\textsuperscript{2, 3}. The incidence has been estimated as approximately one to two per million\textsuperscript{4}. International Headache Society redefined the diagnostic criteria for THS in 2004 specifying demonstration of granuloma by MRI or biopsy as a requisite\textsuperscript{5}. A recent paper by La Mantia et al identified hundred and twenty-four cases of ITHS in the literature\textsuperscript{6}. In this paper we report 4 additional cases of ITHS.

Case presentations

CASE 1.

The 19 year old female patient admitted emergency department complaining of left sided headache accompanied by left sided ptosis and double vision. Her headache began 3 weeks ago and a week later double vision and left sided ptosis emerged. She did not have any previous medical history and her systemic examination was normal. Her neurological examination revealed total left oculomotor palsy. Her sera chemistry and hemogram were normal. Cranial MRI showed a granulomatous lesion expanding from left carotid wall to suborbital apex with homogeneous gadolinium enhancement. Sera markers for vasculitis were negative. She was started on steroids (methylprednisolone 1 g/day IV pulse) with a probable diagnosis of ITHS. On the 3rd day of treatment ocular movements showed evident improvement. Steroid treatment was completed to 7 days followed by oral tapering. She had no signs in neurological examination in last visit approximately 6 years after beginning of her symptoms with no relapses during follow up.

CASE 2.

The 22 year old male patient admitted with pain in the left eye, double vision and ptosis. Pain in the eye started 10 days before his admission and a week later double vision and ptosis developed. His medical history was remarkable except for a history of Bell’s palsy 2 months earlier. His systemic examination was normal. His neurological examination revealed left oculomotor palsy with complete paralysis of eye movements except adduction and ptosis. His cranial MRI showed pathological signal changes and gadolinium enhancement in left cavernous sinus, orbital MRI showed a soft tissue lesion extending from left orbital apex to cavernous sinus (Figure 1.). Sera chemistry and hemogram were normal. His sera investigations for vasculitis

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\caption{Cranial MRI of Case 2. T2 (A), T1 (B) and T1 Gd+ (C) sequences of case 2 showing soft tissue mass in left cavernous sinus}
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and cerebrospinal fluid analysis were normal. He was started on 1 g/day methylprednisolone treatment for 5 days followed by oral tapering. On the 12th day of treatment he had mild ptosis and mild restriction in lateral, up or down gaze of the left eye. During two years follow up period he had no relapses and his neurological status was stable.

CASE 3.

The 73 year old male patient admitted to emergency clinic complaining thrumbling pain in the periorbital region accompanied by nausea and vomiting that began 2 days earlier. The day after his initial symptoms left sided ptosis and double

Figure 2. Cranial MRI of Case 4. T2 (A), T1 (B) and T1 Gd+ (C) sequences of case 4 showing soft tissue mass in right cavernous sinus
vision emerged. He had a history of headache, nausea, vomiting and left sided ptosis one year ago which was diagnosed as Tolosa–Hunt syndrome and completely resolved by methylprednisolone treatment. His neurologic examination revealed restriction of abduction, ptosis and weakened light reaction in the left eye accompanied by hypoesthesia and hypoalgesia in the ophthalmic region of the trigeminal nerve and also rotatory nystagmus on abduction of the left eye. His serum chemistry and hemogram and cerebrospinal fluid investigations were normal. MRI of the brain and orbita showed increased T2 signals in left cavernous sinus concordant with Tolosa-Hunt syndrome. 10 days 1 g/day pulse followed by oral tapered methyl-prednisolone treatment regimen was given. On the 9th day of treatment his complaints progressed and his neurological examination revealed increase in restriction of abduction and also additional restriction of adduction of left eye. On the 20th day of treatment his neurological examination was within normal limits except mildly decreased light reaction in left eye. During one year follow up he had no relapses nor any change in neurological status.

CASE 4.

The 62 year old female patient presented with pain in the right eye and ptosis. Her orbital pain began 2 weeks ago followed by ptosis several days later. She had a medical history of diabetes mellitus and she was on oral antidiabetic treatment. Her systemic examination was normal. Neurological examination showed right ptosis, restriction of up, down and medial gaze of the right eye with hypoesthesia and hypoalgesia in the distribution of 1st and 2nd branches of trigeminal nerve. MRI of the cranium showed granulomatous lesion of right cavernous sinus (Figure 2.). Sera chemistry and hemogram were normal except a fasting glucose level of 120 mg/dl. Sera markers for vasculitis were negative. She was started on 1 g/day steroid treatment for 10 days followed by oral tapering. Her pain ameliorated on the 2nd days of the treatment and by the 3rd day ocular movement restriction started to improve. In follow up visit three months later she had mild ptosis and ocular movement impairment.

Discussion

International Headache Society The Headache Classification Committee defines Tolosa–Hunt syndrome as an 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. IHS re-defined the diagnostic criteria for this disorder. This rare cause of painful ophthalmoplegia effects the cranial nerves due to a granulomatous lesion of unknown etiology in the cavernous sinus or superior orbital fissure. Differential diagnosis of Tolosa–Hunt syndrome include tumours, vasculitis, basal meningitis, sarcoid, diabetes mellitus and ophthalmoplegic “migraine”. Careful investigations and follow up are essential to exclude causes of painful ophthalmoplegia other than ITHS.

A typical clinical course of painful ophthalmoplegia with accompanying symptomatic cavernous sinus enlargement on MRI and resolution of clinical symptoms and MR imaging findings following steroid treatment is highly suggestive of Tolosa–Hunt syndrome. MR investigations are also important to exclude other causes of painful ophthalmoplegia but after all one needs to keep in mind that radiological investigations may be normal in up to 1/4 of the patients with ITHS. Investigations for vasculitis and also in certain cases cerebrospinal fluid analysis are important in differential diagnosis. Unfortunately, there is no consensus for treatment of ITHS and there is very little information on optimal dosage, duration of treatment or alternative forms of treatment.

Recurrent ITHS is a known aspect with the time between relapses varying from months to years. Case 3 had two episodes of ITHS both on the same side and well responding to steroid therapy. The use of immunosuppresants or other forms of prophylactic therapy is debatefull although there is some experience with azathioprine in steroid dependent or steroid resistant cases. Case 2 had an episode of ITHS preceded by Bell’s palsy. There are some cases of ITHS preceded by peripheral facial palsy varying between days to weeks. There is increasing evidence that the main cause of Bell’s palsy is latent herpes viruses. One can speculate that granulomatous inflammation in ITHS emerges as a reaction to viral infection as in the case of Bell’s palsy or the inflammation in ITHS is widespread extending outside the cavernous sinus. However, in case 2 ITHS was 2 years after Bell’s palsy which probably represents a coincidence more than an etiological relationship.

Diabetic ophthalmoplegia is an important consideration in differential diagnosis of painful ophthalmoplegia as ITHS. There are reports noting association of diabetes with ITHS. Case 4 had diabetes mellitus diagnosis several years earlier and
was on oral antidiabetic therapy when her symptoms emerged. The MRI showing soft tissue lesion in cavernous sinus localization and steroid responsiveness favoured diagnosis of ITHS. In cases of painful ophthalmoplegia with diabetes, MRI showing inflammation in cavernous sinus and/or steroid responsiveness may support diagnosis of ITHS.

We report 4 new cases of ITHS followed in our department. IHSS redefined the diagnostic criteria for ITHS but it is still mostly a diagnosis of exclusion. Careful evaluation and follow-up is essential for diagnosis. MRI investigations showing granulomatous inflammation in cavernous sinus region and steroid responsiveness supports the diagnosis of ITHS. Optimal therapy duration and dosage and prophylactic treatment in recurrent cases needs further research.

REFERENCES