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Case Report Open Access

Tolosa Hunt Syndrome: Increased Severity on Second Attack

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Abstract

Tolosa Hunt syndrome (THS) is a rare cause of painful ophthalmoplegia with an estimated annual incidence of 1 case per million per year. It is caused by a nonspecific inflammatory process, of unknown etiology, involving the cavernous sinus, the superior orbital fissure and/or the orbital apex. It is classically described as an episodic orbital pain associated with paralysis of one or more of the 3rd, 4th and 6th cranial nerves, resolving spontaneously or with the commencement of steroids. I report a female patient who had 2 attacks of THS separated by a period of 10 months. She presented with retro-orbital headache, exophthalmos, and ophthalmoplegia of left eye, on both attacks, and was treated with high dose prednisolone. On first attack she improved within 6 weeks of treatment. On second attack, the patient had a higher Erythrocyte sedimentation rate (ESR) and developed 2 relapses on corticosteroids tapering, requiring a prolonged course of treatment, for 27 weeks, which suggests that the disease activity may get more severe on further attacks of the disease.

Keywords: Tolosa-Hunt syndrome; Painful ophthalmoplegia; Proptosis; Headache; Retro-orbital; Ptosis

Introduction

Painful ophthalmoplegia is a condition associated with multiple cranial nerve palsies involving oculomotor, trochlear, abducent, and ophthalmic division of the trigeminal nerve. Various etiologies have been reported; these include infections, inflammations, sphenoid sinus mucocele, tumors, dural arteriovenous malformation, trauma, and diabetes mellitus. Tolosa-Hunt syndrome (THS), a rare cause of painful ophthalmoplegia, is characterized by nonspecific granulomatous inflammation of the cavernous sinus, superior orbital fissure and/or the apex of the orbit [1,2]. The disease is manifested by recurrent periorbital pain, headaches on the same periorbital side and diplopia. Clinical signs include slight exophthalmos, extra ocular palsies involving the third, fourth, and sixth cranial nerves and numbness in the area of V1 and V2 branch of the trigeminal nerve [2,3].

THS is usually reported as unilateral, with no predilection to right or left cavernous sinus, While 4.1-5% of THS is bilateral [3-19]. Uniformly, patients complain of pain, which is a defining symptom. The pain lasts an average of 8 weeks if untreated. Ocular motor cranial nerve palsies may coincide with the onset of pain or follow it within a period of up to 2 weeks. The Pupillary reactions may be normal [16]. The 3rd nerves is involved in 85% of cases, the 6th nerve in 70%, the ophthalmic branch of 5th nerve in 30% and the 4th nerve in 29% [4]. Sympathetic innervation of the pupil is occasionally affected [3]. Facial palsy in not uncommon and systemic symptoms, as back pain, arthralgia, chronic fatigue and gastrointestinal upset, are also noted [5,6]. Clinically, painful ophthalmoplegia and immediate response to steroid therapy are a hallmark of the condition [3]. The aetiology is unknown, although it shares histopathological features with idiopathic orbital pseudo-tumor. However, owing to its anatomical location, it produces characteristic clinical manifestations [1,3]. Over the years, there have been cases reporting the involvement of cranial nerves outside the cavernous sinus [7-10], and some authors raised the possibility that the syndrome is in fact part of a larger spectrum of idiopathic recurrent cranial neuropathy [9,11]. The condition can be classified, according to neuroimaging, in to benign (when no abnormal neuroimaging can be found), inflammatory (when inflammatory findings are shown on MRI or biopsy) and symptomatic (when neuroimaging reveals specific lesion) [12].Treatment should be with high dose steroids (1 mg/kg/d) tapered slowly over 3 to 4 months [13].

The estimated annual incidence of THS is 1 case per million per year [14,15]. It can affect people of age group of 1st to the 8th decades of life, with no sex predilection [4,16]. It was first described by Tolosa, in 1954 [17]. In 1961, Hunt et al. reported six cases of painful ophthalmoplegia; that rapidly improved with the use of steroids [18]. The condition was termed Tolosa-Hunt syndrome by Smith and Taxdal in 1966. In 2004 the international headache society modified the criteria for THS (Table 1) [12].

Case Report

A previously healthy 39 year old female patient presented with left sided retro-orbital and frontal headache for 4 days which was followed by ptosis of left eye, diplopia and numbness of upper part of left side of face. The patient denied any previous similar symptoms, facial or head trauma and drug intake. On examination, there were ptosis of left eye and deviation of eye globe downward and laterally. Loss of adduction, upward and downward movement of left eye globe were evident on extra-ocular muscles examination of left eye (Figure 1), alongside with, exophthalmos and loss of sensation in the area of ophthalmic branch of trigeminal nerve. The pupils were both reactive and of normal size. The visual acquity and fundoscopy, on both eyes, were normal. Further neurologic and general examinations were normal. Brain MRI, Brain MRA and orbital MRI did not reveal any abnormalities except for anteriorly protruding left globe. Erythrocyte sedimentation rate (ESR) was elevated (85 milliliter/1st hour).

Thyroid function test, fasting blood sugar, kidney function test and complete blood count were normal. Anti-nuclear antibodies, anti-dsDNA, anti-neutrophiles cytoplasmic antibodies and rheumatoid

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13.16 Tolosa-Hunt syndrome
Description
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 replase and remit.
Diagnostic criteria
A. One or more episodes of unilateral orbital pain persisting for weeks if untreated
B. Paresis of one or more of the third, fourth and/or sixth cranial nerves and/or demonstration of granulomas by MRI or biopsy
C. Paresis coincides with the onset of pain or follows it within 2 weeks
D. Pain and paresis resolve within 72 h when treated adequately with corticosteroids
E. Other causes have been excluded by appropriate investigations1
Note
1. Other causes of painful ophthalmoplegia include tumors, vasculitis, basal meningitis, sarcoid, diabetes mellitus a ophthalmoplegic 'migraine'.
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 pupil is occasionally affected.
The syndrome has been caused by granulomatous material in the cavernous sinus, superior orbital fissure or orbit in some biopsied cases.
Careful follow-up is required to exclude other possible causes of painful ophthalmoplegia.

Table 1: ICHD-II classification part three. Cranial neuralgias, central and primary facial pain and other headaches.

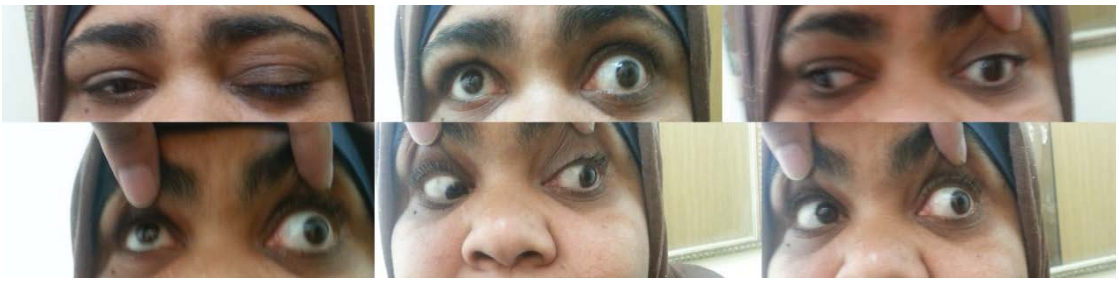

Figure 1: Showing ptosis of left eye and ophthalmoplegia.

factor were all negative. Angiotensin converting enzyme level was 18 microgram/l. A lumbar puncture was done and revealed a normal cell counts and morphology and normal protein and sugar levels level.

On the view of her clinical presentation, imaging and laboratory results, THS was suspected and high dose prednisolone (1 mg/kg) was prescribed. On 3rd day of therapy the patient's headache disappeared completely with partial improvement of ptosis and ophthalmoplegia. Prednisolone therapy was continued for 12 weeks, during which the dose of steroid was tapered at a rate of 7 mg/week. Complete resolution was achieved after 2 weeks of therapy with normalization of ESR, and resolution of left eye ophthalmoplegia and exophthalmos.

Eight months later, the patient's symptoms recurred. She was re-evaluated in the same manner as in her first attack and found to have same clinical findings and same laboratory and imaging results, except for a higher ESR level (110 ml/1st hour). Prednisolone (1 mg/kg) therapy was started with improvement of headache after 2 days and improvement of ptosis after 1 week. Dose tapering by 7 mg/week was done. On the 4th week, the patient started to have retro-orbital headache and, 2 days later, ptosis recurred. The dose was increased by 5 mg and tapering was made at a rate of 4 mg/week with promising improvement on regular follow up. Unfortunately, another relapse of symptoms occurred on reducing the dose below 30 mg. Accordingly, the patient was kept on 30 mg prednisolone for 2 consecutive weeks and the dose was then tapered at a rate of 2 mg/week. A complete resolution of the disease was achieved after 13 weeks of therapy with normalization of ESR and ophthalmoplegia, but steroid therapy was kept for total of 27 weeks because of slow tapering of the dose and relapse of symptoms on higher tapering rate.

On both attacks, ESR was measured on each follow up visit, and of note, the levels were decreasing gradually as the patients symptoms improved with treatment and increased again on relapse of symptoms.

Discussion

In this case report, excluding other causes of painful ophthalmoplegia by the normal MRI findings and laboratory investigations, the positive response to corticosteroid treatment and the 4 days gap between the onset of pain and ophthalmoplegia, were relevant for making the diagnosis and fulfilled the ICHD-3 criteria for THS (Table 1).

THS is a diagnosis of exclusion; diagnostic work-up includes routine blood work, inflammatory markers, fasting glucose, cerebrospinal fluid (CSF) evaluation, anti-nuclear antibodies (ANA), anti-dsDNA, anti-neutrophilic cytoplasmic antibody (ANCA), magnetic resonance imaging (MRI), conventional angiography or magnetic resonance angiography (MRA); and in some cases biopsy [13]. In most cases

it is diagnosed when all other causes of painful ophthalmoplegia are ruled out. The clinical differential diagnosis of steroid responsive painful ophthalmoplegia includes metastases, carotid-cavernous fistulae, thrombosis of cavernous sinus, pituitary adenomas, vasculopathic cranial neuropathy, aspergillus invasion, Wegener's granulomatosis, sarcoidosis, lymphoma and ophthalmoplegic migraine [20]. However, sarcoidosis and lymphoma will often have systemic symptoms and meningiomas will not resolve with steroid therapy. Vascular abnormalities such as arteritides, carotid-cavernous fistulae, ophthalmoplegic migraines and aneurysms are not associated with masses in the cavernous sinus or orbital apex as in THS.

Neuro-imaging - in particular 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 range of differential diagnosis [21]. Therefore, in order to prevent a delay in diagnosis it should be considered as the initial diagnostic imaging modality in this group of patients presenting with external ophthalmoplegia [22]. MRI shows changes in 44% of THS cases only [23]. MRI findings classically show a soft-tissue mass lesion involving the superior orbital fissure or cavernous sinus. Signal characteristics are typically hypointense to fat and isointense to muscle on short TR/TE sequences and isointense to fat on long TR/TE sequences [24]. Significant enhancement of the mass lesion is demonstrated on contrast enhanced sequences. Of particular value are the post-contrast fat-saturated thin-slice coronal images through the orbital apex and cavernous sinus [25]. The MRI findings are nonspecific to THS, as meningioma, lymphoma and sarcoidosis have the same MRI findings, and THS can also have normal MRI Findings [26].

Although spontaneous remission may occur in THS, steroid therapy dramatically improves the retro-orbital pain within 24-48 hours and usually relieves cranial nerve dysfunction within 2 weeks [27]. An unusual chronic variant of THS, requiring low-dose steroid for 11 months, has been reported [28]. The reported prognosis of THS is good. Nevertheless, 30-40% of cases who have been successfully treated for THS may relapse [6]. This usually occurs on same side as the original lesion, but can occur on the opposite side [29]. In the patient reported here, on the first attack she responded well to corticosteroid with complete resolution of ophthalmoplegia after 2 weeks of therapy. On the second attack, a prolonged course of steroid therapy, a delayed resolution of ophthalmoplegia; after 13 weeks of therapy, frequent relapses of symptoms on dose tapering, and a higher ESR with increasing level on each relapse, were all observed, which may suggest that the disease activity may be more severe on recurrent THS cases.

Conclusion

THS is a diagnosis of exclusion. Neuro-imaging is fundamental to be done initially in patients with painful ophthalmoplegia in order not to delay the diagnosis. The disease may recur after successful treatment and the disease activity may be more severe on recurrent attacks, requiring a prolonged course of steroid with slow tapering rate. ESR can be used to monitor the response to treatment and recurrence of the disease.

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