International Journal of Current Medical and Pharmaceutical Research

IJCMPR

ISSN: 2395-6429

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170190

RESEARCH ARTICLE

A CASE OF TOLOSA HUNT SYNDROME: DIAGNOSTIC ALGORITHM AND MANAGEMENT

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ARTICLE INFO

Article History:

Received 17th May, 2017
Received in revised form 3rd June, 2017
Accepted 27th July, 2017
Published online 28th August, 2017

Key words:

Tolosa-Hunt syndrome, Painful ophthalmoplegia, steroid responsive

ABSTRACT

Tolosa-Hunt Syndrome is one of the rare but easily treatable causes of painful ophthalmoplegia. It is due to nonspecific granulomatous inflammation in the cavernous sinus, supra-orbital or orbital fissure. We present a case of a middle aged hypertensive female with acute onset headache, retro-orbital pain, left sided complete ptosis, diplopia and complete ophthalmoplegia. She had no other neurodeficiet. MRI showed enlarged cavernous sinus and soft tissue enhancement on T1. After excluding other causes she was diagnosed as a case of Tolosa-Hunt Syndrome and started on oral steroids to which she responded promptly. In this article we illustrate the various causes and approach to diagnose a case of painful ophthalmoplegia with emphasis on Tolosa-Hunt Syndrome and suggest a regimen of corticosteroids.

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INTRODUCTION

Painful ophthalmoplegia is defined as periorbital or cephalelgia along with one or more ipsilateral ocular motor nerve palsy and sometimes associated with oculo-sympathetic paralysis and sensory loss in distribution of ophthalmic and maxillary division of trigeminal nerve. There are a number of causes of painful ophthalmoplegia like cavernous sinus thrombosis, internal carotid or cerebral aneurysm, carotico-cavernous fistula, diabetic neuritis, ophthalmoplegic migraine etc. One of the rare but treatable causes is Tolosa-Hunt Syndrome (THS) which refers to painful ophthalmoplegia secondary to idiopathic granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbital apex. The hallmark of this disease is prompt and usually complete response to glucocorticoids but there may be relapses and steroid resistant cases [1]. In this article we describe a case of THS, its diagnostic workup and management with follow up after 8 weeks.

Case presentation

Our patient is a 43 year old female previously asymptomatic whose relevant medical history included essential hypertension which was detected 1 year ago for which she was on calcium channel blockers. The patient was admitted to our hospital with left periorbital pain, ipsilateral ocular motor nerve palsies and diplopia. 5 days prior to admission the patient experienced left periorbital pain, 72 hours later she had restricted left eye movements, ipsilateral drooping of eyelids and double vision in both horizontal and vertical axis. There was no history of fever, infection around the paranasal sinuses or trauma. There was no history of similar episode in the past, similar illness in the family, chronic headache, migraine or diabetes mellitus. Prior to admission she had only took NSAIDS to relieve the pain but of no avail. She had no complaints of dimness of vision, difficulty to distinguish colours, loss of sensation on the face or any other neurological or systemic symptoms.

On examination her vitals were stable, BMI 32 kg/m^2. There was left palpebral complete ptosis, exotropia of the primary look of the left eye, paresis of the oculomotor, abducens, trochlear nerve, left pupil was slightly larger in size than the right one. Left eye vision was 6/6, no discromatopsia, fundoscopy was normal, normal direct and consensual light reflex. There was no other cranial nerve palsy, and no other neurological or systemic signs were found.

Keeping in mind the diagnostic possibilities of painful ophthalmoplegia the different tests were carried out. Her routine blood examination showed Haemoglobin 10.9g%, WBC 10000/ml, Platelets 1.53lakhs, Fasting blood sugar 98 mg/dl, Urea 28mg/dl, Creatinine 0.8mg/dl, Liver Function Tests and Thyroid profile was within normal limits. A non contrast CT scan of the brain done at the emergency department of our hospital was normal. So a Gadolinium contrast enhanced MRI of Brain and Orbit with MR Venogram was carried out. Axial and coronal T2-weighted images showed an enlarged left cavernous sinus that was mildly

hypointense to grey matter. Post contrast T1-weighted fat suppressed images showed abnormal soft tissue enhancement. MR Venogram was normal. To detect the etiology different tests were carried out which showed Antinuclear Factor:- Negative, ELISA for HIV negative, serum Angiotensin Converting Enzyme 5.6U/L, Cerebrospinal fluid analysis showed 2 cells/uL , all mononuclear, glucose 91mg/dl, protein 66mg/dl, chloride 99, ADA 4, Gram stain, Zeihl Neelsen stain, India Ink Preparation was negative.

After excluding neoplastic, infectious, vascular, thyroid and metabolic causes of painful ophthalmoplegia she was provisionally diagnosed as a case of Tolosa-Hunt Syndrome. She was started on oral Prednisolone 60 mg which was continued for 2 weeks then tapered by 10 mg every week. After 72 hours there was significant improvement in periorbital pain, ptosis and ocular paresis. She was evaluated at our OPD after 8 weeks when she was asymptomatic and her neurological examination was normal. She was continued on maintenance dose of prednisolone 10 mg/day.

DISCUSSION

Tolosa-Hunt Syndrome (THS) as a rare cause of painful ophthalmoplegia was first described by Tolosa in 1954 in a male patient who had died soon after an operation to explore the sella turcica for left retro-orbital pain and ophthalmoplegia. The autopsy demonstrated nonspecific granulomatuos inflammation in the cavernous sinus, surrounding the intracavernous portion of the left internal carotid artery and cranial nerves III, IV, ophthalmic division of V, and VI [2]. Some years later in 1961 Hunt *et al.* described 6 patients with similar clinical findings and proposed a low-grade non-specific inflammation of the cavernous sinus and its walls as the cause of the syndrome. Pathologically, infiltration of lymphocytes and plasma cells as well as thickening of the dura mater was seen [3]. Later in 1966 Smith and Taxdal described it as a syndrome complex for the first time proposing the eponym Tolosa-Hunt syndrome. They also highlighted the drastic and excellent response to steroids in this condition [4]. The diagnostic guidelines was provided in 1988 by the International Headache

Society (IHS), and further revised in 2004 (Table I) [5].
ICHD –II Classification part 3

Table I

13.16 Tolosa-Hunt syndrome
Diagnostic criteria:
One or more episodes of unilateral orbital pain persisting for weeks if untreated A.
Paresis of one or more of the third, fourth and/or sixth cranial nerves and/or demonstration of granulomas by MRI or biopsy B.
Paresis coincides with the onset of pain or follows it within 2 weeks C.
Pain and paresis resolve within 72 h when treated adequately with corticosteroids D.
Other causes have been excluded by appropriate investigations E.

THS is usually reported unilateral, with no predisposition between right or left sinus cavernous, THS only happens about 5% bilaterally. THS occurs between the ages of 5-75 years without any sex predilection. By order of frequency of involvement of the cranial nerves THS most often affects nerves III, VI, the first branch of nerve V, then nerve IV [6, 7]. THS is basically a diagnosis of exclusion so the other clinical entities in the differential diagnosis are parasellar syndromes and other causes of steroid responsive painful ophthalmoplegia. THS can be distinguished from this conditions based on clinical symptoms and radiology although biopsy from the cavernous sinus and histological evidence like nonspecific granulation tissue in the cavernous sinus, pachymeningitis in the supraorbital fissure and necrotizing inflammation within intracavernous and a part of intracranial internal carotid artery are gold standard.

So usually Gadolinium enhanced MRI of the brain and orbit is done for diagnosis. The abnormal area in the cavernous sinus in THS is of intermediate intensity on T1W1. This is consistent with the pathological process of THS that is granulomatous inflammation [8]. In the appropriate clinical setting of painful ophthalmoplegia, MR findings of a cavernous sinus abnormality that is isointense with muscle on short TR/ TE images and hypointense to isointense with fat on long TR/TE images suggests the diagnosis of THS. However in a recent case report from West Bengal there was normal MRI in a case of THS[9].

Among the parasellar syndromes various vascular causes may produce painful ophthalmoplegia, the most frequent being an intracavernous carotid artery aneurysm. Carotid-cavernous fistula and cavernous sinus thrombosis also have acute onset of symptoms and signs, and must be included in the differential diagnosis. But patients with carotid-cavernous fistulae rarely complain of severe pain instead typically have dramatic ophthalmological signs including proptosis, “arterialised” conjunctival vessels, chemosis, increased intraocular pressure, and retinal vascular abnormalities. A bruit is often present, cerebral angiography is the diagnostic procedure of choice, and interventional angiographic techniques are usually curative. Another common cause is Cavernous sinus thrombosis which may be septic or aseptic in origin. In the first, there may be associated signs of sinusitis, otitis, gingivitis, or orbital cellulitis. Patients are febrile, have a leukocytosis, and if the infectious process spreads intracranially, seizures and altered mental states may occur. Aseptic cavernous sinus thrombosis may be associated with various conditions causing a procoagulant state like Polycythemia vera, sickle cell disease, vasculitis, pregnancy, dehydration, trauma, and intracranial surgery. Regardless of aetiology, cavernous sinus thrombosis is characterised by orbital congestion, proptosis, eyelid swelling, chemosis, lacrimation, and ophthalmoparesis. Pain around or behind the eye is common. Treatment of cavernous sinus thrombosis usually involves anticoagulant drugs, at times thrombolytic agents, and in septic cases, appropriate antibiotic therapy.

Constellation of parasellar syndromes may also be caused by either contiguous or metastatic spread of a neoplasm. Metastatic involvement of the cavernous sinus/superior orbital fissure is generally due to haematogenous dissemination of neoplastic cells. Occasionally, intracranial neoplastic invasion may occur by intraneural or perineural spread, as in the case of squamous cell carcinoma producing painful ophthalmoplegia many months after local excision of a facial skin tumour [10]. High dose corticosteroid therapy may initially improve signs and symptoms due to some neoplasms like lymphoma, chordoma, giant cell tumour.

Inflammatory causes of painful ophthalmoplegia include those due to a specific infectious agent. It is essential that careful CSF examination be done and that cultures (bacterial, fungal, mycobacterial) be obtained. The potential role of a paranasal sinus as a cause of painful ophthalmoplegia requires attention. Sinus disease may lead to cavernous sinus involvement, either

via contiguous spread of infection or due to sphenoid sinus mucocele.

Various orbital diseases or idiopathic orbital inflammation (orbital pseudotumour) can cause painful ophthalmoplegia. Typically, the patient presents with "orbital signs", including proptosis, conjunctival injection, chemosis, and resistance to retrodisplacement of the globe. In addition, the eye may be displaced within the orbit, and there may be abnormalities of the ocular adnexa (for example, lids, lacrimal gland).

Diabetic ophthalmoplegia typically produces an acute, often painful mononeuropathy in either a known or previously undiagnosed diabetic person. Invariably there is recovery of ocular motor cranial nerve function, usually within 3 months. In addition, there are reports of diabetic patients with simultaneous paralysis of multiple ocular motor nerves. But these episodes are not particularly responsive to corticosteroid therapy.

Posterior fossa aneurysms may produce either acute, painful ophthalmoplegia, or may present in a more subacute or chronic fashion. The acute presentation is most often due to an aneurysm in the anterior circulation, typically at the junction of the internal carotid-posterior communicating arteries, whereas the subacute presentation is caused by basilar artery aneurysms. In both, cerebral angiography is diagnostic.

Figure 1 The patient presented with left sided complete ptosis

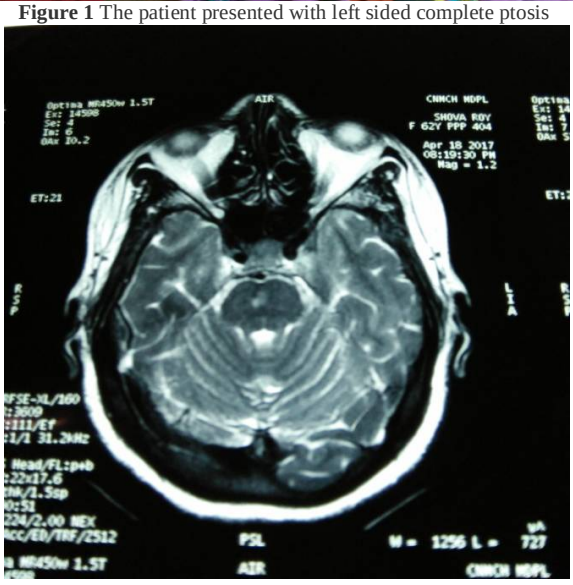

Figure 2 Coronal section showing abnormal Enhancement in left cavernous sinus

Giant cell arteritis may also produce painful ophthalmoplegia. The clinical picture may be one of single or multiple ocular motor nerve palsies. In the only pathological study of ophthalmoplegia occurring in giant cell arteritis, ischaemic necrosis of the extraocular muscles was demonstrated [11].

Ophthalmoplegic migraine typically occurs in a child or young adult with periodic headache, who develops ocular motor cranial nerve palsy at the height of an attack of cephalgia, which is primarily unilateral and in the orbital region. Most often involved is the oculomotor nerve, occasionally the abducens nerve, and rarely the trochlear nerve. The paresis lasts for days to weeks after cessation of a headache; recovery is gradual and tends to be less complete after repeated attacks. A family history of migraine is usually obtained. There are reports of enhancement of the extra-axial portion of the oculomotor nerves of patients with ophthalmoplegic migraine when evaluated with contrast-enhanced MRI but no space occupying lesions [12, 13].

Although spontaneous improvement may occur in THS case, but treatment with corticosteroids are the first choice.THS is exquisitely steroid responsive and usually pain decreases within 24 - 48 hours and cranial nerve paresis improves within

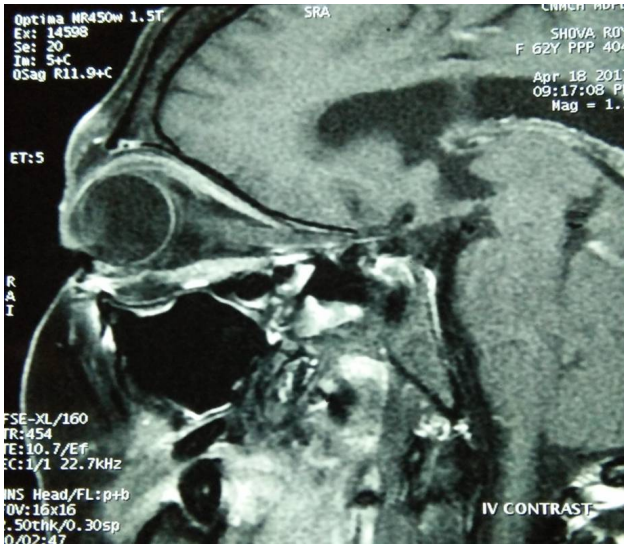

Figure 3 Sagittal section showing hyperintensity in cavernous sinus

Figure 4 the patient after 8 weeks

2 weeks. THS has a good prognosis, but 30-40% of THS cases patients who have been treated will have a relapse. It usually occurs on the same side, but can also occur on the contralateral side and rarely bilateral [14].

Our case is a classical case of first episode of steroid responsive Tolosa Hunt Syndrome and the patient is doing well after a follow up period of 8 weeks.

CONCLUSION

Although the pathological basis of Tolosa-Hunt syndrome still remains unknown, from a practical clinical standpoint it can be regarded as a distinct entity which may be simulated by various other disorders. It cannot be emphasised too strongly that patients suspected of having the syndrome require careful evaluation, appropriate treatment, and scrupulous follow up observation.

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