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THE HUNT FOR TOLOSA-HUNT SYNDROME- A CASE REPORT HIGHLIGHTING A RARE ENTITY

Neurology

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ABSTRACT

Tolosa-Hunt syndrome is a rare cause of painful ophthalmoplegia with an estimated incidence of 1-2 cases per million per year. A wide range of differentials need to be excluded before the diagnosis can be considered. We report the case of a 34-year-old lady who presented with acute onset right-sided retro-orbital and peri-orbital pain for the past 8 weeks. Two weeks after symptom onset, she developed right eye ptosis and complete external ophthalmoplegia. Routine investigations such as the complete hemogram, and liver and renal function tests were normal. HIV and viral markers were non-reactive. The complete autoimmune profile (ANA + ENA profile) was negative and the serum ACE level was normal. Subclinical hypothyroidism and impaired glucose tolerance were the only biochemical abnormalities noted. The cerebrospinal fluid examination was normal. The ultrasound of the abdomen and the contrast-enhanced CT of the paranasal sinuses did not reveal an underlying malignancy. MRI brain and orbit showed an abnormal linear dural enhancement on post-contrast T1W images along the lateral aspect of the superior orbital fissure extending to involve the anterior part of the lateral wall of the cavernous sinus. She was given Inj. Methylprednisolone (MPS) 1 gram IV daily for 5 days followed by oral steroids (1 mg/kg per day) for 2 weeks followed by gradual taper over the next 4 weeks. The patient's headache, ptosis and extraocular movements improved after 48 hours of initiating pulse MPS. Clinicians must be aware of this rare entity when evaluating painful ophthalmoplegia as it is steroid-responsive and potentially treatable.

KEYWORDS

Painful ophthalmoplegia, Cavernous sinus, Tolosa-Hunt syndrome, Granulomatous inflammation, Steroid-responsive

INTRODUCTION

Painful ophthalmoplegia is a relatively rare clinical entity characterized by unilateral periorbital pain/headache and ocular motor cranial nerve palsies.[1] The condition can occur due to a wide range of causes, thus posing a diagnostic challenge. It is imperative to arrive at the correct diagnosis so that appropriate treatment can be timely initiated. Tolosa-Hunt syndrome (THS) is a rare clinical syndrome with an estimated annual incidence of 1-2 cases per million per year.[2]

Establishing the diagnosis of Tolosa Hunt syndrome (THS) requires a comprehensive workup and exclusion of all other causes of painful ophthalmoplegia. We bring forth a case of a middle-aged female presenting with painful ophthalmoplegia who was subsequently diagnosed with THS. Furthermore, the differential diagnostic considerations in patients presenting with painful ophthalmoplegia, diagnostic criteria for THS, and the treatment modalities for THS are subsequently discussed.

Case Report

A 34-year-old lady, vegetarian by diet, without any comorbidities or addictions presented with acute onset, right-sided retro-orbital and peri-orbital gnawing pain for the past 8 weeks. She did not take any analgesics for this pain and kept on continuing her daily activities. The pain was not associated with nausea, vomiting, or photo/phonophobia. Two weeks after the onset of pain she developed double vision that was more for far objects than near objects. The double vision used to disappear on the closure of one eye. She described the two images placed side by side with maximal separation between the images on looking towards the right.

Around the same time, she developed drooping of the right eyelid. There was no history of fatiguability or diurnal variation in symptoms, no conjunctival redness, chemosis, lid swelling, purulent eye discharge, ear ache/discharge, proptosis, fever, diminution of vision, rhinorrhea, nasal stuffiness, or post-nasal drip. The patient denied a history of decreased smell, facial deviation, speech slurring, hearing impairment, swallowing difficulty, and reduced tongue movements. There was no history of weakness, sensory loss of one side of the body, imbalance while walking, joint pain or swelling, photosensitivity, skin rash, dry eyes/dry mouth, oral/genital ulcers, Raynaud's phenomenon, chronic cough, epistaxis, diarrhea, abdominal pain, jaundice, and significant weight loss. The drug and family history were unrevealing, and there was no history of trauma, recent dog bite or vaccination. On examination, there was right-sided ptosis with complete external ophthalmoplegia (III, IV, VI nerve palsy) [Figure 1].

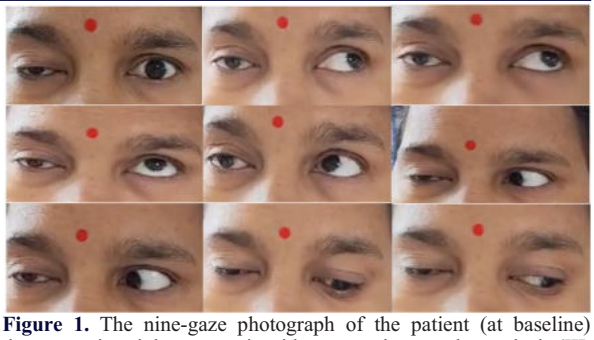

Figure 1. The nine-gaze photograph of the patient (at baseline) demonstrating right eye ptosis with extraocular muscle paralysis (III, IV, VI cranial nerve palsy).

The pupil was mid-dilated and sluggishly reacting to light on the right side compared to the left side. Visual acuity was 6/9 bilaterally and the fundus examination was normal. The rest of the cranial nerve, motor, sensory, deep tendon reflexes, cerebellar and extrapyramidal system examinations were normal.

Her hemoglobin was 12.4 gm/dl with a total leukocyte count (TLC) of 7640/mm^3 and a platelet count of 1.69 lakhs/mm^3. The liver and renal function tests were normal. HIV and viral markers were non-reactive. She had a TSH of 6.9 IU/ml (ref-<5.6). Her fasting blood sugars were 121 mg/dl with an Hba1c of 6.0%. ANA, c-ANCA, p-ANCA, anti-ds-DNA, anti-Ro and anti-La antibodies were negative. The RA factor was non-reactive. Serum ACE levels were normal (33.9 U/L; ref- 8-65). Cerebrospinal fluid (CSF) analysis showed nil cells with a glucose of 78 mg/dl (RBS-118 mg/dl) and protein of 52 mg/dl. The CSF cryptococcal antigen, India ink, Gram stain, Ziehl-Neelsen stain for AFB, pan-neurotropic viral panel, and CB-NAAT were negative. The chest X-ray and ultrasound of the abdomen and pelvis did not reveal any abnormality. Contrast-enhanced CT of the paranasal sinuses was normal. MRI Brain plus orbit revealed an abnormal linear dural enhancement on post-contrast T1W images along the lateral aspect of the superior orbital fissure extending to involve the anterior part of the lateral wall of the cavernous sinus consistent with THS [Figure 2].

The patient was started on Inj. Methylprednisolone (MPS) 1 gram IV daily for 5 days followed by oral steroids (1 mg/kg per day) for 2 weeks followed by gradual taper over the next 4 weeks. The patient's

headache, ptosis and extraocular movements improved after 48 hours of initiating pulse MPS with only residual right LR palsy and diplopia on the right lateral gaze after completing 5 days of pulse steroid therapy [Figure 3]. After four weeks of follow-up, the patient only complained of mild double vision on right lateral gaze.

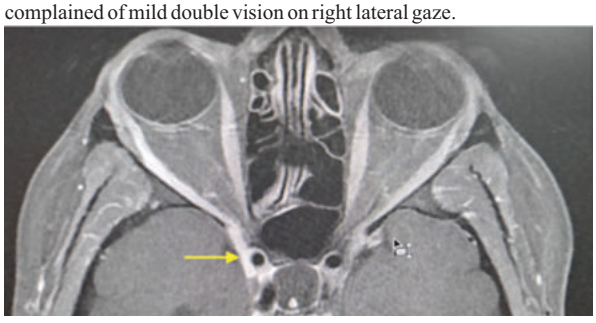

Figure 2. T1 weighted post-contrast MRI image of the brain with orbit demonstrating intense abnormal linear dural enhancement (yellow arrow) along the superior orbital fissure extending into the lateral wall of the anterior part of the right cavernous sinus.

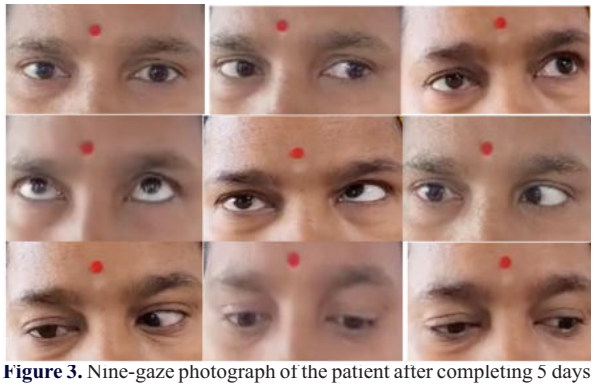

Figure 3. Nine-gaze photograph of the patient after completing 5 days of pulse steroid therapy. There is near complete resolution of right eye ptosis with improvement in upgaze, downgaze and on looking to the left. The right lateral rectus palsy is still persisting.

DISCUSSION

Tolosa-Hunt Syndrome (THS) was first described by Eduardo Tolosa and William Hunt who reported cases of painful ophthalmoplegia characterized by granulomatous inflammation of the cavernous sinus.[3,4] The cavernous sinus, superior orbital fissure, and/or orbital apex involvement can occur due to infections (bacterial or fungal sinusitis, facial or orbital cellulitis, pharyngitis, periodontal infections, ear infections, mastoiditis, basilar meningitis, HIV), immune-inflammatory causes (SLE, RA, Behcet's, sarcoidosis, Granulomatosis polyangiitis, IgG4 disease, orbital pseudotumor, hypertrophic pachymeningitis, Tolosa-Hunt syndrome), vascular lesions (cavernous ICA aneurysm, carotid-cavernous fistula, cavernous sinus thrombosis), neoplastic (nasopharyngeal carcinoma, lymphomas, multiple myeloma, meningiomas, parasellar/orbital metastasis), cranial irradiation-induced, drug-induced (oral contraceptive pill, hormone replacement therapy, steroid use, cancer chemotherapeutic agents), procoagulant states (Factor V Leiden mutation, prothrombin gene mutation, antithrombin III, protein C or S deficiency, acquired states such as nephrotic syndrome, ulcerative colitis, sickle cell anemia, anti-phospholipid antibody, hyperhomocysteinemia, heparin-induced thrombocytopenia, and dehydration), and post-traumatic/post-surgical states (like maxillofacial surgery, and dental extraction procedures).[5,6] Furthermore, diabetic microvascular cranial neuropathy and ophthalmoplegic migraines can result in painful ophthalmoplegia as well. Hence, THS is essentially a diagnosis of exclusion, and a wide range of differentials need to be ruled out.

The current ICHD-3 diagnostic criteria for the diagnosis of THS are highlighted in Table 1.[7]

Table 1. ICHD-3 criteria for Tolosa Hunt Syndrome[7]
A. Unilateral orbital/periorbital headache fulfilling criteria C B. Both B1 and B2 1. Granulomatous inflammation of the cavernous sinus, superior orbital fissure, or orbits, demonstrated by MRI or biopsy 2. Paresis of one or more of the ipsilateral oculomotor, trochlear, and/or abducens nerves
C. Demonstration of evidence of causation fulfilling both C1 and C2 1. Headache ipsilateral to the granulomatous inflammation 2. Headache has preceded the involvement of extraocular motor nerve by ≤2 weeks or developed with it D. Not better accounted by any other cause

Our case fulfilled the ICHD-3 diagnostic criteria for THS and we did not find any evidence (clinical, biochemical or radiological) of a secondary cause that could explain the clinical symptomatology in our patient. Furthermore, the patient's symptoms responded promptly with steroid therapy which was further supportive of THS.

A specialized MRI protocol called the "Tolosa-Hunt Protocol" consists of turbospin echo T2 sequences (T2 w), spin echo T1 w sequence on the axial plane, turbospin echo fat-saturated T2 w sequence on the coronal plane, and turbospin echo T2 w sequence on the sagittal plane. This is followed by spin echo fat-saturated T1 sequences on the axial and coronal planes and the administration of gadolinium contrast.[8] Enlargement of the cavernous sinus due to a soft tissue that is contrast enhancing, a bulging contour of the lateral wall of the cavernous sinus, dural meningeal enhancement, and focal narrowing of the intracavernous ICA are the radiological signs seen in THS.[9] In our case too, there was thick contrast enhancement noted along the lateral wall of the anterior cavernous sinus and the superior orbital fissure consistent with THS.

Consideration of this rare syndrome as a differential of painful ophthalmoplegia is important as it is potentially treatable and exquisitely steroid responsive. In a retrospective study of 31 patients with THS, 64.5% patients showed complete recovery after a median 6.5 weeks of steroid therapy.[10] Recurrences have been described in literature and can occur in upto 39% of cases of THS.[11] Those who recur may require a prolonged course of steroid therapy or rarely secondary immunosuppressives. Focal radiotherapy and/or gamma-knife surgery have been used in certain medically refractory, or steroid intolerant cases.

To conclude, clinicians need to be aware of THS as a possibility when managing patients with painful ophthalmoplegia as the condition is potentially treatable if diagnosed and treated promptly.

Acknowledgements: None

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