CASE REPORT

Clinical presentation and management of Tolosa-Hunt syndrome: a case report

Bisma Qasim[1], Farnaz Siddiqui[2], Maria Saleem[3], Muhammad Zohaib[4], Muhammad Khuzzaim Khan[5], Nisar Ahmed Siyal[6]

Abstract

Tolosa-Hunt Syndrome (THS) is an exceptionally rare disorder characterised by recurrent episodes of excruciating ophthalmoplegia, commonly affecting one side of the face and involving the third, fourth, sixth, and fifth cranial nerves. This syndrome results from non-specific inflammation affecting the cavernous sinus, superior orbital fissure (SOF), and/or orbital apex. In this case report, we present the clinical features, diagnostic evaluation, and management of a 46-year-old female with THS. The patient initially presented with right-sided peri-orbital pain, swelling, chemosis, and headache. Ocular examination revealed mild to moderate proptosis, complete ophthalmoplegia, and normal findings in the left eye. Imaging studies, including CT and contrast-enhanced MRI, confirmed the presence of non-specific inflammation in the cavernous sinus and associated structures. Immediate treatment with oral Prednisolone led to a significant reduction in symptoms within five days, with complete resolution of chemosis and pain. Ocular movements gradually improved over the following week. Long-term follow-up showed no recurrence of symptoms.

Keywords: Chemosis; Ophthalmoplegia; Cavernous Sinus.

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Introduction

Tolosa-Hunt syndrome (THS) is an exceptionally rare disorder with an estimated annual prevalence of one case per million per year.[1] It was initially identified by Tolosa in 1954 and subsequently elaborated on by Hunt in 1961.[2,3] According to the National Organisation for Rare Disorders (NORD), THS is characterised by recurrent episodes of excruciating ophthalmoplegia, typically affecting one side of the face, and involving one or more of the third, fourth, sixth, and fifth cranial nerves (ophthalmic division).[1,3] This syndrome arises due to non-specific granulomatous inflammation affecting the cavernous sinus, superior orbital fissure (SOF), and/or orbital apex.

The diagnosis of THS is primarily one of exclusion, relying on the analysis of clinical manifestations, neuroimaging findings, and the immediate response to corticosteroid treatment.[4] THS is often considered when other potential causes of painful ophthalmoplegia have been eliminated. A comprehensive evaluation is essential to identify characteristic clinical features, such as recurrent or persistent episodes of cranial nerve paresis, localised pain around the eye, and associated symptoms like headache, diplopia or facial pain.[5] Imaging studies, such as magnetic resonance imaging (MRI) and computed tomography (CT) scans, play a crucial role in the diagnosis of THS. These imaging modalities help visualise the affected regions, revealing inflammation or structural abnormalities within the cavernous sinus, SOF, or orbital apex. Additionally, these tests aid in ruling out alternative causes of ophthalmoplegia, such as tumours, vascular lesions, or infections. The immediate and dramatic response to corticosteroid therapy is a hallmark of THS. The administration of high-dose corticosteroids, such as Prednisone or Methylprednisolone, often leads to rapid improvement of symptoms.[6] This therapeutic response is considered both diagnostic and therapeutic, further supporting the diagnosis of THS.

Case Report

In June 2023, a 46-year-old female with no relevant medical history presented to the ophthalmology outpatient department at Dow University Hospital (DUH) in Karachi. She had complaints of right-sided peri-orbital pain, swelling, chemosis, conjunctival congestion, and right-sided headache. The onset of symptoms was preceded by a traumatic occurrence (stone injury) to the right eye two months ago. Initially, she sought treatment at a nearby clinic where she received medication for redness in the right eye. However, the symptoms recurred after two weeks, accompanied by pricking-like pain around the right eye. The patient returned to the same clinic and was prescribed antibiotic treatment. As the symptoms worsened, characterised by severe chemosis, persistent headache, and sudden peri-orbital swelling on the right side (one day before presentation), she was referred to the

[1-3,6]Department of Ophthalmology and Visual Sciences, Dow University of Health Sciences, Karachi, Pakistan; [4]Fourth Year MBBS Student, Dow International Medical College, Dow University of Health Sciences, Karachi, Pakistan; [5]Fourth Year MBBS Student, Dow Medical College, Dow University of Health Sciences, Karachi, Pakistan.

Correspondence: Muhammad Zohaib. **e-mail:** mzobaib292@gmail.com
ORCID ID: 0009-0009-5466-0075

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Figure:-1 Right eye periorbital swelling with severe chemosis.

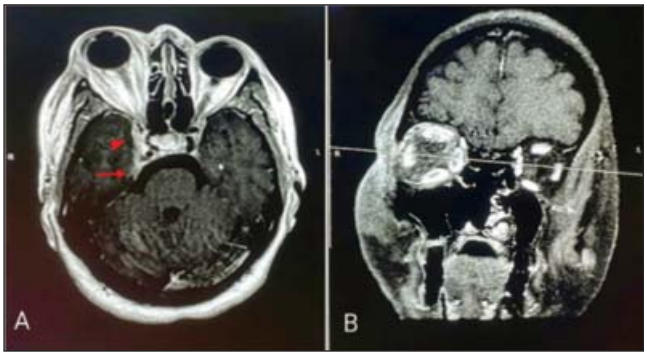

Figure:-2 MRI of the brain and orbit.
A) T1-weighted post-contrast axial sequence shows enhancing nodular thickening involving cavernous sinus reaching up to the orbital apex (arrowhead). Posteriorly, it is reaching up to the posteromedial aspect of the temporal lobe (arrow).
B) T1-weighted post-contrast coronal sequence shows thickening of right-sided ocular muscles including lateral, medial, superior, and inferior rectus muscles.

ophthalmology department at DUH for further evaluation (Figure 1).

Upon ocular examination, the right eye exhibited mild to moderate proptosis (right: 21mm; left: 18mm) with periorbital swelling. Complete ophthalmoplegia without ptosis indicated cranial nerve palsies affecting the fourth (IV), sixth (VI), and partial third (III) nerves. Visual acuity was measured at 6/18 with normal colour vision, and intraocular pressure was 23mmHg. Anterior segment examination revealed chemosis, while the pupil appeared normal (round, reactive, and regular). The posterior segment findings were unremarkable. The ocular examination of the left eye showed normal visual acuity (6/6), intraocular pressure of 14mmHg, and unremarkable findings. All cranial nerves associated with the globe (CNs I, III, IV, V, VI, and VII) were examined. Face sensations were normal. Physical and systemic examinations did not reveal any significant findings. Laboratory investigations, including complete blood count, inflammatory markers, and full biochemistry tests (including thyroid and liver function tests), were within the normal range. The erythrocyte sedimentation rate was not elevated.

A computed tomography (CT) scan revealed mild orbital proptosis on the right side, along with asymmetrical soft tissue thickening involving the inferior, medial, lateral, and superior recti muscles, as well as stretched and thinned optic nerve. To further evaluate the condition, a contrast-enhanced magnetic resonance imaging (MRI) (Figure 2) was performed immediately, which revealed a 2.8 x 0.8 cm (AP x TS) enhanced nodular thickening involving the cavernous sinus extending up to the orbital apex. Posteriorly, it reached the posterior medial aspect of the temporal lobe. Proptosis and thickening of the recti muscles (inferior, medial, lateral, and superior) were also observed on the right side. Magnetic resonance angiography (MRA) did not reveal any significant abnormalities.

The patient was promptly initiated on oral Prednisolone 60mg daily for 11 days, with a planned tapering schedule, and was scheduled for follow-up at the ophthalmology outpatient department. The patient was kept on close follow-up, initially every second day for two weeks, then weekly for two months as signs and symptoms improved. The patient was instructed to report any deterioration in vision, colour vision, or field restriction immediately, while each follow-up visit included a thorough evaluation of optic nerve functions and proptosis measurement. Significant relief in symptoms was observed within 48 hours, with complete resolution of chemosis and pain by day five of treatment. At day 11, improvement in all extraocular movements (EOM) was noted, except for restricted downward gaze, limited to 25 percent of normal. Four weeks after the treatment, the proptosis resolved completely, accompanied by complete restoration of EOM. However, congestion took an additional two weeks to settle down. Further follow-up examinations showed no recurrence of symptoms. Due to significant chemosis and a swollen eyelid during the early visits, only unassisted visual acuity was recorded. Once the chemosis was resolved, full refraction was performed. The best corrected visual acuity was 6/6 for both eyes.

Discussion

In this case, the patient presented with clinical features consistent with Tolosa-Hunt Syndrome (THS), including

right-sided ophthalmoplegia, chemosis, periorbital oedema, headache, and complete reversible paresis of the right abducens nerve (cranial nerve VI). The diagnosis of THS was based on the criteria proposed by the International Classification of Headache Disorders (ICHD) in 2018.[7] To confirm the diagnosis, contrast-enhanced magnetic resonance imaging (MRI) was performed, which revealed raised bump-like thickening indicative of granulomatous inflammation in the cavernous sinus.

The immediate reduction in symptoms observed within five days of initiating oral corticosteroid treatment (Prednisolone 60mg) supports the steroid-responsive nature of THS. However, restricted ocular movements persisted for an additional week before completely resolving.

It is crucial to differentiate THS from other disorders that may present with similar symptoms. Commonly occurring conditions such as pituitary tumours, diabetes, thyroid disease, sarcoidosis, mycobacterium tuberculosis, carotid aneurysm, and cavernous sinus thrombosis should be excluded, as well as other rare disorders including Miller Fischer Syndrome, craniopharyngioma, and carotid cavernous fistula, which share clinical similarities with THS.[8] All the mentioned disorders were ruled out. RBG: 92mg/dl (70 –140 mg/dl), ESR: 21 mm/hr (<20 mm/hr), Thyroid profile was normal; FREE T3: 2.68 pg/dl (1.7–4.2 pg/dl), FREE T4: 1.06 ng/dl (0.17-1.8 pg/dl), Serum TSH: 0.719 uIU/ml (0.3-5.5 uIU/ml), Antithyroglobulin: 8.8 IU/ml (0-10 IU/ml), ANTI-TPO: 8.90 IU/ml (< 9 IU/ml). Chest X-ray was normal excluding TB and sarcoidosis. CT orbit without contrast: suggestive of right orbital metabolic disease most likely thyroid ophthalmopathy which was ruled out as thyroid profile was normal, while findings on MRI with and without contrast were strongly suggestive of Tolosa-Hunt syndrome. No gross sellar or suprasellar mass was detected excluding pituitary tumour or craniopharyngioma. No evidence of intracranial bleed or mass lesion was seen. There was no hydrocephalus, midline shift, or cerebral oedema. Thalami and basal ganglia showed normal signals. Major vascular flow voids and basal cisterns were preserved. MRA revealed no significant abnormality excluding carotid cavernous fistula, cavernous sinus thrombosis, and carotid aneurysm. Miller-Fischer Syndrome was ruled out clinically as the patient had normal deep tendon reflexes and no ataxia.

Glucocorticoids are considered the first-line treatment for THS. However, caution must be exercised to avoid worsening symptoms in cases of misdiagnosis with fungal infections like mucormycosis.[9] In refractory cases of THS, second-line treatments such as immunosuppressants (Mycophenolate Mofetil, Methotrexate), monoclonal antibodies (Infliximab), and radiotherapy may be preferred.[10]

Literature review reveals various unique associations of THS with different diseases. For example, a case was reported in which a young male with haemolytic anaemia, jaundice, diplopia, blurred vision, and left orbital pain was diagnosed with THS based on MRI findings. Further investigations led to the diagnosis of systemic lupus erythematosus and antiphospholipid syndrome.[11] Another case involved a 55-year-old woman with THS presenting as diplopia, right upper eyelid ptosis, erythema nodosum, paralysis of cranial nerves III and VI, hypoesthesia, and allodynia along the route of the ophthalmic branch of the trigeminal nerve. This case was noted to be the initial presentation of systemic sarcoidosis.[12] THS has also been reported in association with other conditions such as myasthenia gravis, diffuse large B-cell lymphoma, and many more.

In summary, THS is diagnosed based on ICHD criteria when a patient exhibits granulomatous inflammation in the cavernous sinus, superior orbital fissure, or orbit, as demonstrated by MRI or biopsy, along with paresis of one or more of the ipsilateral cranial nerves III, IV, and/or VI, and unilateral orbital or periorbital headache ipsilateral to the granulomatous inflammation, or if headache preceded the paresis of the cranial nerves by ≤2 weeks or developed with it.

Conclusion

This case exemplifies the unique presentation of Tolosa-Hunt Syndrome (THS) with characteristic symptoms of ophthalmoplegia, chemosis, periorbital oedema, and headache. The diagnosis was confirmed through contrast-enhanced MRI, which revealed non-specific inflammation in the cavernous sinus. Prompt administration of oral corticosteroid treatment resulted in significant relief of symptoms, although complete resolution of ocular movements required additional time. It is crucial to consider THS as a differential diagnosis and exclude other commonly occurring and rare disorders that may mimic its presentation. The steroid-responsive nature of THS highlights the importance of early recognition and appropriate treatment with glucocorticoids.

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AUTHORS' CONTRIBUTIONS:

BQ, MZ: Concept, design, provide materials, data collection, interpretation, analysis, processing, literature review and writing.

FS: Concept, design, supervision and revision.

MS: Provide materials, data collection, interpretation, analysis and processing.

MKK: Concept, design, data interpretation, analysis, literature review and writing.

NAS: Supervision and revision.