OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Case Report **Ophthalmology**

Tolosa-Hunt Syndrome: A Case Report

Maan Ali Almokdad[1], Ashraf ALakkad[2*]

[1]Department of Ophthalmology, Al Sharq Hospital, Fujairah, United Arab Emirates
[2]Department of Internal Medicine, Madinat Zayed Hospital, AL Dhafra Region, United Arab Emirates

DOI: 10.36348/sjmps.2023.v09i08.006 | **Received:** 27.06.2023 | **Accepted:** 03.08.2023 | **Published:** 09.08.2023

***Corresponding author:** Ashraf ALakkad
Department of Internal Medicine, Madinat Zayed Hospital, AL Dhafra Region, United Arab Emirates

Abstract

Background**:* Idiopathic Orbital Inflammatory Syndrome (OIS) ranks as the third most prevalent orbital disease, following thyroid eye disease and orbital lymphoma. In cases of localized inflammation, various structures within the orbit can be affected. This includes the Extraocular Muscles (orbital myositis), lacrimal gland (dacryoadenitis), sclera (scleritis), uvea (uveitis), as well as the superior orbital fissure and cavernous sinus (Tolosa-Hunt syndrome). ***Case Presentation: In this report, we discuss the case of a 35-year-old man who went to the Emergency Department due to intense, throbbing pain in his eye orbit and half of his head on the right side. He had been experiencing this pain for two days. The pain was aggravated by eye movement and accompanied by ipsilateral redness, mild photophobia, and blurred vision. The patient had no significant medical history prior to this episode. Upon eye evaluation, findings included mild swelling of the right eyelids, painful eye movements, inferior corneal erosions, and conjunctival chemosis with superficial and deep vessel congestion. Visual acuity was reduced due to myopic refractive error. Magnetic Resonance Imaging (MRI) revealed a soft tissue lesion in the right orbital apex extending into the right cavernous sinus, suggesting an inflammatory etiology such as Tolosa-Hunt syndrome. To investigate further, the patient underwent various diagnostic tests, including laboratory investigations, chest X-rays, and serological tests. These tests revealed unremarkable findings, ruling out systemic pathology. The patient received intravenous Solumedrol (Methylprednisolone) followed by oral Prednisolone, resulting in a dramatic improvement in symptoms. ***Conclusion:*** This case highlights the importance of a comprehensive diagnostic approach in evaluating severe orbital and hemi cranial pain. Prompt initiation of corticosteroid therapy can lead to rapid symptom resolution and favorable outcomes in patients with Tolosa-Hunt syndrome.

Keywords: Tolosa-Hunt Syndrome, ophthalmoplegia, cranial nerve palsies, corticosteroids, case report.

INTRODUCTION

Tolosa-Hunt Syndrome (THS) is a rare condition that is known for causing painful ophthalmoplegia. It has been observed that this condition tends to respond well to treatment with steroids [1]. The syndrome was first described by Tolosa in 1954. Later, Hunt conducted further investigations and reported six cases. These cases involved unilateral retro-orbital pain along with extraocular nerve palsies. It was observed that steroid therapy led to significant improvement in these cases. The estimated annual incidence of THS is around one case per million per year [2]. In Tolosa-Hunt Syndrome, patients often feel a continuous, throbbing pain behind the eye. This pain usually starts a few days before they develop ophthalmoplegia [3]. Inflammation within the cavernous sinus can lead to dysfunction of cranial nerves III, IV, VI, and the ophthalmic branch of cranial nerve V [4]. While the condition is typically unilateral, bilateral symptoms can occur in approximately 4 to 5 percent of cases [5]. The diagnosis of Tolosa-Hunt Syndrome (THS) is usually determined by observing the symptoms experienced by the patient, along with the results of neuroimaging tests and the response to corticosteroid treatment [6].

According to the "International Headache Society", the suggested diagnostic criteria for THS involve having a headache on one side and finding proof of "granulomatous inflammation" in the "cavernous sinus", "superior orbital fissure", or orbit. This evidence can be confirmed through magnetic resonance imaging (MRI) or biopsy [7]. Additionally, there should be a weakness affecting one or more of the ipsilateral cranial nerves III, IV, and/or VI [8]. The headache should be on the same side as the site of inflammation and should either develop concurrently or

up to two weeks before the occurrence of oculomotor paresis [9]. Furthermore, the diagnosis of THS should be made only when alternative explanations fail to better account for the observed symptoms [10]. Performing a contrast-enhanced MRI is very important when evaluating patients with painful ophthalmoplegia. This is mainly done to eliminate the possibility of other potential causes [11]. In individuals with Tolosa-Hunt Syndrome (THS), MRI findings may reveal significant features such as cavernous sinus enlargement with enhanced abnormal tissue upon gadolinium administration, abnormal convexity of the "cavernous sinus wall", and "localized narrowing of the intra-cavernous internal carotid artery [12, 13]. Glucocorticoid therapy is important for both diagnosis and treatment purposes. When pain goes away quickly, usually within 24 to 72 hours, it helps to confirm the suspected diagnosis of THS [14]. Moreover, the enhancement of cranial nerve palsies and subsequent reversal of MRI abnormalities within a timeframe of two to eight weeks further strengthens the diagnosis [8].

CASE PRESENTATION

A 35-year-old man came to the Emergency Department due to experiencing intense, throbbing pain in his orbit and half of his head on the right side for the past two days. The pain was exacerbated by eye movement and accompanied by ipsilateral redness in the eye, mild photophobia, and blurred vision. The patient had no significant medical history prior to this episode.

Diagnostic Assessment

Eye Evaluation

During the eye evaluation, several findings were observed. The patient had a Best Corrected Visual Acuity (BCVA) of 0.9/1.0 due to myopic refractive error, while the Intraocular Pressure (IOP) measured within the normal range at 14/15 mmHg. Color vision was normal. Mild swelling of the right eyelids was noted, along with painful eye movements specifically in the right eye. Several inferior corneal erosions were present, which were stained with fluorescein. Temporal conjunctival chemosis and diffuse mild conjunctival superficial and deep vessels were observed, with a Phenylephrine 2.5% eyedrop test indicating mild deep vessel congestion. No discharges were present. The anterior chamber was quiet, and the pupil was round, regular, and reactive. The lens appeared clear, as did the anterior vitreous. Fundoscopy, conducted after pupil dilation, revealed normal findings for the vitreous body, optic disc, macula, optic disc, peripheral retina, and retinal vasculature. Optical Coherence Tomography (OCT) of the macula and optic disc also showed normal results. The examination of the left eye did not reveal any abnormalities. Furthermore, the patient received consultations from an Ear, Nose, and Throat (ENT) specialist and a neurologist, which ultimately led to their admission to the hospital.

Further Diagnostic Assessments:

To investigate the underlying cause, the following diagnostic tests were conducted:

MRI

Magnetic Resonance Imaging (MRI) with and without contrast of the brain, orbits, sinuses, and venogram. The findings showed a soft tissue lesion in the right orbital apex extending into the right cavernous sinus, with a possibility of an inflammatory nature, such as Tolosa-Hunt syndrome. No definite evidence of cavernous sinus thrombosis was noted, and the sinuses appeared clear. Other investigations conducted in this case included a Chest X-ray to assess the chest area. Additionally, a range of laboratory tests were performed, including a Complete Blood Count (CBC), C-reactive protein (CRP), Erythrocyte Sedimentation Rate (ESR), D-Dimer, Prothrombin Time (PT), Partial Thromboplastin Time (PTT), Potassium, Sodium, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Creatine Kinase (CK), Ferritin, Fasting Blood Sugar (FBS), Glycated Hemoglobin (HbA1c), and Cholesterol levels. Serological tests were also conducted, which included Angiotensin-Converting Enzyme (ACE), Venereal Disease Research Laboratory (VDRL), ds-Anti DNA, Anti SS-A, and Anti Smith antibodies. Urinalysis with culture and sensitivity, as well as creatinine levels, were assessed. An eye swab was collected for culture and sensitivity analysis. A Lumbar Puncture procedure was performed. Furthermore, Antiphospholipid Antibodies (APA) testing for IgG and IgM, Myeloperoxidase (MPO) antibodies for P-ANCA, and Proteinase 3 (PR3) antibodies for C-ANCA were carried out. Serological tests for Varicella-Zoster Virus (VZV) IgG and IgM, Dengue Virus IgM, and a COVID-19 swab test were conducted. Additionally, Protein S and C activity, Factor V Leiden, and Factor VIII levels were evaluated. Hematology and serology findings were unremarkable, indicating no significant abnormalities were detected in these investigations.

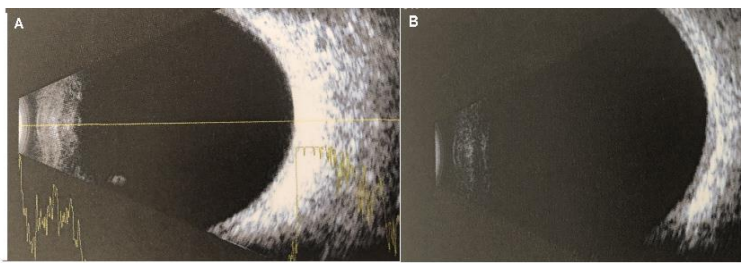

Figure 1: Ultrasound B-scan was within normal limits

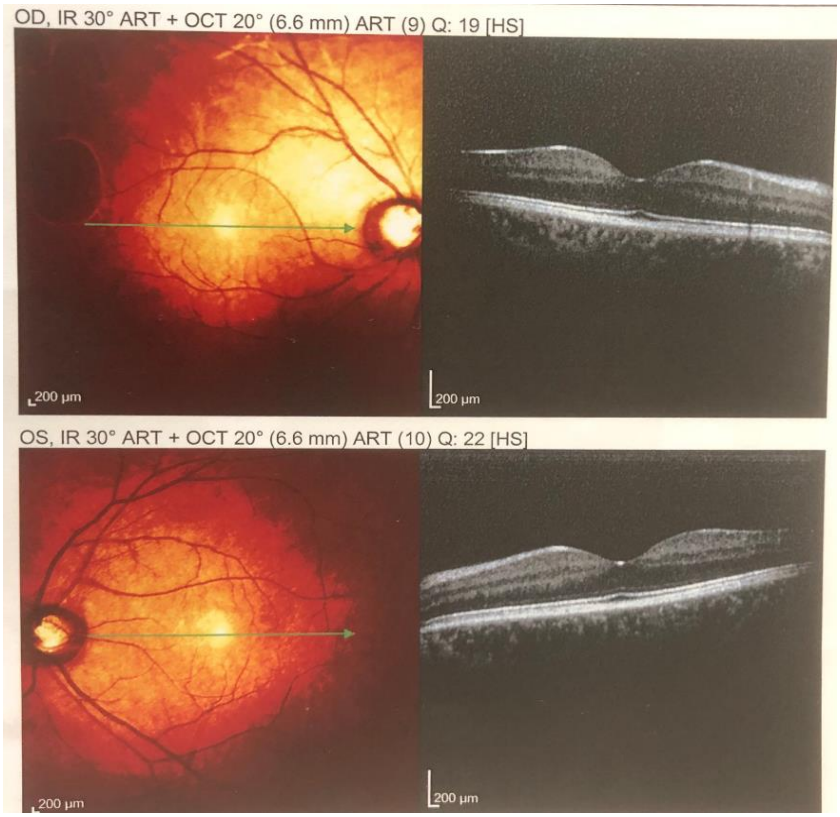

Figure 2: OCT Macula was within normal limits

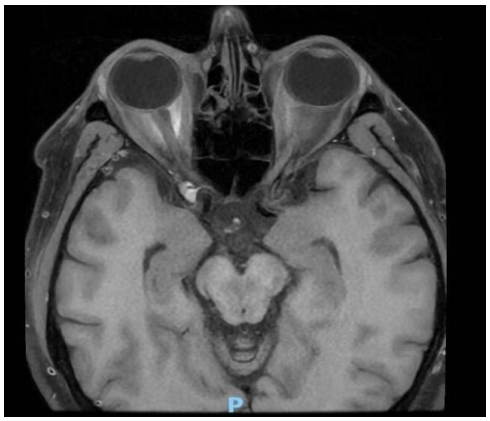

Figure 3: MRI showed a soft tissue lesion in the right orbital apex extending into the right cavernous sinus

Treatment and Management

The patient's treatment plan included administering Intravenous Solumedrol (Methylprednisolone) at a dose of 1 gram for five days. This was followed by taking oral Prednisolone at a dose of 60mg daily for one week. The dosage was then gradually reduced over a three-week period. Gastric protection with Esomeprazole 40mg daily was administered. Topical lubricants and non-steroidal anti-inflammatory eye drops were used. The patient experienced a dramatic improvement in headache symptoms after the first dose of steroids. After six days of hospitalization, the patient had no headache, a quiet eye, and a Best Corrected Visual Acuity (BCVA) of 1.0/1.0, with a normal eye examination.

DISCUSSION

When evaluating patients who have a headache in primary care or the emergency department, our main goal is to make sure there are no alarming symptoms present. These symptoms could be a sign of a more serious underlying cause. The Tolosa-Hunt syndrome (THS) is a cause of craniofacial pain that is not widely known. It is characterized by symptoms such as eye pain, blurred vision, and weakness in the muscles that control eye movement. This condition is associated with the paralysis of one or more cranial nerves that are responsible for eye movement [14]. Different combinations of these “nerve palsies” may occur, indicating the location of the abnormality in the area of

the cavernous sinus or superior orbital fissure [8]. Our patient was also presented with throbbing orbital and hemi cranial pain localized to the right side. The pain was exacerbated by eye movement and accompanied by ipsilateral redness in the eye, mild photophobia, and blurred vision. Even though it is widely recognized as a harmless condition, it is important for patients to be evaluated quickly in order to rule out tumors, vascular issues, and other types of inflammation [9]. Once the diagnosis is confirmed, early treatment can be initiated. After receiving treatment, it has been noticed that around 50% of patients who have been diagnosed with THS might experience a relapse in the near future, either in the coming months or years. Recurrence has the potential to occur at the same site, on the opposite side, or sometimes on both sides [15]. Due to the wide range of possible diagnoses and the potential for misdiagnosis, a definitive diagnosis of THS can only be made after ruling out other conditions that may present similar symptoms. Cavernous sinus thrombosis is a significant differential diagnosis [16].

Aseptic meningitis can happen due to an infection, either septic or as a secondary result of an infectious process [17]. The patient may exhibit proptosis, which is the protrusion of the eyeball, along with swelling of the eyelids, excessive tearing, and chemosis, which is the swelling of the conjunctiva [12]. These symptoms are accompanied by eye pain and ophthalmoplegia, which is the paralysis or weakness of eye muscles [18]. Our patient was also presented with multiple eye complaints and numerous tests were conducted to make the final diagnosis. MRI of the brain with contrast, particularly when viewing it from the coronal perspective, is an essential diagnostic procedure. It aids in ruling out various disease processes, although its specificity is relatively low [19]. Yousem *et al.* conducted a study involving 11 patients, revealing pathological MRI findings in the cavernous sinus of nine individuals [13]. Among these nine patients, six had an enlarged cavernous sinus, and five exhibited a convex lateral wall in the affected sinus. Additionally, eight patients displayed an extension into the orbital apex. In our case, an MRI was also conducted. The MRI revealed a soft tissue lesion located in the right orbital apex, which extends into the right cavernous sinus. Tolosa-Hunt syndrome, characterized by its inflammatory nature, is typically treated with high-dose glucocorticoids as the first-line approach [20]. This treatment has been shown to bring about a swift resolution of orbital pain within 1-3 days, thereby confirming the diagnosis. Our patient demonstrated a similar response, experiencing a significant reduction in pain with the first episode of steroids with a complete resolution of symptoms in six days. According to a study, 40% of patients achieved pain relief within 72 hours, and 78% within one week [21]. However, the resolution of neuropathies may take months, requiring a more extended period of steroid treatment. Following an initial high dose of corticosteroids, a gradual tapering of the oral dosage over several weeks is recommended, accompanied by regular follow-up and subsequent MRI scans to monitor the disease's resolution [22]. Alternatively, immunosuppressive drugs can be considered as another treatment option [15]. Despite treatment efforts, recurrences of Tolosa-Hunt syndrome are common, leading to overall poor quality of life for affected individuals.

CONCLUSION

This case report focuses on a patient with Tolosa-Hunt Syndrome (THS) and highlights their clinical presentation, diagnostic evaluation, and successful management. It underscores the significance of considering THS as a potential diagnosis in patients presenting with unilateral orbital pain and ophthalmoplegia. Further research is necessary to enhance our understanding of the etiology and optimal treatment strategies for this rare condition. However, it is crucial to bear in mind the following considerations when managing THS. THS is a diagnosis of exclusion, as other conditions such as cavernous sinus lesions (aneurysm, fungal infection, meningioma, lymphoma, immunoglobulin G4-related ophthalmic disease, schwannoma, pituitary adenoma with or without apoplexy, carotid-cavernous fistula, metastasis, sarcoidosis, and cavernous sinus thrombosis) should be ruled out. Positive therapeutic responses to systemic steroid therapy can also occur in neoplastic mass lesions like lymphoma. Additionally, prior to initiating steroid therapy, it is important to exclude other infectious conditions such as orbital and sinus infections. Moreover, Long-term follow-up is essential to monitor the patient's progress and ensure appropriate management.

REFERENCES

1. Siddhanta, K. C., Shreeyanta, K. C., Kunwar, P., & Dhungana, K. (2021). Tolosa-Hunt Syndrome: A Case Report. *JNMA: Journal of the Nepal Medical Association*, *59*(238), 604.
2. Murtaza, G., Konowitz, N., Lu, H., Faqah, A., & Kuruvilla, A. (2017). An interesting case of tolosa-hunt syndrome in a young male. *Journal of Investigative Medicine High Impact Case Reports*, *5*(1), 2324709616689478.
3. Paović, J., Paović, P., Bojković, I., Nagulić, M., & Sredović, V. (2012). Tolosa-Hunt syndrome-diagnostic problem of painful ophthalmoplegia. *Vojnosanitetski pregled*, *69*(7), 627-630.
4. Munawar, K., Nayak, G., Fatterpekar, G. M., Sen, C., Zagzag, D., Zan, E., & Hagiwara, M. (2020). Cavernous sinus lesions. *Clinical Imaging*, *68*, 71-89.
5. Zhang, X., Zhou, Z., Steiner, T. J., Zhang, W., Liu, R., Dong, Z., ... & Yu, S. (2014). Validation of ICHD-3 beta diagnostic criteria for 13.7 Tolosa-Hunt syndrome: Analysis of 77 cases of painful ophthalmoplegia. *Cephalalgia*, *34*(8), 624-632.

6. Kline, L. B., & Hoyt, W. F. (2001). The Tolosa-hunt syndrome. *Journal of Neurology, Neurosurgery & Psychiatry*, *71*(5), 577-582.
7. Huseyin, K., Lale, T. S., Burak, Y., Tolga, K., Pinar, K., & Kerem, S. D. (2019). A case of obstructed hemivagina and ipsilateral renal anomaly syndrome complicated with pyometra: tips and tricks for laparoscopic hemihysterectomy. *Fertility and Sterility*, *112*(1), 177-179.
8. Dutta, P., & Anand, K. (2021). Tolosa–Hunt syndrome: A review of diagnostic criteria and unresolved issues. *Journal of Current Ophthalmology*, *33*(2), 104.
9. Kim, H., & Oh, S. Y. (2021). The clinical features and outcomes of Tolosa-Hunt syndrome. *BMC ophthalmology*, *21*(1), 237.
10. Olesen, J., Bendtsen, L., & Goadsby, P. (2018). Comité de clasificación de la cefalea de la Sociedad Internacional de Cefaleas (IHS), III edición de la clasificación internacional de las cefaleas. *Cephalalgia, 38*(1), 1-211.
11. Kapila, A. T., Ray, S., & Lal, V. (2022). Tolosa–Hunt Syndrome and IgG4 diseases in Neuro-Ophthalmology. *Annals of Indian Academy of Neurology*, *25*(Suppl 2), S83.
12. Bugeme, M., Cissé, O., Mukuku, O., & Diop, A. G. (2020). Tolosa–Hunt Syndrome: A Painful Ophthalmoplegia. *Case reports in neurological medicine*, *2020*.
13. Ata, F., Yousaf, Z., Arachchige, S. N. M., Rose, S., Alshurafa, A., Muthanna, B., ... & Zahid, M. (2021). The demographics of Tolosa-Hunt syndrome in Qatar. *Eneurologicalsci*, *24*, 100359.
14. Tsirigotaki, M., Ntoulios, G., Lioumpas, M., Voutoufianakis, S., & Vorgia, P. (2019). Tolosa-Hunt syndrome: clinical manifestations in children. *Pediatric Neurology*, *99*, 60-63.
15. Arthur, A., Sivadasan, A., Mannam, P., Prabakhar, A. T., Aaron, S., Mathew, V., ... & Alexander, M. (2020). Tolosa–Hunt syndrome: long-term outcome and role of steroid-sparing agents. *Annals of Indian Academy of Neurology*, *23*(2), 201.
16. Gogu, A. E., Motoc, A. G., Docu Axelerad, A., Stroe, A. Z., Gogu, A. A., & Jianu, D. C. (2022). Tolosa–Hunt Syndrome and Hemorrhagic Encephalitis Presenting in a Patient after COVID-19 Vaccination Followed by COVID-19 Infection. *Brain Sciences*, *12*(7), 902.
17. Wiener, J., & Cron, R. Q. (2020). Successful treatment of pediatric Tolosa-Hunt syndrome with adalimumab. *European journal of rheumatology*, *7*(Suppl 1), S82.
18. Etheridge, T., Jones, J., Caskey, E. L., Digre, K. B., Warner, J. E., & Seay, M. D. (2022). Tolosa-hunt syndrome after COVID-19 infection. *Cephalalgia Reports*, *5*, 25158163221078977.
19. Hao, R., He, Y., Zhang, H., Zhang, W., Li, X., & Ke, Y. (2015). The evaluation of ICHD-3 beta diagnostic criteria for Tolosa–Hunt syndrome: a study of 22 cases of Tolosa–Hunt syndrome. *Neurological Sciences*, *36*, 899-905.
20. Zhang, X., Zhang, W., Liu, R., Dong, Z., & Yu, S. (2014). Factors that influence Tolosa–Hunt syndrome and the short-term response to steroid pulse treatment. *Journal of the neurological sciences*, *341*(1-2), 13-16.
21. Gama, B. P., & Silva-Néto, R. P. (2020). Tolosa-Hunt syndrome in childhood and adolescence: a literature review in the last 10 years. *Neuropediatrics*, *52*(01), 001-005.
22. Douedi, S., Awad, M., Shenouda, D., Mack, P., & Carson, M. P. (2020). Tolosa-Hunt syndrome: A non-classical presentation of a rare cause of unilateral headache and painful ophthalmoplegia. *Journal of Clinical Medicine Research*, *12*(4), 266.