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Case Series

Ophthalmology Section

Tolosa-hunt Syndrome following COVID-19 Pandemic: A Case Series Describing the Clinical Presentations and Response to Steroids

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ABSTRACT

Tolosa-Hunt Syndrome is a rare condition characterised by unilateral periorbital headache with ophthalmoplegia caused by inflammation of the superior orbital fissure or cavernous sinus. There has been an increase in cases of Tolosa-Hunt Syndrome following the Coranavirus Disease-19 (COVID-19) pandemic. This case series describes the clinical details of three such patients and their response to steroid therapy. The first patient was a 61-year-old woman with a history of post COVID infection who had received two doses of the COVID vaccine. She presented with second, third, fifth, and sixth cranial nerve palsies of the left eye. She received steroid therapy, following which there was recovery of extraocular movements and improvement in vision. The second patient was a 43-year-old male who had received two doses of the COVID vaccine. He presented with multiple cranial nerve palsies affecting the second, partial third, and fifth cranial nerves of the left eye. He reported symptomatic relief and improvement in ptosis after steroid therapy. The third patient was a 40-year-old male who had received two doses of the COVID vaccine. He presented with painful external ophthalmoplegia involving the second, third, fourth, and sixth cranial nerves of the right eye. Following steroid therapy, he experienced symptomatic relief and recovery of extraocular movements.

Keywords: Cavernous sinus, Cranial nerve palsy, Coronavirus Disease-19, Ophthalmoplegia, Periorbital headache, Vaccination

INTRODUCTION

Tolosa-Hunt Syndrome is a rare condition characterised by unilateral periorbital headache with ophthalmoplegia, caused by idiopathic granulomatous inflammation of the superior orbital fissure or cavernous sinus [1]. It presents with painful ophthalmoplegia due to multiple cranial nerve palsies and typically shows an excellent response to steroid therapy. In the past two years, an increased number of patients with a history of COVID infection or vaccination have presented to the Ophthalmology Outpatient Department with unilateral painful ophthalmoplegia, diagnosed by exclusion as Tolosa-Hunt Syndrome. Here, we describe three cases of Tolosa-Hunt Syndrome, their clinical presentations, and the outcomes following steroid therapy. Informed consent was obtained from all three patients.

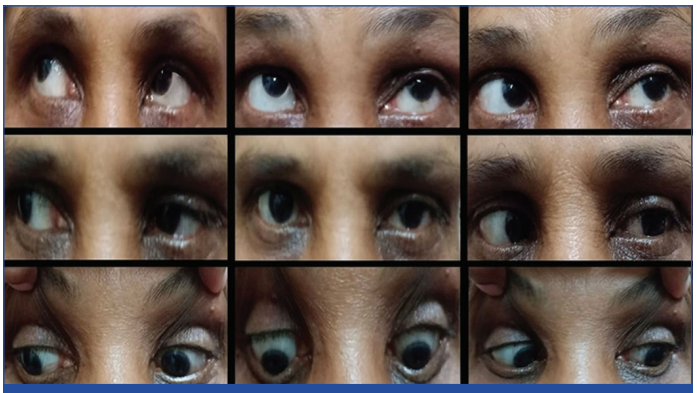
CASE SERIES

Case 1

A 61-year-old woman presented to the Ophthalmology Out Patient Department (OPD) with a two-week history of periorbital pain, ptosis, and decreased vision in the left eye (OS). She has a history of type 2 diabetes mellitus and hypertension, managed with oral medications. The patient also had a COVID-19 infection one year prior and had received two doses of the COVID vaccine ten months ago. On examination, her best-corrected visual acuity was 6/6 in the right eye (OD) and counting fingers close to face in the left eye (OS). The left eye (OS) showed limitation of extraocular movements: -3 in abduction and -1 in elevation [Table/Fig-1], mild ptosis, decreased corneal sensation, Relative Afferent Pupillary Defect (RAPD), and disc edema. The right eye (OD) was normal.

The clinical diagnosis was multiple cranial nerve palsies involving the second, third, fifth, and sixth cranial nerves of the left eye (OS).

The Erythrocyte Sedimentation Rate (ESR) was 70 mm/hour, and C-reactive Protein (CRP) was positive at 10 mg/L. Magnetic Resonance Imaging (MRI) of the brain, orbit, and paranasal sinuses showed increased Protein Density Fat-Saturated (PDFS) signal intensity involving the orbital and canalicular segments of the left optic nerve. Neoplasms, aneurysm, and cavernous sinus thrombosis were excluded. The patient was diagnosed with Tolosa-Hunt syndrome and started on injection dexamethasone 8 mg twice daily for five days, followed by once daily for five days. This was subsequently transitioned to oral prednisolone, starting at 1 mg/kg and tapered over three weeks.



[Table/Fig-1]: Limitation of abduction and elevation in Left eye.

The patient experienced rapid relief of symptoms and demonstrated improvement in extraocular movements in the left eye (OS) from day two of treatment. She regained the full range of extraocular movements after completing the intravenous steroid course. After seven days of oral steroids, she was completely symptom-free, with a best-corrected visual acuity of 6/9 in the left eye (OS). She remained asymptomatic at one-month follow-up.

Case 2

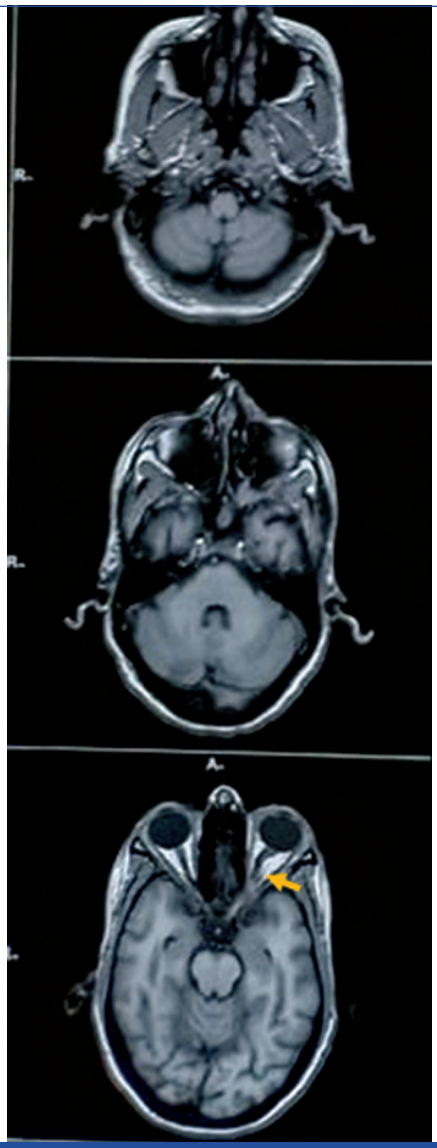
A 43-year-old male with no history of systemic illness presented to the OPD with sudden-onset defective vision in the left eye (OS) that had

developed one month prior. The condition was painful, progressive, and preceded by a two-week history of left-sided headache. He had been on Ayurvedic medications and topical nepafenac eye drops in the left eye (OS) for one month. The patient had no history of COVID infection but had received two doses of COVID vaccination 18 months prior. On examination, best-corrected visual acuity was 6/6 in the right eye (OD) and absent perception of light in the left eye (OS). The left eye (OS) showed 15° exotropia, 10° hypotropia, mild ptosis, decreased corneal sensations, a grade 2 RAPD and partial optic atrophy. The right eye (OD) was normal.

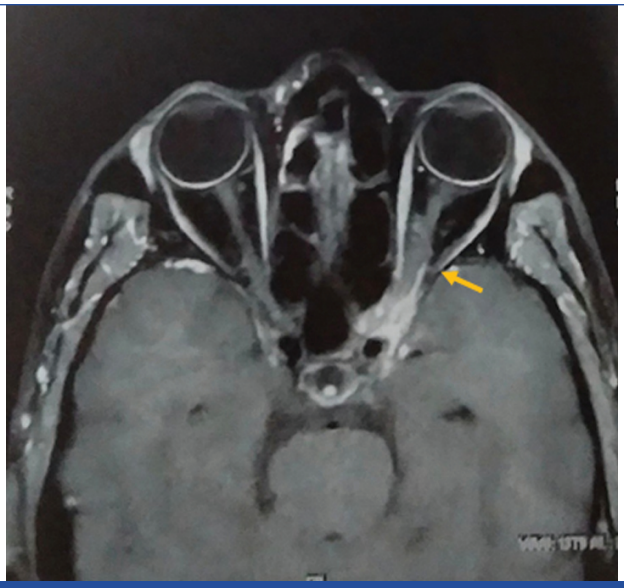
The clinical diagnosis was multiple cranial nerve palsies involving the second, partial third, and fifth cranial nerves of the left eye (OS). MRI brain and orbit with Magnetic Resonance Angiography (MRA) revealed enhancing soft tissue thickening in the left orbital apex and anterior cavernous sinus, with increased stranding of adjacent orbital fat planes causing encasement and compression of the intracanalicular segment of the left optic nerve, suggestive of Tolosa-Hunt Syndrome [Table/Fig-2,3].

Visual Evoked Potential (VEP) showed normal P100 latency in the right eye (OD) and absent waves in the left eye (OS) [Table/Fig-4].

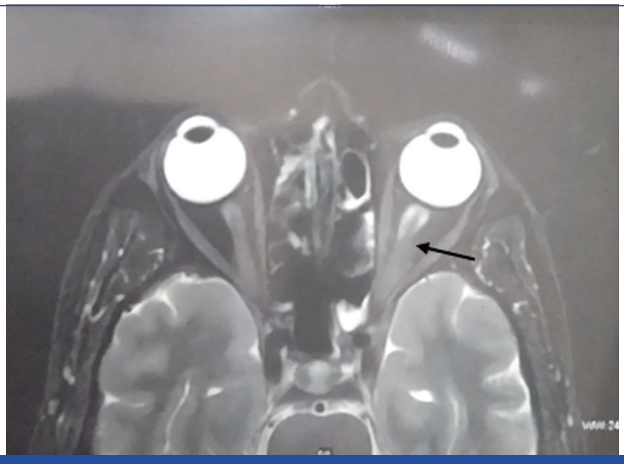
The patient was started on injection dexamethasone 8 mg twice daily for five days, followed by once daily for five days, then transitioned to oral prednisolone starting at 1 mg/kg and tapered over four weeks. Steroid therapy was continued for six weeks. He experienced pain relief and improvement in ptosis in the left eye (OS) at the two-month review; however, vision in the left eye remained absent.



[Table/Fig-2]: MRI brain and orbit- axial section T1 weighted image showing increased Protein Density Fat-Saturated (PDFS) signal intensity involving the orbital and canalicular segment of the left optic nerve (black arrow).



[Table/Fig-3]: MRI brain and orbit- axial section T1 weighted image showing enhancing soft tissue thickening in the left orbital apex and anterior cavernous sinus (black arrow) causing encasement and compression of the intracanalicular segment of the left optic nerve.



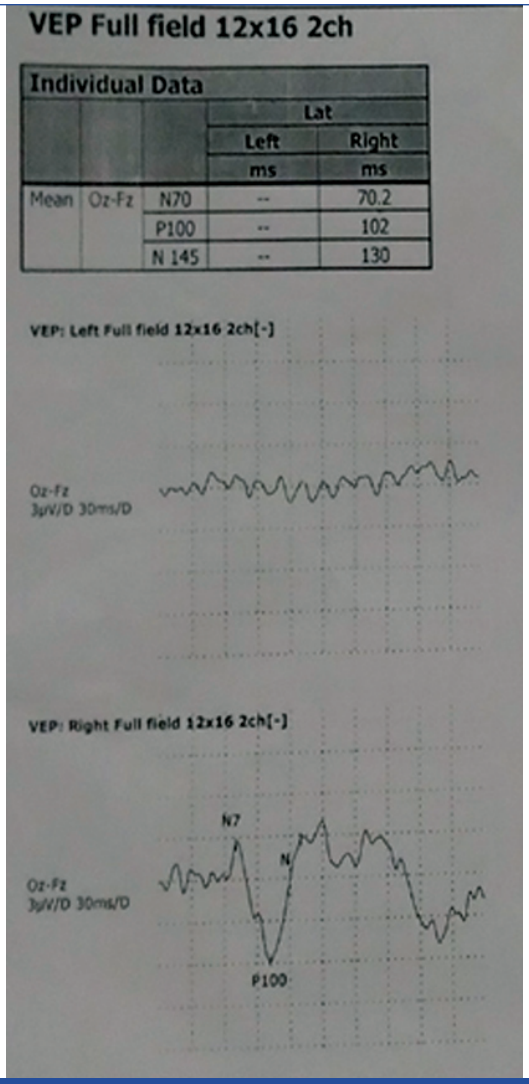
[Table/Fig-4]: MRI brain and orbit- axial section T2 weighted image showing enhancing soft tissue thickening in the left orbital apex and anterior cavernous sinus (black arrow).

Case 3

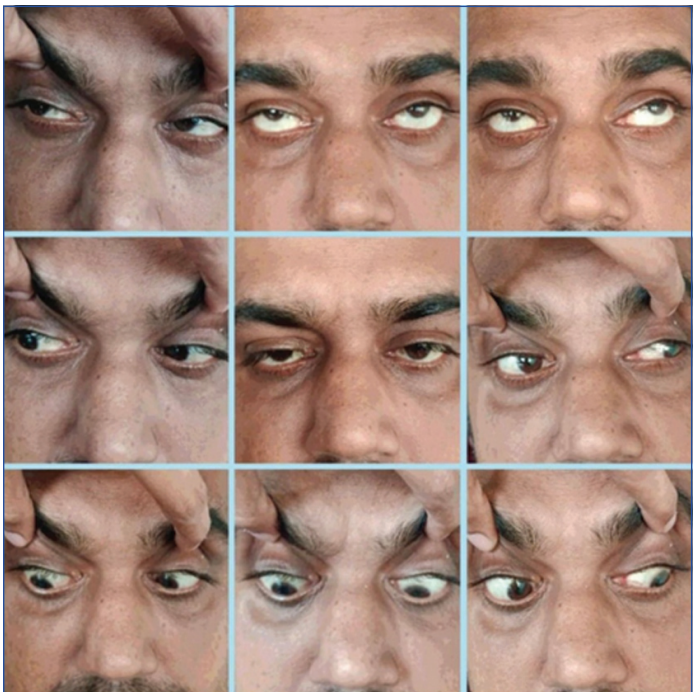
A 40-year-old male was referred from the Department of Neurology with a one-month history of defective vision in the right eye (OD), right-sided headache that developed four days after the onset of vision loss, and drooping of the right upper eyelid. The patient had no history of COVID infection but had received two doses of COVID vaccination one year prior. On examination, vision in the right eye (OD) was absent, and uncorrected visual acuity in the left eye (OS) was 6/6. There was painful ophthalmoplegia involving the second, third, fourth, and sixth cranial nerves of the right eye (OD), with limitation of adduction, abduction, elevation, and depression to –2 in the right eye [Table/Fig-5,6].

Intorsion was absent in the right eye, and a Relative Afferent Pupillary Defect (RAPD) was present. The Erythrocyte Sedimentation Rate (ESR) was 85 mm/hour, and C-reactive Protein (CRP) was positive at 11 mg/L. MRI findings were suggestive of Tolosa-Hunt syndrome [Table/Fig-7].

The patient was started on injection dexamethasone 8 mg twice daily for five days, followed by once daily for five days. Oral prednisolone was then administered, starting at 1 mg/kg and tapered over six weeks. Steroid therapy continued for a total of eight weeks. The patient showed a marked response to treatment: symptoms began to resolve within four days and completely resolved within ten days. However, there was no improvement in vision in the right eye. At the two-month follow-up, his extraocular movements were fully restored.



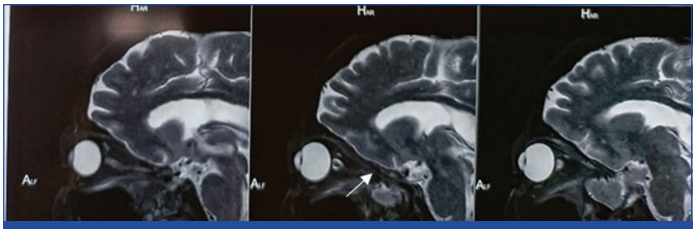
[Table/Fig-5]: Visual Evoked Potential (VEP) showed normal P100 latency in the right eye and absent waves in the left eye.



[Table/Fig-6]: Limitation of extraocular movements in right eye.

DISCUSSION

Tolosa-Hunt syndrome (THS) is characterised by severe unilateral periorbital headache and ipsilateral painful ophthalmoplegia [1]. The International Classification of Headache Disorders defines Tolosa-Hunt syndrome as a unilateral headache followed by third, fourth, and/or sixth cranial nerve palsies within two weeks or occurring simultaneously, localising around the ipsilateral eye. It is caused by granulomatous inflammation involving the superior orbital fissure, cavernous sinus, or orbit, detectable via MRI or biopsy. THS is characterised by palsies involving one or more of the ipsilateral third, fourth, and/or sixth cranial nerves, and cannot be explained by any alternate etiology of headache [2].



[Table/Fig-7]: MRI brain and orbit- sagittal section T2 weighted image showing enhancing soft tissue thickening in the right orbital apex and anterior cavernous sinus (white arrow).

In this case series, the first patient was an elderly woman with a history of COVID infection and vaccination, who developed multiple cranial nerve palsies involving the second, third, fifth, and sixth cranial nerves in the left eye (OS). Intravenous steroids followed by a gradually tapered oral steroid regimen led to significant improvement in vision and recovery of extraocular movements. The second and third patients were young males with a history of COVID vaccination who unfortunately lost vision in one eye, also presenting with multiple cranial nerve palsies. Following steroid therapy, they experienced pain relief and recovery of extraocular movements, but no improvement in vision. Oral steroids were continued for a longer duration to prevent recurrence. Around 50% of THS patients may experience recurrence, and in such cases, long-term oral steroids or steroid-sparing agents may be required.

Rapid pain relief with steroids is characteristic of Tolosa-Hunt syndrome. A study by Zhang X et al., (2014) reported that younger patients exhibited a more effective short-term response of cranial nerve palsies to steroid therapy [3]. A study published in 2023 by Ramirez JA et al., described MRI findings in THS, which help exclude other lesions such as lymphoma involving the cavernous sinus. MRI features of THS include enlargement with dural margin convexity, T1-isointense abnormal tissue, and T2 isointense to hypointense signal changes [4]. Kmeid M et al., studied the diagnostic criteria and management of THS. In steroid-resistant patients, newer management strategies include steroid-sparing agents or radiotherapy [5]. As reported in a 2022 case by Etheridge T et al., a 12-year-old otherwise healthy girl developed THS after COVID-19 infection, presenting with partial right third cranial nerve palsy, likely due to COVID-19-related immune dysregulation [6].

Vardanyan & Khachatryan reported a case of a 65-year-old female with COVID-19 infection who developed painful left ophthalmoparesis with third and sixth cranial nerve palsies suggestive of THS. She was treated with corticosteroids and experienced relief of pain [7]. Gogu AE et al., (2022) described a 45-year-old man who, nine days after receiving the COVID-19 vaccination and being COVID-positive, developed second, third, fourth, fifth, and sixth cranial nerve palsies suggestive of THS. Steroid therapy provided significant pain relief, with minimal improvement in eye motility and visual acuity [8]. A retrospective case series by Ang T et al., (2023) reported THS following COVID-19 infection and vaccination. Symptoms developed five to thirty-five days after COVID vaccination, although delayed presentation could not be excluded. Several cases of orbital inflammation were reported after the first dose of COVID-19 vaccination. Repeated exposure to the vaccine, acting as an immunogenic stimulus, may have precipitated orbital inflammation following the second or third dose [9]. The differential diagnoses of Tolosa-Hunt syndrome include neoplasms, aneurysm, vasculitis, cavernous sinus thrombosis, carotid-cavernous fistula, infection, and sarcoidosis [10].

Interestingly, we have now observed a marked reduction in cases of orbital inflammation, including Tolosa-Hunt syndrome. This suggests that COVID-19-related immune dysregulation may have contributed to the increased incidence of these cases in the post-pandemic period. Further research is needed to explore the relationship between viral infections and immune dysregulation leading to orbital inflammation, including Tolosa-Hunt syndrome.

CONCLUSION(S)

In this case series, we described three patients with Tolosa-Hunt syndrome presenting with painful ophthalmoplegia and multiple cranial nerve palsies. An increase in cases of Tolosa-Hunt syndrome was noted following the COVID-19 pandemic. Diagnosis was based on clinical symptoms and MRI findings, and prompt steroid therapy resulted in excellent recovery in terms of pain relief and restoration of extraocular movements. However, the second and third patients unfortunately lost vision in one eye.

Further research is needed to investigate the role of viral infections and associated immune dysregulation in the development of orbital inflammation, including Tolosa-Hunt syndrome.

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