Case Report

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Recurrent Tolosa-Hunt syndrome: a case report

Shashank Neupane, MBBS[a], Prasamsa Pudasaini, MBBS[a], Bishal Dhakal, MBBS[a], Pasang Sherpa, MBBS[b], Pooja Rokaya, MBBS[a,*], Anukul Subedi, MBBS[c]

Introduction and importance: Tolosa-Hunt syndrome is a rare condition with unknown aetiology that manifests clinically as unilateral orbital pain and ophthalmoplegia. It is a diagnosis of exclusion that resolves spontaneously but can recur and respond dramatically to systemic steroids.

Case presentation: The authors herein report a case of a 38-year-old male who presented with horizontal diplopia, limited outward movement of the right eye, and blurry vision for two days which was managed with oral Prednisolone. The patient visited 3 months later with progressive ptosis and vertical diplopia with periorbital pain over the right eye. It was eventually diagnosed via magnetic imaging resonance studies and successfully treated for Tolosa-Hunt syndrome with IV methylprednisolone followed by oral prednisolone.

Clinical discussion: Hence, the typical clinical presentation of the case with significant response to steroids, exclusion of other conditions from investigation and imaging, and subsequent recurrence of similar symptoms were crucial for making the diagnosis of Tolosa-Hunt syndrome.

Conclusion: Tolosa-Hunt syndrome is a syndrome of painful ophthalmoplegia which responds well to steroid therapy but has a tendency to recur. Hence, patients must be adequately informed about the reoccurrence and kept under follow-up.

Keywords: case report, diplopia, painful ophthalmoplegia, recurrence, tolosa-hunt syndrome

Introduction

Tolosa and Hunt independently described a condition of unilateral painful ophthalmoplegia causing periorbital or hemicranial pain with ipsilateral oculomotor nerve palsies, in the years 1954 and 1961 respectively[1–3]. It has since been occasionally identified and described and has been recognised by the National Organisation for Rare Disorders (NORD) as a rare disorder, with an estimated annual incidence of approximately one case per one million people[4]. Although classically referred to as a unilateral entity, bilateral involvement occurs in ~5% of cases. The average age of onset for this syndrome is 41 years, but it can occur at any age from the first to eight decades of life[5] with no gender preference[1,4,6]. Here, we report a case of Tolosa-Hunt Syndrome in an adult male presenting with horizontal diplopia and restricted eye movements.

HIGHLIGHTS

- Tolosa-Hunt syndrome is nonspecific granulomatous inflammation characterised by lymphocyte and plasma cell infiltration, primarily in and around the cavernous sinus, with variable extent into and beyond the superior orbital fissure/apex.
- Patient presented with horizontal diplopia, restriction of movement, watery discharge from the right eye with blurring of vision during first episode and periorbital pain, ptosis, and ophthalmoplegia during recurrent episode.
- The typical clinical presentation of the case with significant response to steroids, recurrence of similar symptoms, and exclusion of other conditions from investigation and imaging were crucial for making the diagnosis.
- Symptoms usually resolve without intervention but may recur. Therefore, follow-up even after recovery is very crucial.

Case presentation

A 38-year-old gentleman presented to the emergency department with complaints of double vision and watery discharge from the right eye for two days. The patient also had a history of redness in the right eye for the same duration. He denied any weakness in her arms and legs, slurred speech, or difficulty swallowing. There was not any associated fever, headache, vomiting, limb weakness/numbness or trauma.

On examination, his vital signs were within the normal range, except for an elevated blood pressure of 170/120 mm of Hg. The neurological examination showed intact motor and sensory functions. However, eye examination revealed ophthalmoplegia of the right eye, with sluggish light reflex. The left eye examination was normal. His cardiac enzymes and electrocardiogram

[a]Nepalese Army Institute of Health Sciences, [b]Department of Medicine, Nepal Medical College and [c]Kathmandu Medical College and Teaching Hospital, Sinamangal, Kathmandu, Nepal

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*Corresponding author. Address: Nepalese Army Institute of Health Sciences, Kathmandu, Nepal. Tel.: +977 984 566 2307. E-mail: rokaya.pooja47@gmail.com. (P. Rokaya).

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(ECG) were normal. The patient was discharged on request but advised to follow-up in eye OPD the next day.

The following day, detailed history and ophthalmological examination showed double horizontal vision, limited outward movement of the right eye, and blurry vision. Complete blood count, inflammatory markers, and full biochemistry tests, including thyroid and liver function tests, were within the normal range. Chest X-ray and computed tomography head scan were also normal. A provisional diagnosis of right lateral rectus palsy was made, and then discharged with oral acyclovir (400 mg) and Prednisolone (8 mg) and counselled about regular ocular exercise.

On the third day following discharge, he again presented to the emergency department with complaints of blurred vision, dizziness, and increased blood pressure. His right and left eyes had 15 and 14 mm of Hg intraocular pressure.

Non-contrast computed tomography (NCCT) head revealed a small soft tissue lesion measuring 8 ×6 mm on the roof of the sphenoid sinus. Similarly, MRI demonstrated a small mucous retention cyst in the left sphenoidal sinus. Laboratory investigations were normal for muscle-specific tyrosine kinase antibodies, acetylcholine receptor binding proteins, and p-ANCA. He was medicated with oral prednisolone 60 mg (tapered over three months) and thiamine supplementation. His symptoms subsequently improved. So, he was discharged and was asked for outpatient follow-up.

Three months after the initial visit, the patients again presented to our hospital with progressive ptosis and vertical diplopia complaints. An associated headache and periorbital burning sensation over the right eye that progressed over to the left nasal bridge, left zygoma, left jaw, and left face. A detailed physical and ocular examination was done.

Ocular symptoms were found to be more severe than during the previous visit. Visual acuity was 6/12 on the right and 6/18 on the left. An ocular examination of the right eye revealed ptosis, and complete restrictions of eye movements, as seen in Fig. 1; the corneal sensation was normal, the pupil was reactive to light, and a relatively apparent pupillary defect was absent. Slit-lamp examination showed no significant anterior and posterior segment findings.

Laboratory investigations that were done at this visit are shown in the (Table 1).

On investigation, his liver function test, lipid profile, protein electrophoresis, CBC, magnesium, urea, creatinine, sodium, potassium, Anti-Ds-DNA antibody, p-ANCA, and c-ANCA were normal. Lyme disease antibodies Borrelia IgG was positive and IgM negative. Serology, including human immunodeficiency virus, hepatitis C virus, hepatitis B surface antigen, and venereal disease research laboratory test (VDRL), were non-reactive.

We repeated an MRI of the brain, and this time, there were features suggestive of Tolosa-Hunt Syndrome. There was a homogeneously enhancing soft tissue component in the left cavernous sinus in the inferolateral aspect, causing a lateral bulge of the cavernous sinus wall and laterally displacing the medial temporal lobe with mild white matter oedema.

Hence, through clinical presentation of periorbital pain, paresis of third and sixth cranial nerves, features suggestive of Tolosa-Hunt syndrome and pain and paresis resolving with corticosteroids, a diagnosis of Tolosa-Hunt syndrome was made and the patient was then started on IV methylprednisolone 1 gm/day for 3 days. The patient showed rapid improvement in his symptoms. On the third day of methylprednisolone therapy, there was decreased ptosis, diplopia, and ocular pain. Likewise, oral prednisolone 60 mg daily and gastroprotective agent, pantoprazole 40 mg daily, were started on the fourth day. Despite features of steroid-induced bilateral central serous chorioretinopathy (Fig. 2), a follow-up study of the patient showed remarkable improvements in his symptoms (Table 1).

Discussion

The Tolosa-Hunt syndrome is also known as painful ophthalmoplegia, recurrent ophthalmoplegia, and ophthalmoplegia syndrome[4,6]. The syndrome of painful ophthalmoplegia consists of periorbital or hemicranial pain combined with ipsilateral ocular motor nerve palsies, oculosympathetic paralysis, and sensory loss in the distribution of the ophthalmic and occasionally maxillary parts of the trigeminal nerve[1].

Dr Eduardo Tolosa, a Spanish neurosurgeon, first reported a patient with left orbital pain, ipsilateral progressive visual loss, total left ophthalmoplegia, and reduced sensation over the first division of the trigeminal nerve in 1954. Postmortem examination revealed granulomatous inflammation of the left carotid artery and cavernous sinus[1,2]. Hunt *et al.*[3] reported similar cases in 1961. Smith and Taxdal coined "Tolosa Hunt Syndrome" in 1966[1,7].

The exact cause of Tolosa-Hunt syndrome is not known. However, it is thought to be associated with inflammation of specific areas behind the eye (cavernous sinus and superior orbital fissure)[6]. The disease begins with continuous pain caused by pressure and dysfunction of structures within the cavernous sinus, superior orbital fissure, or orbital apex[1,4,8].

The most common symptoms of Tolosa-Hunt syndrome are chronic periorbital headache[5,9], double vision[9,10], paralysis (palsy) of certain cranial nerves, and chronic fatigue. Affected individuals may also have proptosis, ptosis, and diminished vision[4,8].

Many individuals with Tolosa-Hunt syndrome experience severe periorbital pain, which is later followed by painful and decreased eye movement (ophthalmoplegia)[10]. Pain is usually the presenting symptom and can occur up to 30 days before ophthalmoplegia[6]. However, ophthalmological symptoms preceded pain in our patient as in other cases. Our patient had horizontal diplopia and watery discharge from the right eye for two days. Pain is usually located in the periorbital region[10] but can also be retroorbital[10,11] with extension into the frontal and temporal areas. Pain is usually unilateral[4,8,12] but may be bilateral[6]. The patient had unilateral periorbital pain over the right eye, which progressed to the left nasal bridge, zygoma, jaw, and face.

Tolosa-Hunt Syndrome also causes involvement in all three ocular motor nerves (oculomotor, trochlear, and abducens nerves) in various combinations, resulting in ophthalmoplegia. The ophthalmic branch of the trigeminal nerve is often involved[6]. Our patient had progressive ptosis and diplopia. A similar finding of ptosis and diplopia was seen in the case reported by K.C *et al.*[12]. This was accompanied by headache and periorbital burning sensation in our case. Ocular symptoms were found to be more severe than at the previous visit, as our patient experienced complete limitation of right eye movement at the latter visit.

Diagnostic criteria as established by the International Headache Society in 2004 are one or more episodes of unilateral orbital pain lasting for weeks if untreated; Paresis of one or more of the third,

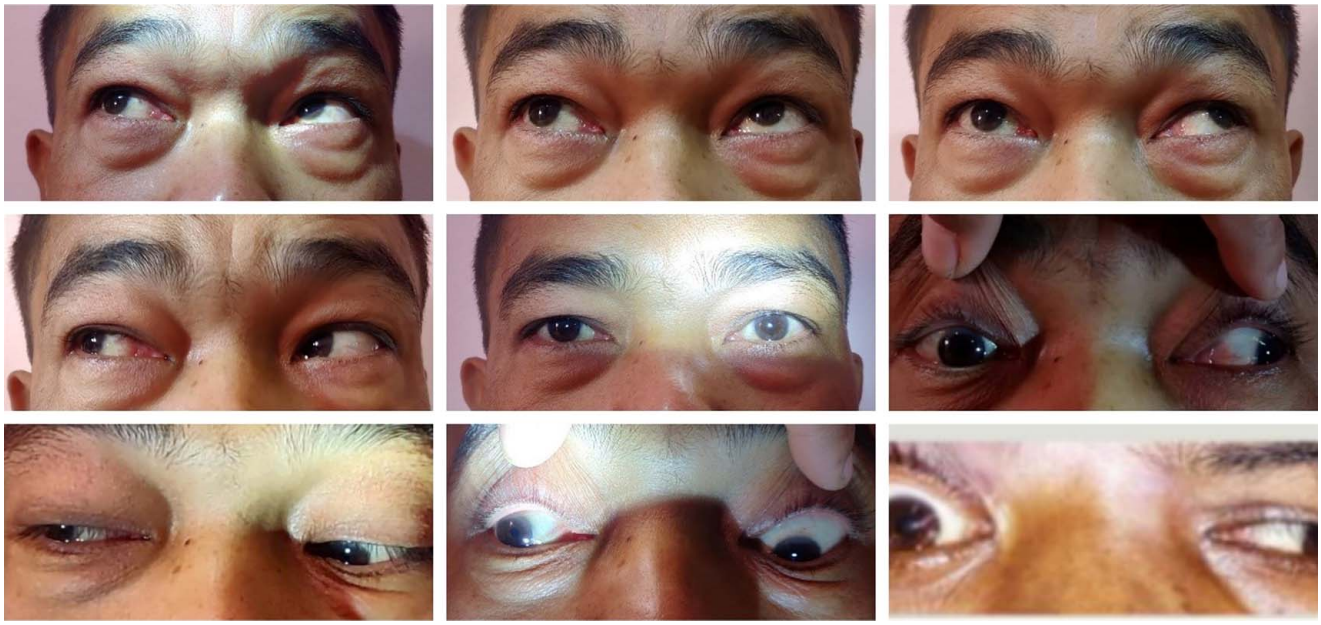

Figure 1. Extraocular movement in nine cardinal gazes. Simultaneous paralysis of Third and fourth cranial nerves in the right side.

fourth, and sixth cranial nerves, with or without evidence of a granuloma by MRI or biopsy; paresis coincident or within two weeks of the onset of pain; pain and paresis resolve within 72 h when treated with corticosteroids; and other causes ruled out by appropriate investigations[13]. Painful ophthalmoplegia has a broad differential diagnosis that includes orbital inflammatory syndromes, neoplasms, vascular anomalies, and autoimmune diseases[4,6,14]. Hence, if Tolosa-Hunt syndrome is suspected based on clinical presentation and MRI, blood and cerebrospinal fluid (CSF) tests should be performed to rule out other causes of painful ophthalmoplegia[4].

Contrast-enhanced Magnetic Resonance Imaging of the brain, particularly the coronal view, is an important diagnostic study. It

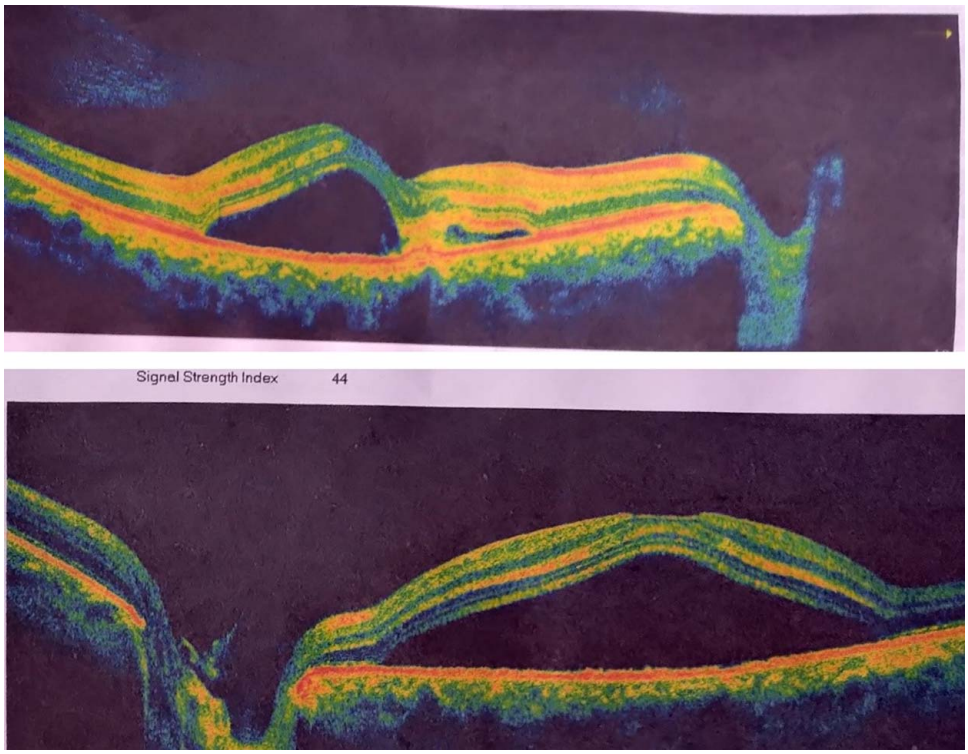

Figure 2. Optical coherence tomography bilateral eye: showing subretinal fluid in the macular area suggestive of central serous chorioretinopathy.

Table 1

Laboratory investigations of the patient during hospital visit due to recurrence of symptoms.

Lab investigation	Value of the patient	Normal lab values	Unit
Erythrocyte sedimentation rate	23	15 mm/hr.	mm
C-reactive protein	14.45	0–6.45	mg/l
Free triiodothyronine	9.4	1.4–4.2	pg/ml
Free thyroxine	2.7	0.8–2	ng/dl
Thyroid Stimulating Hormone (TSH)	0.01	0.4–6.1	micro-IU/ml
Tuberculosis (TB)-Gold Interferon-gamma release assay	213.49	> 25.0	%
Active B1 (holotranscobalamine)	32.30	25.10–165.00	pmol/l
Angiotensin-converting enzyme	31	8.0–52.0	U/l
Cholinesterase serum	9.28 kU/l	4.62–11.50	kU/l
Acetylcholine receptor binding antibody	0.17 nmol/L	< 0.40	nmol/l
Smith antibody	0.105	0.0–0.9	

helps to rule out other diseases that have caused painful ophthalmoplegia, as is rarely normal in cases of Tolosa-Hunt syndrome[15]. MRI can show thickening of the cavernous sinus due to abnormal soft tissue that is isointense on T1, iso, or hypointense on T2 and enhances with contrast. Additional MRI findings include convexity of the lateral wall of the cavernous sinus and extension into the orbital apex[6]. Sometimes, there is no finding in the earlier phase, as in our patient. Kobor and colleagues recommend repeating MRI in a patient with an initially normal MRI to detect new signs of inflammation, which may appear months after the initial presentation[12,15]. At the later visit after 3 months, a repeat MRI examination was performed, which showed a homogeneously enhancing soft tissue component in the left cavernous sinus in the inferolateral area, resulting in a lateral bulging of the cavernous sinus wall and a lateral displacement of the medial temporal lobe with mild white matter oedema.

Symptoms usually resolve without intervention but may recur[4]. High-dose glucocorticoids are the first-line treatment for Tolosa-Hunt syndrome considering its inflammatory pathology[4,6]. It relives orbital pain rapidly within 1–3 days, also serving as diagnostic confirmation[5,10,11]. Since Tolosa-Hunt syndrome responds well to steroid treatment and early cases are reversible[5], early detection is beneficial. Some patients may experience steroid-related side effects, as evidenced by our patient symptoms of steroid-induced bilateral central serous chorioretinopathy. Despite this, a follow-up study of the patient revealed remarkable improvements in his symptoms, and he was discharged home with the recommendation of follow-up.

There was clear evidence that spontaneous remissions occurred before using systemic corticosteroids. However, recurrences are common, occurring in about half of the reported patients with no clear pattern, which was also observed in this patient[16]. Therefore, patients should be informed that relapses can occur, and that patient follow-up is crucial[1,4,11].

Conclusion

Tolosa-Hunt syndrome is a painful ophthalmoplegia caused by nonspecific cavernous sinus inflammation. The Tolosa-Hunt syndrome is nonspecific granulomatous inflammation characterised by lymphocyte and plasma cell infiltration, primarily in and around the cavernous sinus, with variable extent into and beyond the superior orbital fissure/apex. Our patient's clinical presentation, particularly the involvement of oculomotor, trochlear, trigeminal, and abducens cranial nerve palsies, suggested a Tolosa-Hunt-like syndrome. This case demonstrates the importance of including Tolosa-Hunt syndrome as a differential diagnosis after all other diagnostic studies have ruled out more common etiologies for ipsilateral periorbital pain with oculomotor nerve palsy. We would also like to emphasise the importance of steroid treatment and patient follow-up even after recovery.

Ethical approval

This is a case report; therefore, it did not require ethical approval from ethics committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-chief of this journal on request.

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Author contribution

S.N., P.P., B.D. were involved in the conceptualization of the study, data collection, and writing case details. S.N., P.P. collected the data. P.S., P.R. were involved in the literature review and prepared the initial manuscript draft. P.P., A.S. and B.D. prepared the final manuscript after revising and editing the initial draft. S.N. supervised the study. All authors accepted the final version of the manuscript.

Conflicts of interest disclosure

The authors report no conflicts of interest.

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