

Ophthalmoplegia and cranial nerve deficits in an adolescent with headache

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Abstract

Tolosa–Hunt syndrome is an idiopathic, inflammatory condition involving the cavernous sinus and is characterized by unilateral, painful ophthalmoparesis. The condition often begins with retro-orbital pain followed by select cranial nerve involvement. We report the case of a 17-year-old female whose presentation with progressive left-sided headache and ophthalmoparesis culminated in the diagnosis of Tolosa–Hunt syndrome. While many of her signs and symptoms have been previously reported in the rare pediatric cases of Tolosa–Hunt syndrome described in the literature, this case illustrates a unique presentation involving cranial nerves V and VII in addition to the more commonly reported cranial nerve III, IV, and VI palsies.

Keywords

Tolosa–Hunt syndrome, ophthalmoparesis, ophthalmoplegia, cranial nerve deficit, cranial nerve palsy, headache, adolescent, pediatric

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Introduction

Tolosa–Hunt syndrome (THS), first described by Drs Tolosa (1954) and Hunt (1961), is extremely rare, with an incidence of one to two cases per million people.^{1–3} In a series of 77 patients, the mean age of onset was 44 ± 15 years, making THS in children even rarer.⁴

In both adults and children, THS typically presents with unilateral, retro-orbital, “boring” or “stabbing” pain followed by cranial nerve (CN) III, IV, and VI palsies.^{1,2,5} The time from onset of pain to noticeable neurologic deficit is variable, with a median of 2 days in adults.⁴ The painful ophthalmoparesis is almost exclusively unilateral, with a small number of bilateral cases described.⁶ Diagnostic criteria (Table 1) require involvement of one or more of the third, fourth, or sixth CNs, which are most common, but involvement of CN V and CN VII has also been reported in adults.^{7–9} In a review of 16 pediatric cases, 81% involved CN III, 56% CN VI, 13% CN IV, and 31% both CN III and CN VI.⁵ Two pediatric cases have described CN VII involvement,^{10,11} and one other case reports pain (with intact light touch and pinprick sensation) in branches V1 and V2 of the fifth CN.¹² With this case, we aim to contribute to the limited literature describing THS in children, with the unique presentation of a child who demonstrated findings of a CN VII palsy and hyperesthesia of CN V.

The differential diagnostic possibilities in THS are important and necessitate an extensive workup to rule out more sinister processes. Categories to consider include those of migrainous, vascular, malignant, infectious, and demyelinating origin. Necessary evaluations to assess these potential etiologies include serum and cerebrospinal fluid (CSF) studies as well as advanced neuroimaging with magnetic resonance imaging (MRI).

Case report

A 17-year-old female with history of obesity, pre-diabetes, and marijuana use presented for care in the setting of progressive left-sided ophthalmoparesis and worsening headache. Prior to admission, she had a 1-month history of left frontotemporal and retro-orbital headaches accompanied by photophobia, nausea, vomiting, and localized numbness over the left temple. The headaches often woke her up from

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Table 1. Diagnostic criteria.

Description
Unilateral orbital or periorbital pain associated with paresis of one or more of the third, fourth, and/or fifth cranial nerves caused by a granulomatous inflammation in the cavernous sinus, superior orbital fissure, or orbit
Diagnostic criteria (ICHD-3)
A. Unilateral orbital or periorbital headache fulfilling criterion C
B. Both of the following: <ol style="list-style-type: none"> 1. Granulomatous inflammation of the cavernous sinus, superior orbital fissure, or orbit, demonstrated by MRI or biopsy 2. Paresis of one or more of the ipsilateral third, fourth, and/or fifth cranial nerves
C. Evidence of causation demonstrated by both of the following: <ol style="list-style-type: none"> 1. Headache is ipsilateral to the granulomatous inflammation 2. Headache has preceded paresis of the third, fourth, and/or fifth nerves by ≤ 2 weeks, or developed with it
D. Not better accounted for by another ICHD-3 diagnosis

Source: <https://www.ichd-3.org/13-painful-cranial-neuropathies-and-other-facial-pains/13-8-paratrigeminal-oculosympathetic-raeders-syndrome/>
MRI: magnetic resonance imaging; ICHD: International Classification of Headache Disorders.

sleep, and while previously intermittent, they had been constant for the 3 weeks prior to presentation. Over the preceding 2 weeks, the patient developed persistent, binocular diplopia, which eventually progressed to complete ophthalmoplegia. She also reported 1 week of intermittent left-sided mandibular pain and finally developed sensory changes over the maxillary (V2) division of the left trigeminal nerve. On examination, she was found to have CN III and VI palsies despite an unremarkable head computed tomography (CT). The patient was transferred to our hospital for inpatient evaluation and management.

At admission, she was afebrile, with a blood pressure of 156/83 mmHg; vital signs were otherwise normal for age. She was mildly ill-appearing and obese, weighing 112 kg. Pupils were 5 mm and briskly reactive to direct light, with sluggish restriction of the left pupil to indirect light. Funduscopic examination revealed sharp optic margins without pallor. Extraocular movements were markedly abnormal in the left eye with near-complete ophthalmoplegia and minimal upward and downward gaze. She had marked ptosis of the left eye, most consistent with severe oculomotor and abducens nerve palsies. Visual fields were full bilaterally. No facial asymmetry was noted. Trigeminal sensory examination revealed left-sided hyperesthesia in the V1 and V2 distributions.

Following consultation with Pediatric Neurology and Ophthalmology, the patient underwent an extensive workup revealing a normal complete blood count (CBC) and comprehensive metabolic panel (CMP) (except for glucose of 170), HbA1C of 6.1, angiotensin-converting enzyme (ACE) of 14 U/L (adult range, 16–85 U/L), negative serum autoimmune studies (antinuclear antibody (ANA), cyclic citrullinated peptide (CCP), anti-SSA/Ro (Sjögren's syndrome-related antigen A) Ab, anti-SSB/Ro (Sjögren's syndrome-related antigen B) Ab, Smith antibody (Sm Ab), ribonucleoprotein antibody (RNP Ab), topoisomerase I antibody (Scl 70 Ab), topoisomerase I antibody (Jo1 Ab), rheumatoid factor (RF), myeloperoxidase antibody (MPO Ab), proteinase 3 Ab), normal lactate dehydrogenase (LDH) and uric acid, and negative serum

electrophoresis for monoclonal proteins. Infectious workup was negative for *Borrelia burgdorferi*, syphilis IgG Ab, CSF-VDRL (Venereal Disease Research Laboratory), and QFT-TB (QuantiFERON-TB) Gold. Bacterial, fungal, and mycobacterial cultures and acid-fast smear were negative. A lumbar puncture demonstrated normal CSF studies other than lymphocytosis (92%). CSF ACE was negative, and IgG, albumin, and flow cytometry were normal.

MRI of the brain and orbits demonstrated an extra-axial enhancing, ill-defined lesion centered in the left cavernous sinus (CS), including involvement of Meckel's cave, superior orbital fissure, orbital apex, foramen rotundum, foramen ovale, and middle cranial fossa (Figure 1). Mild narrowing of the patent right cavernous internal carotid artery was also described. The lesion was noted to approach but not involve the optic nerve.

Findings were consistent with THS and the patient was initiated on high-dose oral steroids. She demonstrated improvement in severity of headache within 12 hours of steroid initiation and complete resolution of headache by 24 hours. CN deficits remained unchanged at discharge (24 hours after initiation of steroids).

One month following discharge, the patient described resolution of headache and improved extraocular movements and diplopia. Repeat imaging at this time noted a "slight decrease in the size of the lesion." Unfortunately, the patient discontinued her 10-week steroid course after approximately 1 month. Shortly after discontinuing treatment, she began to experience new-onset, left-sided facial droop, consistent with a CN VII palsy, as well as recurrence of ptosis, diplopia, ophthalmoplegia, and hyperalgesia in V2. Follow-up imaging revealed mildly expanded asymmetric enhancement in the left cavernous sinus and Meckel's cave with extension along V3 through foramen ovale and V2 through foramen rotundum to the pterygopalatine fossa. New enhancement visualized in the distal left internal auditory canal, extending along the facial nerve inferiorly to the visualized upper parotid gland.

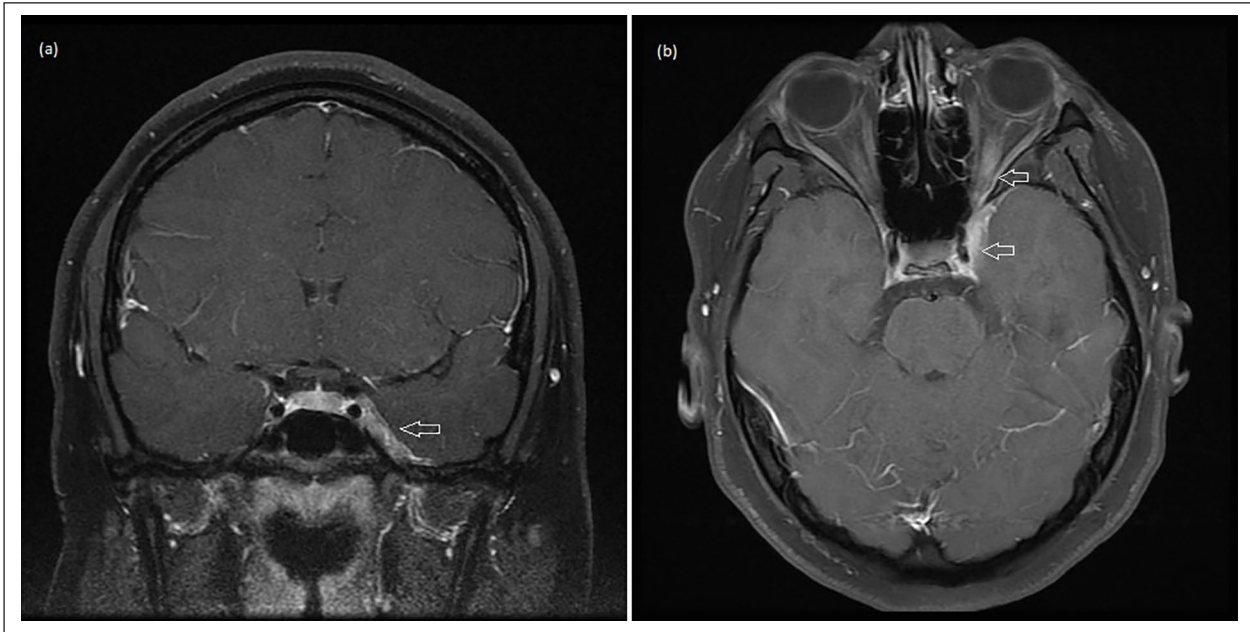


Figure 1. (a) Magnetic resonance imaging of the orbits revealing an enhancing, ill-defined lesion centered in the left CS, including involvement of Meckel's cave, superior orbital fissure, orbital apex, foramen rotundum, foramen ovale, and middle cranial fossa. This creates mild narrowing of the patent right cavernous internal carotid artery. (b) Magnetic resonance imaging of the brain revealing enhancing, ill-defined lesion centered in the left cavernous sinus, including involvement of Meckel's cave, superior orbital fissure, and orbital apex. The lesion approaches, but does not primarily or significantly involve the optic nerve.

High-dose steroids were initiated once more. The patient was followed by Pediatric Neurology at 1 and 2 years since completion of treatment and noted to have complete resolution of symptoms.

Discussion

While THS is considered idiopathic, it is characterized by granulomatous inflammation of the CS identified on contrast-enhanced MRI or biopsy.⁴ Histopathologic diagnosis is difficult and generally not necessary as MRI findings are typically adequate to confirm the suspected clinical diagnosis. More importantly, MRI alleviates the need for invasive diagnostic procedures by ruling out other potential CS lesions.¹³ In a review of adults, MRI revealed inflammatory tissue in >90% of patients with THS. The authors use these data to note that while biopsy may be necessary in some cases, MRI findings of inflammation “in conjunction with clinical findings” should be used to make the diagnosis.¹⁴ A review by Jain et al.¹⁵ showed near-universal CS involvement on MRI. Indeed, diagnostic criteria require evidence of inflammation in the CS, superior orbital fissure, or orbit (Table 1). Other imaging findings that can be seen in THS include carotid artery narrowing¹⁶ or stenosis, as well as findings within the orbital apex, orbit, and/or Meckel's cave.¹⁵

Although no specific treatment guidelines for THS in children exist, extrapolated data from adult literature and pediatric case reports denote steroids as the treatment of choice. Typical treatment consists of high-dose steroids following a

thoughtful and complete evaluation, including MRI and CSF studies.⁵ Rapid and often marked improvement in pain after initiating therapy is characteristic of THS. CN deficits generally resolve completely but may take weeks to months.⁵ In children, initial therapy with high-dose prednisone, or its equivalent, has resulted in a lower risk of relapse than low-dose treatment,⁵ although additional studies are necessary to more clearly define an appropriate treatment regimen.¹⁷ THS has been described as a commonly recurring condition, more likely to recur but also more likely to respond to steroid treatment in younger patients.¹⁸ While THS characteristically responds to steroid therapy, future directions include investigative use of non-steroid immunomodulators as novel therapies for THS. For instance, one pediatric case report of a patient with recurring THS describes achievement of symptom remission on adalimumab monotherapy.¹⁹

Conclusion

THS is a rare, idiopathic, inflammatory condition characterized by painful ophthalmoparesis involving the third, fourth, and sixth CNs. CN V involvement has been reported in adults but only once reported in a pediatric patient. We aim to contribute to the limited data regarding course and outcomes of this disease process by presenting what is, to the best of our knowledge, the first reported case of hyperesthesia of the fifth CN and third case of CN VII palsy in a child with THS.

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