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## Case Report

# Tolosa-Hunt Syndrome - Case Report

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## Abstract

**Background:** Tolosa-Hunt syndrome (THS) is an uncommon disease caused by non-specific inflammation of the cavernous sinus, superior orbital fissure and the apex of the orbit. The disease is characterized by periorbital pain, paresis of the bulbomotor and quick response to steroid treatment.

**Case reports:** We presented 38-year old male patient, with THS. The patient had severe frontal headache and left-sided periorbital pain. Examination showed upper left-sided eyelid ptosis, left-sided oculomotor cranial nerve palsy and partial left sided abducens nerve palsy. MRI of the head showed asymmetric enhancement of the cavernous sinus. The clinical diagnosis satisfies the criteria for THS. After steroid therapy her symptoms and clinical signs dramatically reverses.

**Conclusion:** THS is an entity that occurs rarely, its etiopathogenesis is unknown, and it is manifested clinically by unilateral orbital pain associated with simple or multiple oculomotor paralyses, which resolves spontaneously but may recur. MRI orbital phlebography and biopsy are the recommended methods for making diagnosis. In our patient clinical presentation MRI findings and positive response to the corticosteroid treatment were relevant for making the diagnosis.

## Introduction

Tolosa-Hunt syndrome (THS) is a painful ophthalmoparesis or ophthalmoplegia, usually unilateral, caused by non specific inflammation of the cavernous sinus or superior orbital fissure. Severe orbital or peri-orbital pain, constant or episodic, is the initial feature of THS that usually resolve spontaneously or under treatment but tend to relapse. Diplopia related to ophthalmoparesis or disordered eye movement occurs when the oculomotor (III), trochlear (IV) and abducens (VI) nerves are damaged by granulomatous inflammation. Signs of incomplete nerve palsy with or without pupillary sparing may be present. A ptosis can be observed due to oculomotor paralysis [1].

The etiology of THS remains unknown, although it may be commonly associated with trauma, tumor, aneurysm, and inflammation. It is known that THS responds well to systemic corticosteroids. THS is rare in the first two decades of life and subsequently appears to have a uniform distribution. According to the International Headache Society 2013 classification, THS is described as unilateral orbital pain associated with paresis of one or more of the third, fourth and / or fifth cranial nerves due to granulomatous inflammation in the cavernous sinus, upper orbital crack or orbit.

The diagnostic criteria for the diagnosis of THS, defined by the 3rd edition of the International Classification of Headache Disorders (ICHD-3), include:

- A. unilateral headache meeting criterion C;
- B. Both of the following:
  - 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 third, fourth and / or fifth ipsilateral cranial nerves;
- C. Evidence of causality demonstrated by the following two elements:
  - 1) Headache preceded paresis of the third, fourth and / or sixth nerves of  $\leq 2$  weeks or developed with it;
  - 2) Headaches are localized around the eyebrow and the eye and
- D. Not better explained by another diagnosis ICHD-3 [2]

The dysfunction of the pupil is related to the lesion of the sympathetic fibers in the cavernous portion of the internal carotid artery or parasympathetic fibers surrounding the oculomotor nerve. Inflammatory involvement of the sympathetic nerves running through the interior of the cavernous

sinus can cause Horner syndrome with miosis. The combination of unilateral oculomotor palsy and Horner syndrome increases the localization specificity of the cavernous sinus.

The sympathetic innervation of the pupil is sometimes affected. The involvement of the trigeminal nerve of the first division (mainly V1) can cause paresthesia of the forehead. The loss of the ipsilateral reflex of the cornea suggests involvement of the trigeminal nerve. Swelling of the eyelids is more likely to occur with orbital disease than with inflammation limited to the cavernous sinus.

There is no pathognomonic characteristic of THS, so it is often considered a diagnosis of exclusion. A large number of differential diagnoses of THS include tumors, vasculitis, basal meningitis, sarcoidosis, diabetes mellitus and ophthalmoplegic migraine.

Here we report a 38-year-old man with painful left eye ophthalmoplegia secondary to THS, his diagnostic procedures and his treatment.

### Case Report

A 38 year-old previously healthy man was admitted to the Neurology Department with a 3 week history of severe frontal headache and left-sided periorbital pain, with the right eyelid ptosis and paresis of the left oculomotor cranial nerve. Pain was sharp and continuous. This was associated with of blurry vision, without vomiting, dizziness, loss of consciousness or limb weakness. There was no history of fever, facial pain or hearing loss on the affected side.

At admission, the patient complained of left supraorbital pain extending into the infraorbital area. During the history, the patient reported that he had already been hospitalized 6 months ago in an ophthalmic department in the south of the country, for sub-acute appearance of a right eyelid ptosis. The medical history revealed that despite the neurological and diagnostic analysis the diagnosis was not derived. After leaving the hospital, the evolution was towards the regression of the symptomatology, without any treatment. Her medical history only included smoking 15 packs/ years. She had not history of headaches, diabetes, hypertension or any another illness. Physical and neurological examination performed at admission verified upper left-sided eyelid ptosis, left-sided oculomotor cranial nerve palsy and partial left sided abducens nerve palsy without nystagmus. The right eye had normal ocular movements, visual acuity

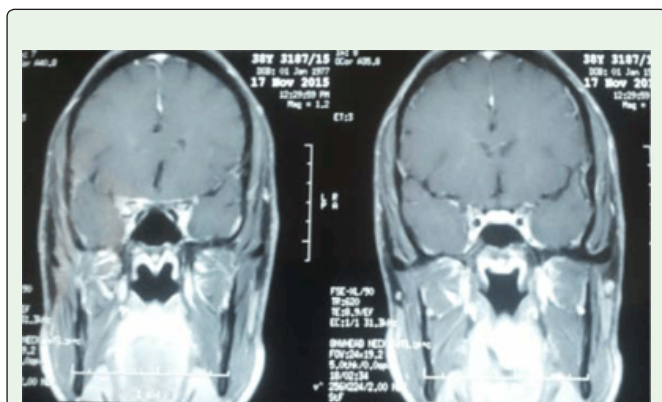
and visual field. Fundoscopy was normal in both eyes. Complete ophthalmological evaluation was performed to rule out glaucoma and other local eye pathologies. The rest of the neurological and systemic examination was unremarkable. Family history was negative for any neurological disease. He didn't have any risk factors for sexually transmitted diseases. He was not using any medications at the time of presentation.

We performed the following complementary studies: complete blood count showed mild leucocytosis (white cell count of 11 300/mL) and haemoglobin of 15.2 g/dL (haematocrit 50%). Erythrocyte sedimentation rate was 14 mm/h. Serum chemistry, including liver function tests, was normal. Vasculitis markers, thyroid function tests, anti-thyroglobulin, anti-microsomal receptor were normal. A Cranial Tomography (CT) scan of brain and paranasal sinus, were normal. Contrast enhanced Magnetic Resonance Imaging (MRI) with different sequences was performed. Post contrast T1 MRI weighted images detected diffuse enhancement in the area of the cavernous sinus (Figure 1). Analysis of Cerebrospinal Fluid (CSF) showed normal opening pressure, cellularity, glucose, proteins and red blood cells. Systemic intravenous corticosteroid therapy with 500 mg methyl prednisolone was administered for 5 consecutive days, along with gastroprotective therapy and monitoring of steroid-related adverse effects. Systemic intravenous corticosteroid therapy resulted in complete regression of symptoms and the patient was discharged from the hospital. He was recommended to take oral corticosteroids daily, and the dose was gradually decreased for 2 months.

### Discussion

Tolosa first described the condition in 1954, in a patient with unilateral recurrent painful ophthalmoplegia involving cranial nerves III, IV, VI and V1. The patient was imaged using carotid angiography, and segmental narrowing of the carotid siphon was seen [3]. Hunt et al., [4] described 6 patients with similar clinical findings in 1961, and proposed a low-grade non-specific inflammation of the cavernous sinus and its walls as the cause of the syndrome. Pathologically, infiltration of lymphocytes and plasma cells as well as thickening of the dura mater was seen. The condition was termed Tolosa-Hunt syndrome by Smith and Taxdal in 1966 [4]. The latter authors stressed the importance of the dramatic rapid response to steroid therapy [5,6].

The aetiology of Tolosa-Hunt syndrome is largely unknown [7]. As described above, the hallmark of this disease is the nonspecific granulomatous inflammation characterised by infiltration of lymphocytes and plasma cells primarily in and around the cavernous sinus, with variable extension into and beyond the superior orbital fissure/orbital apex. What incites this inflammatory reaction is still unclear. It is considered a very benign illness, but exclusion of more malignant diseases bears utmost importance whenever any patient presents with such clinical features [8,9]. Knowing the differential diagnoses is more important to rule out other causes than to rule in the syndrome itself. The differential diagnosis includes many etiologies including vascular, tumoral (pituitary adenoma, sarcoma, neurofibroma, epidermoid, craniopharyngioma, meningioma, chordoma, chondroma, giant cell tumor, metastases, lymphoma, carcinomatous meningitis, metastases local or distant), inflammatory (sarcoidosis, Wegener's granulomatosis, orbital pseudo tumor of THS, giant cell arteritis) and infectious etiologies (bacterial sinusitis,



**Figure 1:** MRI of the brain (coronal section) with enhancement demonstrates non specific fullness involving cavernous sinus, consistent with Tolosa-Hunt syndrome.

periostitis, mucormycosis, syphilis, fungi and mycobacteria), as well as other conditions (ophthalmoplegic migraine, trauma and microvascular infarction secondary to diabetes).

Neuroimaging and LCR are important in differential diagnosis. It is also important to ask for the complete blood count, ESR protein, C-reactive protein, complete biochemical tests, including functional tests of the thyroid and liver. Chest X-ray and sinus CT are sometimes indicated. Brain and orbital imaging includes MRI and CT. MRI (T2-weighted, including fat suppression, STIR sequence) helps identify high signals in an extra-ocular active muscle. Inflammatory causes of painful ophthalmoplegia include those due to a specific infectious agent. It is essential to conduct a careful examination of CSF and obtain cultures (bacterial, fungal, mycobacterial) [10].

The management of patients with THS is complex and difficult. Neurologists, ophthalmologists and neuroradiologists play an important role in establishing the correct diagnosis. The diagnosis of THS should be used rarely and with great caution, since most cases are ultimately attributable to defined pathological processes, such as infection, granulomatous inflammation or neoplasm. Patients suspected of having the syndrome require careful evaluation, appropriate treatment and careful follow-up observation [1].

High-dose corticosteroid therapy is the first-line therapy for Tolosa-Hunt syndrome given its inflammatory pathology [1]. There is no evidence sufficient for the appropriate dose, route of administration and duration of therapy [11]. A remarkable feature of glucocorticoid therapy is the rapid resolution of orbital pain within 1-3 days, which also serves as confirmation of a diagnosis [12]. Our patient answered the same way. In one study, 40% of patients achieved pain relief within 72 hours and 78% in the week. On the other hand, the resolution of neuropathies is delayed by several months, which requires a longer treatment with steroids. Radiological improvement takes even longer to resolve; therefore, the persistence of the MRI results, unless it is not in decline, should not change the duration of the treatment. After an initial high-dose of corticosteroid, an oral taper over the course of several weeks is recommended, along with regular follow-up with subsequent MRI studies to document the resolution of the disease. Immunosuppressive drugs are the other therapeutic modality of Tolosa-Hunt syndrome. The recurrence of the disease occurs in about 50% of patients, which is quite alarming [13].

## Conclusion

THS is an entity that occurs rarely, its etiopathogenesis is unknown, it is manifested clinically by unilateral orbital pain associated with simple or multiple oculomotor paralyses, which resolves spontaneously but may recur. In this case clinical presentation MRI and positive response to the treatment with corticosteroids were relevant for making the diagnosis.

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