

Tolosa Hunt Syndrome, a painful ophthalmoplegia

Síndrome de Tolosa-Hunt, uma oftalmoplegia dolorosa

Maxuel Nogueira dos Santos Junior¹ <https://orcid.org/0000-0002-3451-6107>

Alex Eduardo Siva¹ <https://orcid.org/0000-0002-0999-0165>

Renata Cristina Franzon Bonatti¹ <https://orcid.org/0000-0001-7452-2563>

ABSTRACT

Tolosa-Hunt syndrome (STH) is a rare disease characterized by sudden onset unilateral painful ophthalmoplegia caused by non-specific granulomatous inflammation in the cavernous sinus or superior orbital fissure (or both). Ophthalmoparesis occurs when the cranial nerves III, IV and VI are affected by inflammation. Pupillary dysfunctions may be present and is related to involvement of the sympathetic fibers that pass through the cavernous sinus in the portion of the internal carotid artery or parasympathetic fibers around the oculomotor nerve. The involvement of the first branch of the trigeminal can cause paresthesia corresponding to the distribution from the first branch (forehead). Rarely, there may be extension of inflammation beyond the cavernous sinus or superior orbital fissure and may also affect the optic nerve. There is a good response with the use of corticosteroids and there may be spontaneous remissions. Relapses occur in 40% of cases. The disease is most common after the second decade of life. It affects both genders equally. The present study is a case report of a patient who presented with painful ophthalmoplegia of sudden onset on the right with 4 days of evolution followed by ipsilateral amaurosis after one day of onset of pain.

Keywords: Tolosa-Hunt syndrome; Ophthalmoplegia; Headache; Cranial nerves syndrome

RESUMO

A síndrome de Tolosa-Hunt (STH) é uma doença rara caracterizada por oftalmoplegia dolorosa unilateral de início súbito causada por uma inflamação granulomatosa inespecífica no seio cavernoso ou fissura orbital superior (ou ambos). A oftalmoparesia ocorre quando os nervos cranianos III, IV e VI são acometidos pela inflamação. Disfunções pupilares podem estar presentes e está relacionado com acometimento das fibras simpáticas que passam pelo seio cavernoso na porção da artéria carótida interna ou fibras parassimpáticas ao redor do nervo oculomotor. O acometimento do primeiro ramo do trigêmeo pode provocar parestesia território correspondente à distribuição desde ramo (testa). Raramente, pode haver extensão da inflamação para além do seio cavernoso ou fissura orbital superior podendo acometer também o nervo óptico. Há uma boa resposta com o uso de corticoides e pode haver remissões espontâneas. Recidivas ocorrem em 40% dos casos. A doença é mais comum após a segunda década de vida. Afeta ambos os gêneros de forma igualitária. O presente estudo trata-se de um relato de caso de um paciente que se apresentou com oftalmoplegia dolorosa de início súbito à direita com 4 dias de evolução seguido de amaurose ipsilateral após um dia do início da dor.

Descritores: Síndrome de Tolosa-Hunt; Oftalmoplegia; Cefaleia; Síndrome de nervos cranianos

¹ Department of Neurology, Universidade Federal do Triângulo Mineiro, Uberaba, MG, Brazil.

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INTRODUCTION

The THS is a rare disease with an incidence of 1 case per 1 million per year, and characterized by painful ophthalmoplegia caused by an idiopathic granulomatous inflammation in the cavernous sinus with good response to the use of glucocorticoids that was known some years after its first description in 1954 by Tolosa.⁽¹⁻³⁾ It is generally considered a benign condition, but permanent neurological deficits may occur, and relapses are frequent requiring prolonged immunosuppressive therapy in these cases.⁽⁴⁾

The present study aims to describe the pathophysiological and clinical characteristics, and the differential diagnosis, considering that it is an exclusion diagnosis and therapeutic measures according to the International Headache Society (IHS-2013) with the presentation of a clinical case.⁽⁵⁻⁷⁾

CASE REPORT

The study describes the case of a patient treated in the ambulatory by the ophthalmology team of Hospital Escola da Universidade Federal do Triângulo Mineiro (UFTM), being hospitalized and transferred to the neurology service of said hospital. Diagnostic criteria was used according to the international classification of headache - The International Classification of Headache Disorders 3 Beta (ICHD-3 beta 2013) were used.⁽⁷⁾ After excluding other differential diagnoses, the patient was treated with steroid therapy with good response. The follow-up time was only two months due to patient non-attendance to the ambulatory follow-up.

Male patient, 58 years old, hypertensive with chronic kidney disorder with previous transplantation (1998), with placement of 2 stents in the circumflex artery 2 months before, alcoholic and smoker. He was on tacrolimus, prednisone 5mg daily, furosemide, clonidine, ASA, clopidogrel, and simvastatin when admitted to the UFTM Hospital after appointment with an ophthalmology team with report of intense periocular pain on the right started 4 days before with progress in hours for ophthalmoplegia due to involvement of the III, IV and VI cranial nerves on the right, followed by ipsilateral amaurosis by involvement of the II cranial nerve within 24 hours after the onset of pain. The following laboratory tests were carried out with normal results: hemogram, fasting glycemia, glycated hemoglobin, electrolytes, ESR, PRC, FAN, anti-HIV, VDRL, FTA-ABS, P-ANCA, C-ANCA, protein electrophoresis, and thyroid function. Lumbar puncture was also carried out to study cerebrospinal fluid with normal results, including cultures. Then, an imaging study was performed by magnetic resonance imaging (MRI) of the brain (Figures 1 and 2), which demonstrated inflammatory alterations in superior orbital fissure and in the right cavernous sinus, consistent with THS according to the clinical condition after exclusion of other differential diagnoses. Corticosteroid therapy was initiated with prednisone 1mg/kg/day until solving the pain, which occurred 10 days after initiation of therapy, and then the corticosteroid therapy dose was gradually reduced for a period of 2 weeks. Hospitalization lasted 12 days, and 2 months after discharge the patient had a new MRI of the encephalon with significant reduction of the alterations when compared to the initial examination. It evolved with significant improvement of ophthalmoplegia and mild improvement of visual acuity, remaining with mild ophthalmoparesia after 2 months. There was

improvement of direct photomotor response in the right eye, and cure of paresthesia in the territory of the ophthalmic branch of the trigeminal nerve.

DISCUSSION

The case reported initially presented painful ophthalmoplegia to be studied, and with laboratory and imaging examinations it was possible to suggest the diagnostic hypothesis of THS, with the choice for treatment in immunosuppressive doses with glucocorticoids.⁽⁸⁻¹⁰⁾

THS is a rare disease of unknown etiology of equal distribution between genders, with a higher incidence after the age of 20 years. The most affected nerves are the oculomotor (85%), abducent (70%), ophthalmic branch of the trigeminal nerve (30%), and trochlear (29%). The syndrome is usually unilateral, but can rarely be presented bilaterally (4-5%).⁽³⁾ Involvement of the maxillary and mandibular branches of the trigeminal as well as oculomotor nerve (present in the case reported) and facial nerve have also been reported when there is an extension of the inflammatory process beyond the cavernous sinus.⁽³⁾ Without treatment, symptoms usually regress spontaneously within 8 weeks in most cases. It is important to emphasize that most patients with painful ophthalmoplegia (> 75% of cases) will not be diagnosed with THS. Tumors and vascular causes are the most common ones.⁽¹²⁾ The vast majority of differential diagnoses can be made with an MRI of the encephalon.^(7,11,12) The diagnosis is made based on 3 pillars: clinical presentation, image examination, and response to corticosteroid therapy.⁽³⁾ Biopsy is rarely performed due to technical difficulties.⁽²⁾

The diagnostic criteria for THS according to the ICHD-3 beta 2013 are:

- A. Unilateral pain 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 III, IV and/or IV ipsilateral cranial nerves
- C. Evidence of causality demonstrated by both of the following:
 1. Headache preceding paresis of the III, IV and/or VI nerves for <2 weeks or developed with it
 2. Headache located around the eye and ipsilateral eyebrow
- D. Not better explained by another diagnosis of ICHD-3 beta.⁽⁷⁾

There is usually a dramatic response with corticosteroid therapy, with resolution of pain in 24-72 hours (40% in the first 72 hours, and 78% in up to 1 week). Ophthalmoplegia presents a slower resolution (2-8 weeks).⁽¹³⁾ Infrequently, residual neurological deficits may persist indefinitely. Relapses usually occur in half of the patients, ranging from months to years, and are more common in young people, and always require additional investigations to rule out inflammatory and neoplastic diseases.⁽¹⁴⁾ There is no evidence that corticosteroid therapy alters the prognosis in frequency of relapses or persistent ophthalmoplegia. Regarding patients not responding to corticosteroid therapy, it is possible to use second-line therapy options. Therefore, a small group of patients will need association with immunosuppressants (acting as a corticosteroid sparer or as a potentiator in patients not responsive to corticosteroids).⁽¹³⁾ The most commonly used medications are cyclosporine, azathioprine, methotrexate, mycophenolate mofetil,

and infliximab. There are some reports on use of radiotherapy in cases of relapse and in cases where initial treatment with corticosteroids is contraindicated.⁽¹³⁾ Follow-up is carried out with encephalon MRI every 2 months to ensure the treatment is being effective and that no evidence of another etiology develops. Typically, radiological improvement comes much later than clinical improvement. After radiological normalization, MRI is suggested every 6 months for a period of 2 years.⁽¹⁴⁾

We then conclude with the present case study that due to the lack of a high specificity for the diagnosis of this pathology it is still necessary that it is made as an exclusion diagnosis. However, it should always be suspected in light of a suggestive clinical presentation based on the ICHD-3 beta criteria.⁽⁷⁾



Figure 1: Axial cut of MRI in T2 enlargement and hypersignal sequence in cavernous sinus and right orbit.

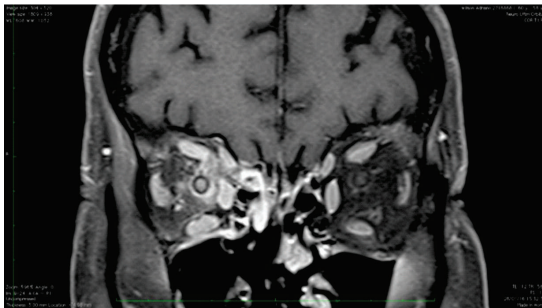


Figure 2: Coronal MRI cut in post-contrast T1 sequence showing enlargement and contrast hypercaptation in cavernous sinus region and right orbit.

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Corresponding author:

Maxuel Nogueira dos Santos Junior

R. Jangadeiros Alagoanos, n. 1521, Pajuçara. Maceió – AL, Brazil.

E-mail: max_nogueira@hotmail.com