Tolosa-Hunt Syndrome with Facial Nerve Paresis

Mohsen Pirastehfar, MD1 and Jin Jun Luo, MD, PhD1,2,*

Abstract—Tolosa-Hunt syndrome (THS) is a rare idiopathic non-specific inflammatory disorder of cavernous sinus or supraorbital fissure causing headache and painful ophthalmoplegia. Usually THS involves several cranial nerves including IIIrd, IVth, VIth, and V1 and V2 of the Vth when they are traveling through the wall of the cavernous sinus and supraorbital fissure. Involvement of a cranial nerve beyond this anatomical location is uncommon. We described a 27 years old previously healthy woman presenting with right temporal persistent headache and right retro-orbital pain for 10 days. She also complained of right face and right forehead numbness and loss of sensation in the right aspect of her nose. She was found to have mild right facial, the VIIth, nerve paresis in addition to her IIIrd, VIth, V1 and V2 involvement. Brain MRI showed a gadolinium enhanced lesion in the right cavernous sinus. Her symptoms were improved with steroid treatment which was consistent with previous reports that THS responds well to steroid therapy. Our case also supports the notion that THS may affect a cranial nerve beyond cavernous sinus in location.

Keywords — Cranial nerve paresis, inflammation, painful ophthalmoplegia, Tolosa-Hunt syndrome.

I. INTRODUCTION

The eponym Tolosa-Hunt syndrome (THS) was named after Dr. Eduardo Tolosa, a Spanish neurosurgeon who was first reported this entity in 1954 [1], and Dr William Hunt [2], an American neurologist and neurosurgeon who described it with more cases in 1961. Pathologically, THS is caused by an idiopathic non-specific inflammation in the wall of cavernous sinus or supraorbital fissure. THS is a rare neurologic disorder and its incidence is estimated one case per one million populations [3]. THS involves worldwide and at all ages. Males and females appear to be equally affected. The age distribution is fairly uniform except for being rare before age 20 years [4]. Typical clinical features of THS are painful ophthalmoplegia with involvement of multiple cranial nerves (oculomotor, the IIIrd; trochlear, the IVth; abducens, the VIth and ophthalmic and maxillary divisions, the V1, V2 of the trigeminal Vth nerves). We report a case of THS with facial nerve paresis.

II. CASE REPORT

A 27 years old previously healthy Spanish-speaking woman presented for persistent right sided headache with retro-orbital pain for 10 days. She also complained of numbness in her right face and right forehead, loss of sensation in the right aspect of her nose, and with symptoms of nausea, vomiting, photophobia, phonophobia and blurry vision, which were not responding to nonsteroidal anti-inflammatory drug treatment. She denied any weakness or numbness in her arms and legs. No traumatic injury to the head or orbital area nor viral infectious symptoms involving respiratory and digestive system was reported.

On examination, she was afebrile with normal vital signs. Speech and language were normal. She was found to have a horizontal diplopia with painful eye movement and limited lateral gaze in the right eye, suggesting the right VIth nerve paresis. She had normal visual acuity, normal appearance of the optic discs, isocoria with normal pupillary light reflexes. No exophthalmos and nor ocular bruits were noted. Mild right eye ptosis with mild depression of her right nasolabial fold and decrease wrinkles on the right forehead were evident, suggesting discrete right peripheral IIIrd and VIIth nerve dysfunction. She was found to have decreased sensation to light touch, pinprick and temperature on right side of her face which was consistent with dysfunction in V1 and V2 territories of the Vth nerve. The remaining neurologic examinations were all normal including taste, hearing, gag reflex, muscle strength, coordination, sensation in the limbs, Romberg sign, gait and stance.

Laboratory studies showed an abnormal serum level of erythrocyte sedimentation rate (49 mm/hour, normal: 0-20) C-reactive protein (4.2 mg/dl, normal 0-3), but all others including chemistry profile, hematogram with differentials, glycosylated hemoglobin A1c, hepatic and thyroid functions, and angiotensin converting enzyme, were normal. A lumbar puncture was performed showing normal opening pressure and normal results of cerebral spinal fluid profile including glucose...
and protein. Her non-contrast brain CT scan didn't show intracranial abnormality but brain magnetic resonance imaging (MRI) (1.5 Tesla) disclosed a gadolinium-enhanced pathology in the right cavernous sinus (Figure 1A and 1C). Brain MRA and MRV showed normal findings. The provisional diagnosis of THS was made.

Intravenous infusion of corticosteroid (Methylprednisolone 500 mg daily for 3 doses) was initiated. She responded very well to the treatment. Her symptoms of headaches, blurry vision, and the right VIth nerve palsy began to improve one day after initiating the treatment and markedly improved after having received three doses of iv corticosteroid. She was discharged home with oral steroid (prednisone 60 mg per day with a plan of gradually tapering down to off). She had completely symptoms-free at her 1 month follow-up. A follow-up brain MRI in 2-months after discharge demonstrated significantly reducing inflammation in size in the right cavernous sinus (Figure 1B and 1D). During the course of tapering off steroid, however, she complained of right eye pain and blurry vision indicative of a relapse, which was quickly relieved by resuming a slightly higher dose of oral steroid (prednisone 20 mg/day). She was maintained at low dose of steroid (prednisone 5 mg every other day) and symptom-free at the 6-months follow-ups. Her clinical course with typical presentation of headache and painful ophthalmoplegia. Neurologic examination showed multiple cranial nerve involvement. Laboratory findings of increased levels of erythrocyte sedimentation rate and C-reactive protein and neuroimaging studies disclosing an enhanced lesion in the cavernous sinus, and exquisite responses to corticosteroid treatment are consistent with those of THS.

### III. Discussion

In this case report, we present a rare case of THS in a young woman with painful ophthalmoplegia and the VIIth nerve involvement, in addition to the classical presentation involving cranial nerves of the IIIrd, IVth, Vth, and/or VIth cranial nerves. The patient responded well to the corticosteroid treatment.

THS is a rare neurologic disorder with its incidence estimated one case per one million populations [3], as low as that of Creutzfeldt-Jakob disease [5]. THS is caused by an inflammatory process of unknown etiology. Pathologically, there is a nonspecific inflammation of the septa and wall of the cavernous sinus, with non-caseating giant cell granulomas, lymphocytes and plasma cell infiltration and proliferation of fibroblasts [1,2]. The inflammation produces pressure and secondary dysfunction of the structures within the cavernous sinus, susceptible to those cranial (IIIrd, IVth, VIth, and/or VIth) nerves passing through. Our patient was found to have her right nasolabial fold depression and decreased wrinkles on the right forehead, suggestive of a peripheral VIIth nerve paresis; and numbness in her forehead and loss of sensation in her right face and nose indicative of Vth nerve palsy. Notably, the VIIth nerve paresis was not included in the revised 2013 diagnostic criteria (Table 1) [4]. In supporting our observation, previous case reports have shown involvement of the optic, V1 and V2, VIIth or VIIIth nerves [3]. Thus, a cranial nerve involvement in a location beyond cavernous sinus should not pre-exclude THS in the differential. On the other hand, THS may result from an expanded, rather than a localized, inflammation. The mechanism by which multiple cranial nerve involvement beyond the location of cavernous sinus may be due to the underlying non-specific inflammation which is supported by clinical observation that the symptoms, such as pain, blurry vision, and muscle weakness, resolve when it is

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<td>ICHD-3 CRITERIA FOR THS [4]</td>
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A. Unilateral headache fulfilling 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. Paralysis of one or more of ipsilateral IIIrd, IVth and/or VIth cranial nerves.

C. Evidence of causation demonstrated by both of the following:
1. Headache has preceded paresis of IIIrd, IVth and/or VIth nerves by ≤ 2 weeks, or developed with it.
2. Headache is localized around the ipsilateral brow and eye.

D. Not better accounted for another ICHD-3 diagnosis.

Fig. 1. Brain MRI with gadolinium enhanced T1 weighted images showing a lesion in the right cavernous sinus which was reduced in size after treatment. Coronal (A and B) and axial (C and D), prior to (A and C) and post of (B and D) corticosteroid treatment.
treated adequately with corticosteroids.

Headache in THS can mimic a scenario of migraine. Initial presenting symptoms in our patient such as headaches with nausea, vomiting, photophobia, phonophobia and blurry vision may be confused with an attack of a complicated migraine but the presentation of painful ophthalmoplegia with ipsilateral multiple cranial nerve involvement suggestive of a structural lesion related event. Clinical findings in our patient fulfilled the ICHD-3 criteria for THS (Table 1) with the presentation of multiple cranial nerve dysfunction of the IIIth, VIth, and V1 and V2; and abnormal MRI findings in the region of cavernous sinus. The presentation of VIIth nerve paresis suggested that inflammation was not limited in the cavernous sinus in location. A marked radiological and clinical improvement to steroid was also evident. Our patient did not have any comorbidity such migraine, infection, diabetes, or sarcoidosis. Notably, the patient needed a low dose steroid to prevent a relapse, as the latter may occur in up to 40% of the patients [6].

Neuroimaging study, particularly brain MRI, the diagnostic modality of choice, is critical in establishing the diagnosis. Although a granuloma demonstrated by either MRI or biopsy is required for diagnosis (Table 1) [4]. La Mantia and colleagues have argued against this commandment [7]. After having reviewed the literature on a pooled 124 THS cases published from 1988 (year of publication of first THS criteria) to 2002 and analyzed individual cases in relation to the new THS criteria, La Mantia and colleagues found that approximately only one third (35%, 44/124) were with inflammation on MRI or biotic evidence of granuloma, while one third (33%, 41/124) with normal neuroimaging findings, and the remaining one third (31%, 39/124) due to a secondary specific lesion. They argued that application of clinical criteria for THS alone does not guarantee a correct diagnosis [7].

The Headache Classification Subcommittee of the International Headache Society describes the course and features of THS as "episodic orbital pain associated with paralysis of one or more of the IIIth, IVth, and/or VIth which usually resolves spontaneously but tends to relapse and remit [4]. On the other hand, THS may be an initial presentation of systemic inflammatory disorders such as sarcoidosis and Wegener's granulomatosis; or can be concomitant with other autoimmune inflammatory disorders, such as lupus erythematosus [8]. Guidelines for diagnosis and management of THS have been published with several revisions [4,9,10]. However, THS is essentially the clinical diagnosis and the diagnosis of exclusion plus a clinical favorable response to corticosteroid treatment. Usually patients with THS respond to corticosteroid treatment exquisitely well. If the symptoms do not improve in 7 days with corticosteroid treatment, an entity other than THS should be considered [11,12].

IV. CONCLUSIONS

In summary, THS may affect a cranial nerve beyond cavernous sinus in location. The neuroimaging study, particularly brain MRI with gadolinium enhancement, is the diagnostic modality of choice. Corticosteroid is the cornerstone treatment for THS which usually results in rapid clinical relief of the symptoms within days.

V. ACKNOWLEDGEMENT

This article is dedicated to Mrs. Ethel Lombard for her outstanding service to the Department of Neurology at Temple University Hospital for 60 years.

References
1 Tolosa E: Periarteritic lesions of the carotid siphon with the clinical features of a carotid infraclinoid aneurysm. J Neurol Neurosurg Psychiatry 1954;17:300-302.
Questions (please choose a single answer):

1- Which of the following statements is NOT correct in Tolosa-Hunt Syndrome?

   A. Granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbit, demonstrated by MRI or biopsy
   B. Paresis of one or more of ipsilateral IIIrd, IVth and/or VIth cranial nerves
   C. Headache precedes paresis of IIIrd, IVth and/or VIth nerves by ≤ 2 weeks,
   D. Headache can evolve into ipsilateral neck pain causing neck rigidity.

2- All of the following diseases have been reported relevant to Tolosa-Hunt Syndrome Except?

   A. Sarcoidosis
   B. Wegner disease
   C. HIV
   D. SLE

3- Which of the following statements is incorrect about Tolosa-Hunt Syndrome?

   A. The best diagnostic radiologic modality is MRI with contrast.
   B. THS may affect cranial nerves beyond cavernous sinus.
   C. THS could be relapsing-remitting in clinical course.
   D. THS is always started with a headache before cranial nerves involvement.

Correct answer: 1: D; 2: C; 3 D.