International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Isolated Complete-Pupil Involved- Third Nerve Palsy as Presentation of Tolosa-Hunt Syndrome: Case Report

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Abstract— Introduction*: Tolosa-Hunt syndrome (THS) is a rare, painful ophthalmoplegia associated with paresis of one or more of the third, fourth and/or sixth cranial nerves that in some uncommon cases dysfunction of the optic, trigeminal, facial, acoustic nerves and sympathetic innervation of the pupil can be seen. THS is a diagnosis of exclusion and treatment should be with high dose steroid.* ***Case presentation****: We describe the case of a 55-year-old Egyptian male that was admitted to our hospital for painful ophthalmoplegia of the right eye. After the diagnostic work-up, we concluded that the patient had an inflammatory form of Tolosa-Hunt syndrome. We initiated treatment with IV steroids and showed great response.* ***Discussion****: The etiologies of headache in association with third cranial nerve palsy—pupillary involvement are: Tolosa-Hunt syndrome (THS), recurrent painful ophthalmoplegic neuropathy (RPON) formerly named ophthalmoplegic migraine (OM), posterior communicating artery aneurysms (PCAs), pituitary apoplexy.* ***Conclusion****: Finally, we concluded that the patient had Tolosa-Hunt syndrome because he completely fulfilled HIS 2018 diagnostic criteria, and the treatment with steroids at a dose of 1 mg/kg/day tapered slowly and has been well received.*

I. Introduction

In a patient with the clinical characteristics of an anterior intracavernous carotid aneurysm, Eduardo Tolosa described a granulomatous inflammatory process encircling the carotid siphon in 1954[1]. After a few years, Hunt et al. reported in 1961 that 6 patients had successfully responded to steroids[2]. The eponymous Tolosa-Hunt syndrome (THS) was first coined in 1966 by Smith *et al.,* to describe the triad of unilateral ocular discomfort, associated cranial nerves (CNs) palsies, and a remarkable improvement in symptoms after receiving systemic steroids therapy[3].

THS is a rare, painful ophthalmoplegia associated with paresis of one or more of the third, fourth and/or sixth cranial nerves that in some uncommon cases dysfunction of the optic, trigeminal, facial, acoustic nerves and sympathetic innervation of the pupil can be seen. Other than pain-induced nausea, vomiting, systemic symptoms can occur rarely[4]. It responds to steroids and is caused by granulomatous inflammation—unknown etiology of the cavernous sinus or orbital apex[5,6]. The exact prevalence remains unknown, with an estimated annual incidence of one to two case(s) per million per year[7]. The International Headache Society (IHS) first offered THS criteria in 1988[8] and changed it in the 2004[9], 2018[10] revisions of the IHS classification.

THS can be classified according to neuroimaging as benign (when no abnormal neuroimaging can be found), inflammatory (when inflammatory findings are shown on MRI or biopsy) and symptomatic (when neuroimaging reveals a specific lesion)[11].

THS is a significantly understudied topic in the Middle East, with little information available beyond a few case reports[12-15]. In this case we report a patient with painful ophthalmoplegia of the right eye with emphasis on the Tolosa-Hunt syndrome: its findings, work-up, and treatment. Furthermore, we will tackle briefly on pupil involvement in painful third cranial nerve palsy.

II. Case Presentation

We are reporting a case of 55 years old, Egyptian gentleman, not known to have any previous medical disease who is admitted to our hospital after he experienced around three weeks history of right retro-orbital headache, gradually increased until he failed using over the counter painkillers to alleviate the pain. Few days after his headache, he started to have subjective double vision mainly in near vision associated with complete right eyelid droop for which he decided to seek medical evaluation.

The patient denies history of fever, sensory or other neurological symptoms, as well as systemic review were unremarkable.

On examination: he looked in pain, with normal range vital signs.

He was conscious alert and fully oriented with normal other higher mental components.

His neurological examination remarkable for complete right palpebral ptosis, very dilated, non-reactive pupil and extropic, hypotropic right eye in primary gaze, horizontal binocular diplopia with no other cranial nerves or Horner were involved (figure 1, 2).

All his other motor, sensory, cerebellar as well as systemic examinations are normal. The patient was admitted and

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investigated thoroughly as approach of painful ophthalmoplegia of isolated, pupil involved third cranial nerve palsy (failure of inferior oblique, superior rectus, inferior rectus, medial rectus, parasympathetic).

Fig. 1. Complete right palpebral ptosis, Right fixed dilated pupil

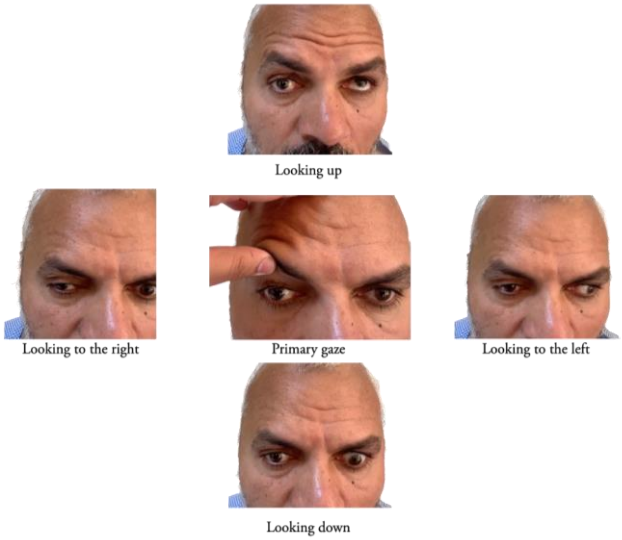

Fig. 2. Neuro-ophthalmologic examination prior treatment shows right palpebral ptosis, exotropia, hypotropia of the primary look of the right eye, paresis of the third cranial nerve.
*Right eyelid is elevated because it was moved by the examiner.

His labs workup revealed normal renal, liver function as well as basic chemistry including lipids profile. His complete blood count, coagulation profile and thyroid function tests found to be within normal limit. His HbA1c was 5.7%, ESR of 47 and normal CRP. All vasculitis screening and serology workup were negative. Lumbar puncture was done and cerebrospinal fluid protein, glucose, cell count, microbiology including tuberculosis screening were within normal values.

Radiologically, X-ray of the chest is normal, and urgent CT/CTA/CTV showed normal brain parenchyma, patent arterial and venous circulations.

MRI brain + IV Gadolinium with different sequences with were obtained, demonstrating enhancing soft tissue thickening along right cavernous sinus, without any filling defect in the cavernous sinus or dilated SOV, suggestive of Tolosa-Hunt syndrome (figure 3).

Since the studies showed no abnormalities and we excluded neoplastic, infectious, vascular, thyroid, and metabolic causes of painful ophthalmoplegia, we decided to start the patient on intravenous Methylprednisolone (1G, intravenous, once daily) for five days after rest of the differential diagnoses were ruled out based on history, physical examination, and relevant investigations.

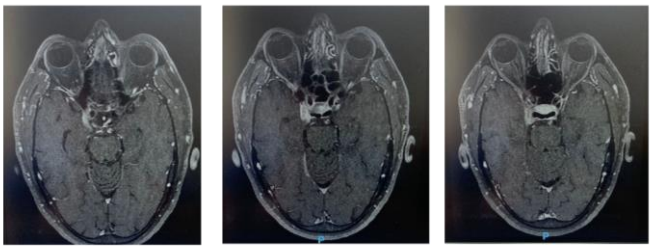

Fig. 3. MRI brain axial T1 post-contrast images from his initial presentation. shows an enhancing soft tissue thickening along right cavernous sinus, without any filling defect in the cavernous sinus or dilated SOV.

The patient afterwards reported dramatically improvement as his headache was almost subsided within first 24-48 hours, and his dilated pupil, droopy right eyelid.

After he finished the five days course, he was discharged on oral Prednisolone (1mg/Kg) with gradual tapering every two weeks. On follow up assessment three weeks later he had complete resolution of the headache and ophthalmoplegia (figure 4).

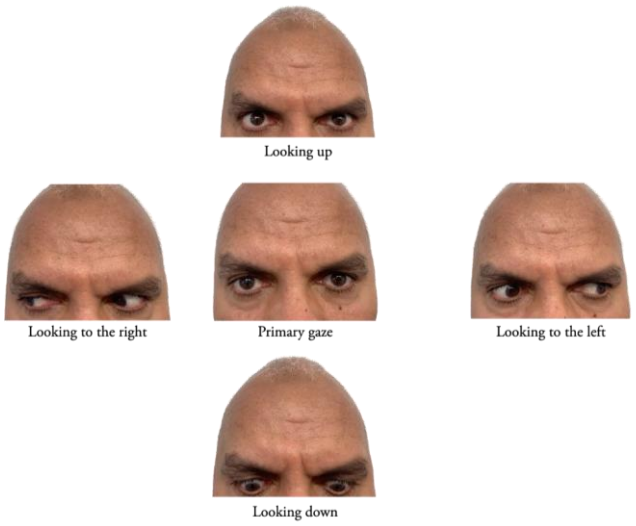

Fig. 4. Neuro-ophthalmologic examination after treatment shows improvement of the right palpebral ptosis and right eye movements after 3 weeks of steroid treatment.

III. Discussion

Tolosa-Hunt syndrome is described as a unilateral orbital or periorbital pain associated with paresis of one or more of the IIIrd, IVth and/or VIth cranial nerves caused by a granulomatous inflammation in the cavernous sinus, superior orbital fissure or orbit[10]. This case presented to our emergency room and admitted under the care of neurology team. Our hospital is considered to be the largest secondary hospital in the city of Jeddah to receive neurological cases.

Our patient fulfilled completely the ICHD-3 diagnostic criteria, he had right retro-orbital headache that preceded the

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paresis of oculomotor nerve by less than 2 weeks. Furthermore, it was ipsilateral to the granulomatous inflammation that was evident by MRI (criterion A, C). MRI with gadolinium demonstrated enhanced soft tissue thickening along right cavernous sinus, paresis of the ipsilateral oculomotor nerve (criterion B). Finally, after thorough history, examination, lab investigations we ruled out any another ICHD-3 diagnosis (criterion D). Also, in the literature review, no standard dose or duration of use for steroid treatment has been established. Our patient responded on day 2 with improvement of his headache and oculomotor nerve palsy on intravenous pulse Methylprednisolone 1G which is consistent with literature and previous studies[16,17]. Studies have shown that older patients are more likely to have a slower improvement in their oculomotor palsy, which couldn't explain our patient's almost complete resolution of symptoms within 2 days of steroid treatment[18]. Prognosis in THS is good as stated in previous studies and one recent demographic study in Qatar with a recurrence-rate of 9.7%[19] and that was evident in our patient with short term follow up after 3 weeks of presentation with complete resolution of neurological signs and symptoms without relapses, resistance to treatment or sequalae.

However, permanent ocular motor deficits may remain in some patients. Relapse can occur in as many as 40% of patients successfully treated with steroids for THS. Gimenez-Roldan *et al.* have reported that relapses may occur as long as 13 years after initial diagnosis and treatment.[20]

The etiologies of headache in association with third cranial nerve palsy—pupillary involvement are: Tolosa-Hunt syndrome (THS), recurrent painful ophthalmoplegic neuropathy (RPON) formerly named ophthalmoplegic migraine (OM)[21-23], posterior communicating artery aneurysms (PCAs)[24], pituitary apoplexy[25].

The clinical features of pupil involvement in painful third cranial nerve palsy are: Ptosis due to paralysis of levator palpebrae superioris muscle (LPS)[26], ocular deviation resulting in exotropia and hypotropia, pupils can be spared or dilated, diplopia, headache.[27]

There is limited regional literature on its varied presentations, diagnosis, and management especially in Saudi Arabia, we're only aware of a single case report here in Jeddah[28]. We hope our case report will give some insight about this rare disease.

IV. Conclusion

We concluded that the patient had Tolosa-Hunt syndrome because he completely fulfilled HIS 2018 diagnostic criteria, and since no abnormalities were found in his laboratory tests, except neuroimaging which showed enhancing soft tissue thickening along right cavernous sinus, hence, we classified him as an inflammatory variety of Tolosa-Hunt syndrome and was treated successfully with Methylprednisolone.

Abbreviations

CSF, cerebrospinal fluid; CTA/V, computerized tomography angiography/venography, ESR, erythrocyte sedimentation rate, IHS, international headache society; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; SOV, superior ophthalmic vein. TSH, Tolosa-Hunt syndrome.

Competing interests:

The authors declare that they have no competing interests.

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