Case report
Tolosa-Hunt syndrome in Libyan female patient

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■ **Abstract:**

Background: Tolosa Hunt syndrome is an extremely rare disorder typically presents with painful unilateral ophthalmoplegia, caused by non-specific inflammation affecting the cavernous sinus and superior orbital fissure leading to third, fourth, with or without sixth cranial nerve palsy. Case: this report describes a case of 27-years old female with Tolosa Hunt syndrome who was firstly diagnosed as seronegative myasthenia gravis. She developed right supra-orbital pain and diplopia; on examination, she had right-sided complete ophthalmoplagia with ptosis. Conclusion: clinical findings were consistent with diagnosis of Tolosa-Hunt Syndrome (THS). The patient responded dramatically to steroids with alleviation of the orbital pain within 24 hours followed by significant improvement in the ocular movements in few days.

● **Key words**: Ophthalmoplagia, Orbital pain, ptosis, Tolosa-Hunt syndrome

■ **المستخلص:**

متلازمة الخاصية تولوسا هانت هو مرض نادر يسبب شللا في عضلات العين وألما عند محاولة تحريكها وارتخاء في جفن العين. سبب المرض التهاب في الجيب الدموي الذي يمر خلاله العصب الثالث والرابع والسادس والفرع الأول والثاني من العصب الخامس. الخاصية الأساسية لهذا المرض هو اختفاء الأعراض خلال أيام من اخذ عقار الكرتيزون.

● **الكلمات المفتاحية:** شلل العين المؤلم، تدلي الجفون. متلازمة تولوزا هانت.

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Introduction

Tolosa-Hunt syndrome is an extremely rare idiopathic condition, characterized by painful unilateral ophthalmoplegia. It is usually associated with third, fourth, with or without sixth cranial nerve palsy and usually, there is no visual impairment. It was first described by a Spanish physician, Tolosa in 1954, in a patient with painful ophthalmoplegia associated with 3rd, 4th and 6th carotid nerve palsies (Tolosa, 1954). Thereafter, in 1961, Hunt described the association between similar cases and low-grade, non-specific inflammation of cavernous sinus (Hunt et al., 1961).

Tolosa-Hunt syndrome is considered as a non-specific inflammatory (granulomatous or non-granulomatous) reaction in the cavernous sinus, supra orbital fissure or in the orbit. It responds promptly to corticosteroids in most cases though recurrences can occur (Hoes et al., 1981; Hunt et al., 1988). The revised diagnositic criteria for THS by the international headache society include one or more episodes of pain in unilateral orbital area that persisted for several weeks or longer if not treated, followed by paresis of one or more of the third, fourth, and sixth cranial nerves. Some cases, present with paresis of the first branch of the fifth cranial nerve (ophthalmic nerve) and rarely may be associated with disorders of the optic nerve and proptosis (Shahrizalia, et al., 2010). The magnetic resonance imaging (MRI) or biopsy examination show nonspecific inflammation (Ramli et al., 2010).

However, ophthalmoplegia in association with pain in the retro-orbital or periorbital region is commonly seen in some pathologies, other than Tolosa-Hunt syndrome. These include internal carotid artery and cerebral aneurysm (Cogan and Mount, 1963), carotid-cavernous fistula (Li et al., 2019; Ghosh, 2015), tumors (Maciá et al., 2005; Daigavane and Abhishek, 2021), infection (Hajjar et al., 2022) and ophthalmoplegic migraine (Arur et al., 2007). Furthermore, cranial neuropathies in poorly controlled diabetic patients are extremely rare and Tolosa-Hunt-like syndrome in some cases of diabetes mellitus is challenging for physicians regarding diagnosis and treatment (Lasam and Kapur, 2016).

This report presents an interesting case of Tolosa-Hunt syndrome in a Libyan female patient treated successfully with corticosteroids.

■Case report

A 27 years old Libyan female patient presented with pain in the right eye for 10 days, followed by difficulty in opening the eye with double vision. The patient's anti-acetyl choline antibodies test was negative, therefore; the diagnosis was seronegative myasthenia gravis and the patient was treated with pyridostigmine that made her lethargic with no improvement in her periorbital pain and ptosis. Since clinical history was not consistent with myasthenia gravis, the patient was then referred to the neurologist for opinion. The clinical examination of the patient reviled complete ophthalmoplegia and incomplete ptosis of right eye (Figure 1).

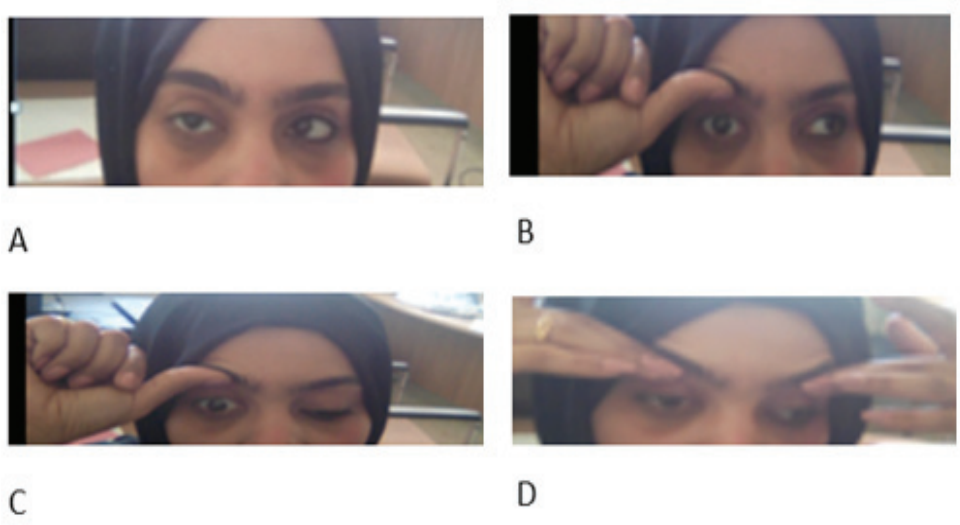

Figure 2: Eye examination showing complete ophthalmoplegia and incomplete ptosis of right eye

A. Looking to the right: right eye ptosis and right lateral rectus palsy
B. Looking to the left: right medial rectus paralysis, left eye normal
C. Looking down: right inferior rectus paralysis
D. Looking to left and down side: right superior oblique paralysis

The patient's complete blood picture, urea, creatinine, liver function test, ESR, CRP, angiotensin-converting enzyme, antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, and double stranded antibodies were all negative.

Based on clinical picture, the patient was diagnosed as Tolosa-Hunt

syndrome and started on prednisolone 80mg/day for 3 days followed by tapering the dose slowly during her 8 weeks course of treatment. The periorbital pain was resolved within 24 hours, and the diplopia, ptosis and ophthalmoplegia resolved within few days (Figure 2).

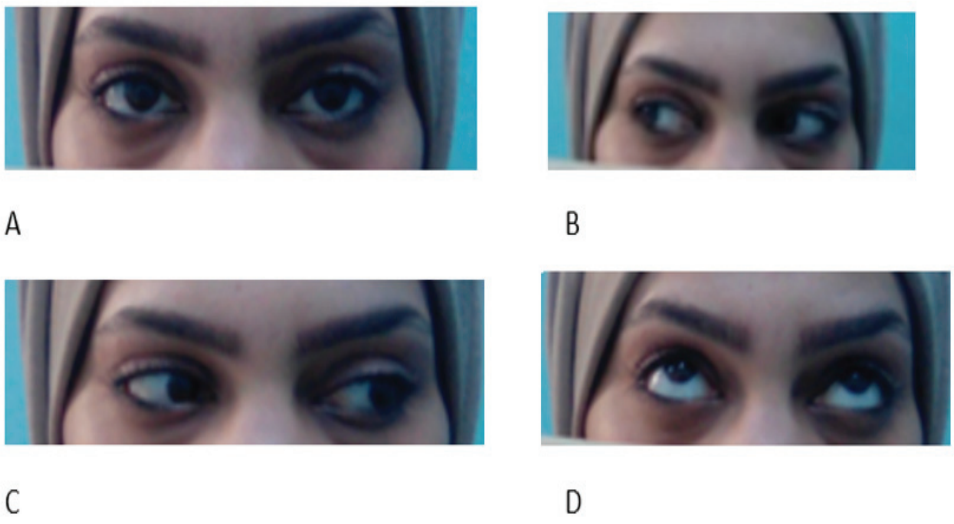

Figure 2: Post-treatment eye examination revealed improvement in right palpebral ptosis and cranial nerve paresis of the right eye.

A. No right eye ptosis

B, **C**, and **D** Normal right eye movement in different directions

■ Discussion

Tolosa, a Spanish doctor described the condition in 1954 in a patient with recurrent painful ophthalmoplegia involving 3rd, 4th and 6th cranial nerves, the patient's carotid angiography showed segmental narrowing of carotid siphon (Tolosa, 1954).

In 1961, Hunt et al described six patients with similar clinical findings, and proposed a low-grade nonspecific inflammation of the cavernous sinus and its walls as the cause of the syndrome (Hunt et al., 1961). About five years later, Simith and Taxdal termed the condition Tolosa – Hunt syndrome (Smith and Taxdal, 1966).

While the exact cause of Tolosa-Hunt syndrome is unknown, infection and autoimmune response linked with an inflammation in the cavernous sinus have been suggested (Sharma et al., 2006; Seidenberg and Leib, 1990). Histologically,

there is a nonspecific inflammation of the septa and wall of the cavernous sinus, with a lymphocyte and plasma cell infiltration, giant cell granulomas, and proliferation of fibroblasts and thickening of the dura matter (Tolosa, 1954, Hunt et al., 1961). The inflammation produces pressure and secondary dysfunction of the structures within the cavernous sinus, including cranial nerves III, IV, and VI, as well as the superior divisions of cranial nerve V.

The diagnosis of Tolosa-Hunt syndrome usually based on thorough clinical evaluation and detailed patient history that revealed the presence of characteristic features (e.g., pain, headache, ophthalmoplegia). The diagnosis may be confirmed by specialized radiologic tests including computed tomography (CT) scan, and magnetic resonance imaging (MRI). These examinations may reveal characteristic enlargement or inflammation of cavernous sinus and superior orbital fissure. According to the international headache society guidelines (1988, revised 2004); the diagnostic criteria for Tolosa-Hunt syndrome include retro-orbital pain persisting for weeks if untreated. Usually associated with 3rd 4th and or 6th cranial nerves palsy, granulomatous inflammation within the cavernous sinus, superior orbital fissure or orbit. The diagnosis usually confirmed by MRI or tissue biopsy, in addition, the onset of the nerve palsy must coincide with onset of pain or follow it within 2 weeks of its onset, and the paresis resolve within 72 hours when treated adequately with steroid and other causes have been excluded by appropriate investigation (Hung et al., 2015).

Other causes of orbital pain, ophthalmoplegia and cranial nerve palsies such as trauma, vascular Ceuses (e.g. intra-cavernous carotid artery aneurysm), neoplasm (e.g. primary intracranial tumor, pituitary adenoma, meningioma and metastasis), infection, Wegener's granulomatosis, eosinophilic granuloma, diabetic ophthalmoplegia and giant cell arteritis must be excluded by appropriate investigations. The clinical picture of the patient reported here met the diagnostic criteria and most of other differential diagnosis were ruled out making a diagnosis of Tolosa-Hunt syndrome most likely.

The patient retro-orbital pain has been completely resolve within 24 hours of starting steroid treatment, however, diplopia, ptosis and ophthalmoplegia improved within few days. The time needed for improvement of the cranial

nerve palsies may take up to 3-4 weeks (Zhang et al., 2014).

Tolosa-Hunt syndrome follows a variable course that can last from days, weeks to months if untreated. The prognosis is generally good and the residual deficit is unusual though, recurrences are common and may occur in 50 % of cases and can be either unilateral or bilateral (Hannerz, 1992). For follow up it is recommended to repeat MRI of the brain every 1 to 2 months until MRI is normal, then every 6 to 12 months for 2 years.

■ Conclusion

Tolosa Hunt syndrome is a rare condition, patients with THS present with painful ophthalmoplegia with a dramatic response to systemic corticosteroids. As THS essentially remains a diagnosis of exclusion, clinicians need to be aware of the different causes of painful ophthalmoplegia, including the less common presentations. Neurologists, ophthalmologists and neuroradiologists play an important role in establishing the correct diagnosis. It is usually self-limited. Relapses may occur (30-40 % of patients may experience relapse); high-dose corticosteroid therapy is the first-line therapy (Kline and Hoyt, 2001; Zhang et al., 2014). There is no evidence sufficient for the appropriate dose, route of administration and duration of therapy (Kirbas et al., 2008). A remarkable feature of glucocorticoid therapy is the rapid resolution of orbital pain within 1-3 days, which also serves as confirmation of The diagnosis (Hung et al., 2013). Prognosis is good with unusual residual deficit.

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