

<https://doi.org/10.31288/oftalmolzh202355355>

Neuro-ophthalmological aspect of Tolosa-Hunt Syndrome: A Case Report

V. A. Vasyuta ¹, O. P. Vitovska ², T. A. Iovenko¹, S. A. Verbovska ¹, L. O. Dunaievska ¹

¹ State Institution "Romodanov Neurosurgery Institute of NAMS of Ukraine»

² Bogomolets National Medical University
Kyiv (Ukraine)

Keywords:

cavernous sinus, fissura orbitalis superior, ocular pain, ocular motility abnormalities

Tolosa-Hunt Syndrome is an idiopathic granulomatous inflammatory disease of the cavernous sinus, superior orbital fissure, or orbit which is manifested by ocular pain and ophthalmoplegia. Granulomatous inflammation of the dural wall of the cavernous sinus and/or superior orbital fissure is the basis of the pathological process. The disease is clinically manifested by orbital pain, diplopia, exophthalmos, and/or oculomotor abnormalities. The syndrome is also called painful ophthalmoplegia with a key symptom being neuropathic periorbital or retro-orbital pain, and paresthesias along the first branch of the trigeminal nerve. We present a case of this syndrome. The patient was administered hormonal therapy, Medrol at a daily dose of 1 mg/kg body weight/day intravenously for five days, with subsequent transition within a month to oral Medrol. The pain in the eye completely relieved and restoration of normal ocular motility was observed in the presence of hormonal therapy. Tolosa-Hunt syndrome is a clinical diagnosis of exclusion (i.e., it is diagnosed after excluding other causes of painful ophthalmoplegia).

Management of ocular and periorbital pain (ophthalmalgia) is a multidisciplinary issue that must include collaboration amongst ophthalmologists, neurologists and adjacent specialties in medicine. The eye is highly pain sensitive since it is extremely important for the human being. In addition, it must be preserved to the maximal extent since approximately 90 percent of an individual's information is obtained through vision [1].

Ophthalmologists are commonly aware of the ophthalmic causes of ophthalmalgia, but the diagnosis and management become challenging when the cause is not ophthalmic but is more related to neurology, neurosurgery or rheumatology. Extraocular causes of ophthalmalgia are variable and require a detailed differential diagnosis made by a multidisciplinary team comprising, besides the ophthalmologist, neurologist, neurosurgeon, oral and maxillofacial surgeon, etc [1].

Ophthalmalgia may be a symptom of eye disease (glaucoma, retrobulbar neuritis or ocular inflammatory disorder), trigeminal neuralgia, the Barré-Liéou syndrome (vertebral artery syndrome), or trigeminal autonomic cephalalgia. Painful ophthalmoplegia may be seen in patients with cerebral vascular aneurysm, carotid-cavernous fistula, giant cell arteritis, sarcoidosis, orbital

pseudotumor and the superior orbital fissure syndrome (also known as Rochon-Duvigneaud syndrome). Tolosa-Hunt syndrome is a rare cause of ophthalmalgia.

It is an idiopathic granulomatous inflammatory disease of the cavernous sinus, superior orbital fissure, or orbit associated with ocular pain and ophthalmoplegia [2]. The syndrome was initially described by Eduardo Tolosa, a Spanish neurosurgeon, in 1954 [3] and then by the American neurosurgeon William Hunt et al in 1961 [4]. Granulomatous inflammation of the dural wall of the cavernous sinus and/or superior orbital fissure is the basis of the pathological process. The disease is clinically manifested by orbital pain, diplopia, exophthalmos, and/or oculomotor abnormalities. The syndrome is also called painful ophthalmoplegia with a key symptom being periorbital or retro-orbital pain, and paresthesias along the first branch of the trigeminal nerve. Pain is intense, described as sharp, penetrating or drilling and can precede ophthalmoplegia by up to 30 days.

Tolosa Hunt syndrome tends to have a relapsing and remitting course, with attacks recurring every few

months or years. The oculomotor nerve is most commonly involved (approximately 80%), followed by abducens nerve (approximately 70%), and an ophthalmic branch of trigeminal nerve (approximately 30%). There can also be sympathetic (third order neuron Horner syndrome) or parasympathetic (oculomotor) involvement which leads to pupillary abnormalities. In 2004, the International Headache Society (IHS) re-defined the diagnostic criteria of Tolosa-Hunt syndrome. The diagnostic criteria were modified by expert consensus, subsequently, in 2018 [5, 6, 7]. According to the criteria, the diagnosis of Tolosa-Hunt syndrome is substantiated if there is magnetic resonance imaging (MRI) or biopsy evidence of granulomatous inflammatory disease of the cavernous sinus, superior orbital fissure, or orbit.

Diagnostic criteria of Tolosa-Hunt syndrome according to the International Classification of Headache Disorders (ICHD) (2018) [7] are as follows:

A. Unilateral orbital or periorbital 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. paresis of one or more of the ipsilateral IIIrd, IVth and/or VIth cranial nerves

C. Evidence of causation demonstrated by both of the following:

1. headache is ipsilateral to the granulomatous inflammation

2. headache has preceded paresis of the IIIrd, IVth and/or VIth nerves by 2 weeks, or developed with it

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

Some reported cases of Tolosa-Hunt syndrome had additional involvement of the Vth nerve (commonly the first division) or optic, VIIth or VIIIth nerves. Sympathetic innervation of the pupil is occasionally affected. The diagnosis of Tolosa-Hunt syndrome can only be made by exclusion, and careful follow-up is required to exclude other causes of painful ophthalmoplegia such as tumors, vasculitis, basal meningitis, sarcoid or diabetes mellitus and ophthalmoplegic migraine [2, 5].

The syndrome is characterized by the dramatic symptomatic improvement seen with glucocorticoids. Medrol and its analogues are used at a daily dose of 1-1.5 mg/kg body weight/day or 500-1000 mg/day intravenously, with subsequent transition to oral glucocorticoids.

The differential diagnosis of ophthalmalgia should include eye pathology accompanied by pain in the eye. Inflammatory eye disorders (e.g. keratitis, scleritis, and optic neuritis) and an acute glaucoma attack should be excluded. In addition, the differential diagnosis should include neurologic disorders accompanied by pain in the eye (neuralgia of the first division of the trigeminal nerve and trigeminal autonomic cephalalgias) [1]. Moreover, painful ocular motility disorders should be

excluded: craniocerebral trauma; orbital apex syndrome (of traumatic, inflammatory, neoplastic or vascular origin), orbital tumor or pseudotumor, cavernous sinus disorders (carotidocavernous fistula and cavernous sinus thrombosis), intracranial neoplasms (meningioma, craniopharyngioma, neurogenic tumor, hemangioma, lymphoma, schwannoma, and pituitary adenoma), metastatic tumors, nasopharyngeal carcinoma; inflammatory disorders (chronic inflammation of the petrous bone, sinusitis, syphilis, basal meningitis, herpetic disorders (herpes zoster virus)). Cerebral vascular aneurysm and Chiari malformation should be also excluded. Other causes of painful ophthalmoplegia include sarcoidosis, granulomatosis with polyangiitis (Wegener's granulomatosis), Behçet disease, systemic lupus erythematosus, multiple sclerosis, diabetes mellitus and thyroid gland disorders [8, 9, 10, 11].

Case Description

A 65-year-old patient presented to us in 2021 complaining of a droopy left upper eyelid, double vision, and retroorbital and periorbital pain within a month before presentation. He also suffered from an intense diffused headache within a week before presentation. In 2019 and 2020, he experienced several-day episodes of an intense headache followed by oculomotor abnormalities and diplopia. The patient reported that he was treated by a neurologist for oculomotor neuropathy. Intracranial neoplasms, inflammatory central nervous system and ear, nose and throat disorders and rheumatologic pathology were excluded. A full blood count was obtained and cerebrospinal fluid examination was performed. This time, the patient experienced a longer episode of headache and oculomotor abnormalities (as long as a month), these abnormalities became more severe (droopy eyelid and failure to move the globe upward, downward and inward), and the diplopia and headache also increased in severity. The patient had also type 2 diabetes mellitus and grade two hypertension. He underwent a general clinical examination and neuroimaging, and was consulted by a rheumatologist, a cardiologist and an endocrinologist. A brain MRI found no symptoms of a focal lesion, but a 2-mm thickening of the left cavernous sinus. The latter was isointense on T1 and hypointense on T2 imaging, and better seen with contrast-enhanced MRI. Doppler ultrasound of the head and neck vessels showed moderate non-stenotic lesions of the major head and neck vessels. He was admitted to the in-patient neurology service and received a two-week treatment (including vascular, nootropic and vitamin therapy) for recurrent oculomotor neuropathy, with no improvement in his symptoms.

The patient was examined by an ophthalmologist. On examination, uncorrected visual acuity (UCVA) OD was 1.0; UCVA OS, 0.3-0.4 and best-corrected visual acuity (BCVA) OS, 0.5 with a spherical correction of +2.0 D; no visual field defect was noted, and intraocular pressure (IOP) OU was 15 mm Hg.

The patient was diagnosed with ophthalmoplegia in the left eye and referred for consultation to the Romodanov institute.

On neuroophthalmological examination, UCVA OD was 1.0; UCVA OS, 0.9, and there was binocular diplopia. In addition, the left eye showed mydriasis, grade 2 ptosis, and limited upward, downward and inward extraocular movements. The Schirmer test was normal. The conjunctiva was pale pink, the cornea transparent, and corneal reflex, normal. The media were transparent. On funduscopy, the optic discs were pale pink, with well-defined margins; the retinal arteries, narrow, venous deflection at arteriovenous crossing, and the macula was normal.

The patient was diagnosed with Tolosa-Hunt syndrome with a left oculomotor nerve lesion because (1) clinical features included pain and oculomotor abnormalities and (2) other causes of painful ophthalmoplegia were excluded. He was administered hormonal therapy, Medrol at a daily dose of 1 mg/kg body weight/day intravenously for five days, with subsequent transition within a month to oral Medrol. The pain in the eye completely relieved on day 3, and restoration of normal ocular motility in all fields of gaze was observed after two weeks of hormonal therapy. The patient was followed for 12 months after this treatment.

Conclusion

Tolosa-Hunt syndrome is a clinical diagnosis of exclusion (i.e., it is diagnosed after excluding other causes of painful ophthalmoplegia). A combination of pain in the eye and adjacent (retrobulbar, retroorbital and/or periorbital) areas with oculomotor abnormalities is a feature of this syndrome. The disease does not require treatment with vascular, nootropic or vitamin therapy. Glucocorticoid therapy at an optimal dose significantly improves disease symptoms, with complete resolution of pain and oculomotor abnormalities within a few days. Tolosa-Hunt syndrome is not a pure eye disease, but patients with this disorder present their symptoms to ophthalmologists, and it is on the latter depends whether a diagnosis will be correct and whether the patient will be referred promptly to appropriate allied health professionals. Collaboration with neurologists, neurosurgeons, rheumatologists, hematologists and infectionists is a must for ophthalmologists. The successful management of Tolosa-Hunt syndrome requires a multidisciplinary approach, with the involvement of health care professionals of various specialties.

References

1. Vasyuta VA, Biloshytsky VV. Differential diagnosis of patients presenting with ocular and periorbital pain: a multidisciplinary approach. *J Ophthalmol (Ukraine)*. 2018;5:66-71. doi: 10.31288/oftalmolzh201856671.

2. Kim H, Oh SY. The clinical features and outcomes of Tolosa-Hunt syndrome. *BMC Ophthalmology*. 2021;21:237. doi: 10.1186/s12886-021-02007-0.

3. Tolosa E. Periarteritic lesions of the carotid siphon with the clinical features of a carotid infraclinoidal aneurysm. *J*

Neurol Neurosurg Psychiatry. 1954;17:300-2. doi: 10.1136/jnnp.17.4.300. PMID: 13212421. PMCID: PMC503202.

4. Hunt WE, Meagher JN, LeFever HE, Zeman W. Painful ophthalmoplegia. Its relation to indolent inflammation of the cavernous sinus. *Neurology*. 1961;11:56-62. doi: 10.1212/wnl.11.1.56. PMID: 13716871.

5. La Mantia L, Curone M, Rapaport AM, Bussone G. Tolosa-Hunt syndrome: critical literature review based on IHS 2004 criteria. *Cephalalgia*. 2006;26(7):772-81. doi: 10.1111/j.1468-2982.2006.01115.x. PMID: 16776691.

6. Colnaghi S, Versino M, Marchioni E, Pichiecchio A, Bastianello S, Cosi V, Nappi G. ICHD-II diagnostic criteria for Tolosa-Hunt syndrome in idiopathic inflammatory syndromes of the orbit and/or the cavernous sinus. *Cephalalgia*. 2008;28(6):577-84. doi: 10.1111/j.1468-2982.2008.01569.x. PMID: 18384413.

7. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(3):177.

8. Kim H, Oh SY. The clinical features and outcomes of Tolosa-Hunt syndrome. *BMC Ophthalmol*. 2021; 21(237):101. <https://doi.org/10.1186/s12886-021-02007-0>

9. Kline LB, Hoyt WF. The Tolosa-Hunt syndrome. *J Neurol Neurosurg Psychiatry*. 2001;71:577-582.

10. Olsen K, Johnson A, Castillo S, Bennett J, Ryan MF. Diagnosis and treatment of Tolosa-Hunt Syndrome in the Emergency Department. *Open J Emerg Med*. 2017;5:1-7.

11. Zurawski J, Akhondi H. Tolosa-Hunt syndrome--a rare cause of headache and ophthalmoplegia. *Lancet*. 2013; 382:912.

Disclosures

Received 14.08.2023

Accepted 15.09.2023

Corresponding Author: Vira A Vasyuta, Department for Science and Organization, Romodanov Neurosurgery Institute, National Academy of Medical Science of Ukraine, Kyiv. E-mail: vasyuta.v@ukr.net

Author Contributions: VAV: Conceptualization, Writing-original draft, Formal Analysis, Writing-review & editing; OPV: Methodology, Writing-original draft, Formal Analysis, Writing-review & editing; TAI: Writing-review & editing; SAV: Writing-review & editing; LOD: Writing-review & editing. All authors reviewed the results and approved the final version of the manuscript.

The study conformed to the principles of the Declaration of Helsinki.

Informed consent was obtained from the participant

Conflict of interest: There are no competing interests to declare.