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Diagnosis and Treatment of Tolosa-Hunt Syndrome in the Emergency Department

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Abstract

We describe herein a patient who presented with painful ophthalmoplegia and was ultimately diagnosed via magnetic imaging resonance studies and successfully treated for Tolosa-Hunt syndrome. Tolosa-Hunt syndrome is a rare, reversible and painful ophthalmoplegia characterized by recurrent unilateral orbital pain, ipsilateral oculomotor paralysis and prompt response to steroids. Specific criteria for its diagnosis exist and are discussed herein. Individuals affected may display signs of select cranial nerve palsies, ptosis, facial numbness, diplopia, midrosis, and proptosis. Appropriate recognition of the disease can allow for immediate intervention and thus decrease the length and severity of symptoms especially as symptoms may not spontaneously resolve without treatment which leads to unnecessary suffering through pain, anxiety, and decreased vision. We describe the case presentation and keys for diagnosis emergency medicine that physicians should know for this potentially devastating condition.

Keywords

Tolosa-Hunt Syndrome, Ophthalmoplegia, Vision Loss, MRI, MRA, Cranial Nerve Deficits

1. Introduction

Tolosa-Hunt syndrome is a painful ophthalmoplegia characterized by recurrent unilateral orbital pain, ipsilateral oculomotor paralysis and its prompt response to steroids [1]. The diagnostic criteria according to the 2004 International Headache Society include: a) one or more episodes of unilateral orbital pain persisting for weeks if untreated; b) paresis of one or more of the third, fourth and/or sixth cranial nerves and/or demonstration of granuloma by MRI or bi-

opsy; c) paresis which coincides with the onset of pain or follows it within two weeks; d) pain and paresis which resolve within 72 hours when treated adequately with corticosteroids; e) other causes have been excluded by appropriate investigations [2]. Patients may present with some of all of these findings and here clinical suspicion and appropriate imaging and ophthalmology consultation are requisite.

Tolosa-Hunt Syndrome is a rare but important reversible cause of vision loss which may elude detection on primary examination. Individuals affected may display signs of paralysis of certain cranial nerves (CN), exhibited by ptosis, facial numbness, diplopia, midrosis, and/or proptosis that may initially point to an alternate diagnosis: including malignancy, infection or vascular occulsion. Quick recognition of the disease through the appropriate diagnostic imaging and laboratory studies can allow for intervention aimed at decreasing the length and severity of symptoms, rule out more sinister disease processes that may need immediate surgical intervention or other interventions and relieve anxiety for the patient. While symptoms may resolve without intervention, withholding treatment may cause weeks of unnecessary suffering through pain, anxiety, and decreased vision [3] which can be debilitating. Of note there is no universal patient presentation other than ophthalmoplegia for Tolosa-Hunt syndrome that may afflict patients of any age and gender [2]. Moreover, there is no specific study or test as Tolosa-Hunt syndrome is often a diagnosis of exclusion which makes it critical for the emergency medicine physician to recognize its presentation and treatment.

Key aspects of this case are discussed herein as well as important differential diagnoses the emergency medicine physician should be aware of regarding a patient who presents with painful, atraumatic vision loss.

2. Case Presentation

A 61-year-old woman presented to our Emergency Department with worsening left periorbital eye pain, visual disturbances and diplopia where the left eye would not cross the midline medially. The pain was described as throbbing in nature with episodes of extremely sharp pain worsened with even gentle palpation of the eye. The patient's symptoms started roughly one month ago with the onset of double vision and pain around the orbit. The patient was recently seen by her primary care provider and was given levofloxacin for suspected sinusitis. The patient completed the course of antibiotics without improvement of her symptoms.

Four days prior to presentation, the patient was seen again by another provider because her diplopia and pain were worsening. At this second encounter the patient underwent a computed tomography scan of her head and orbits that was read as normal with no evidence for intracranial bleeding, masses or other findings that could explain her symptoms. She was prescribed naproxen sodium for pain and inflammation for suspected chronic sinusitis and discharged.

Upon presentation to our emergency department (ED), the patient's relevant

past medical history was reviewed which included a remote episode of Bell's palsy. She denied prior history of head injury or other cranial nerve involvement, fever, illness, foreign travel, nausea, vomiting, vertigo, or any constitutional symptoms. She indicated she was a former smoker with no history of illicit drug use and social alcohol use. The patient had no known medical issues or chronic diseases including diabetes, hypertension or vascular disease and stated she saw her primary care physician regularly. She had no significant family history for chronic illness and she took no medications. On physical examination she appeared well except for her chief complaint. Her vital signs were within normal limits as was her pulse oximetry reading. Her neurological exam save the cranial nerve deficits noted was unremarkable as was the rest of her physical exam including her head and neck exam.

Because of the concern for her continued vision loss, laboratory studies were ordered which included a basic metabolic panel (BMP), complete blood count (CBC) and coagulation studies to assess for infectious and thrombotic causes, respectively. Also, indirect markers of inflammation were assessed which included an erythrocyte sedimentation rate (ESR) and a C-reactive protein level (CRP). Magnetic resonance imaging of her brain and orbits with and without intravenous contrast was also ordered in order to further integrate the cause of the patients worsening symptoms.

Her laboratory values were remarkable for an elevated CRP of 7.5 mg/L, fibrinogen of 534 mg/dL and an ESR of 33 mm/h. All other lab values including a white blood cell count were within normal limits. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the brain demonstrated (Figure 1 and Figure 2) no evidence of mass lesions, cortical edema or hemorrhage and revealed normal optic pathways and normal optic nerve anatomy. The anterior pathway of the left cavernous sinus in the marrow space appeared thicker and showed some asymmetry. The constellation of MRA findings combined with history and physical exam suggested a diagnosis of Tolosa-Hunt

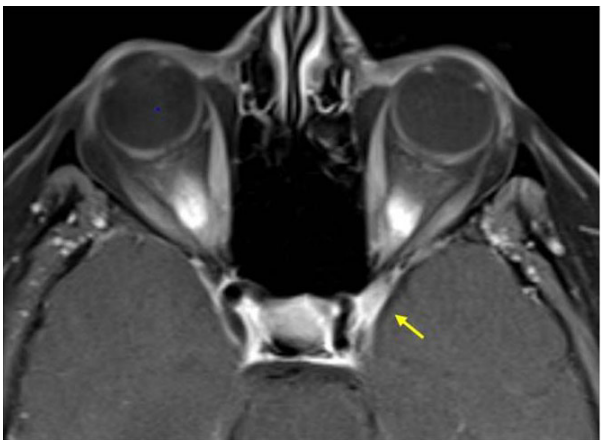

Figure 1. MRA images consistent with the findings in Tolosa-Hunt Syndrome. Axial fat-suppressed post contrast imaging showing asymmetric thickening and enhancement of the left cavernous sinus (arrow), although a nonspecific finding, in the given clinical setting consistent with Tolosa-Hunt syndrome.

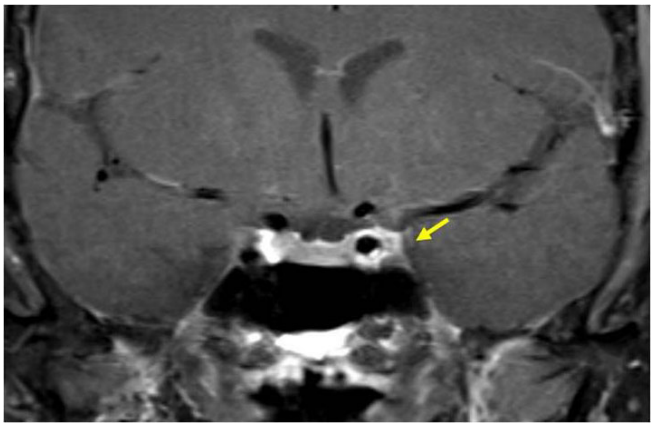

Figure 2. MRA images consistent with the findings in Tolosa-Hunt Syndrome. Coronal fat-suppressed post contrast imaging showing asymmetric thickening and enhancement of the left cavernous sinus (arrow).

syndrome versus lymphoma.

Accordingly, an ophthalmologist was consulted to urgently see the patient while in the emergency department who made the recommendation for prednisone 50 mg daily for five days based on the diagnosis of Tolosa-Hunt syndrome. At her two week follow-up appointment with the ophthalmologist, the patient's symptoms had completely resolved without sequela or further need for intervention.

3. Discussion

Acute and worsening painful vision loss is a cause for concern in the emergency department and it is crucial to identify the precipitating cause in order to properly intervene in a timely manner. Possible causes such as acute angle-closure glaucoma, iritis, corneal ulcer, giant cell arteritis, central retinal artery occlusion, orbital cellulitis, retinal detachment, endophthalmitis and optic neuritis must be evaluated and treated promptly as acute vision loss is a true medical emergency.

Patients with Tolosa-Hunt Syndrome often present with severe headaches and painful episodic opthalmoplegia which can involve the cranial nerves III through VI. The symptoms often are self resolving but tend to relapse and remit. It is caused by an idiopathic granulomatous inflammation of the cavernous sinus and is usually unilateral. Tolosa-Hunt syndrome is a diagnosis of exclusion, however magnetic resonance or computed tomographic scans can be used to detect inflammatory changes in the cavernous sinus or orbital fissure and a biopsy can be used to confirm the diagnosis. The treatment for Tolosa-Hunt syndrome is high-dose oral corticosteroids which typically results in rapid improvement of symptoms through reduction associated inflammation [4]. Failure of symptoms to resolve with high-dose oral steroids suggests an alternative diagnosis.

A complete physical exam with emphasis on the eye and neurologic portions of the exam including a fundoscopic exam are an essential part of the management for a patient who presents with vision loss. An initial work-up in the emergency department is best guided clinically by signs, symptoms, patient age

and past medical history. Here, based on our patient's presentation, we considered a CBC, inflammatory markers, BMP and appropriate head and orbit imaging: the patient already had a recent negative head computed tomographic scan so MRI and MRA were logically undertaken to further interrogate the patients underlying vision issues. Ophthalmologic consultation and specialized exam is vital for early identification and intervention of acute and painful visual loss. Once emergent causes of painful acute vision loss are ruled out, other less-emergent causes that do not cause a threat to life or sight can be considered and treated appropriately.

Our differential diagnoses for this patient involved various causes of both diplopia and orbital pain. One of the classic diseases to cause diplopia is oculomotor nerve or CN third nerve palsy. Oculomotor nerve palsy results in the characteristic "down and out" position of the affected eye due to the paralysis of the medial rectus, the superior rectus, inferior rectus and inferior oblique muscles. The paralysis of the medial rectus muscle leads to uninhibited muscle tone of the lateral rectus muscle, which is innervated by the Abducens nerve, causing the affected eye to be laterally deviated. The affected eye would also be displaced inferiorly due to the uninhibited action of the superior oblique muscle, innervated by the Trochlear nerve. Oculomotor palsy can be the result of various causes from diabetes, ischemic injury, trauma or space occupying lesions nevertheless, most causes are idiopathic. However, pain is not an associated symptom of oculomotor nerve palsy, therefore making this diagnosis less likely as pain is a significant symptom in this case.

If we review some of the possible common differentials to cause both orbital and facial pain, they include infections, orbital cellulitis, cavernous-sinus thrombosis and various neoplastic diseases. Cavernous-sinus thrombosis can be septic or non-septic in etiology. Septic cases, and to a lesser extent non-septic cases, present with a frequency of 80% to 100% with acute onset of fever, proptosis, chemosis, ptosis, and CN III, IV, and/or VI nerve palsies; note, initially there can be isolated involvement of the VI nerve, which is especially true in chronic, indolent cases. In addition, 50% to 80% of cases of cavernous-sinus thrombosis present with evidence of periorbital edema, headache, lethargy, altered sensorium, optic disc edema, and venous engorgement [5]. It is caused by a formation of a blood clot inside the cavernous sinus often the result of a spreading infection by gram-positive bacteria. Due to the intercavernous sinus, spread to the opposite side is common in the first days [6] and bilateral symptoms help to distinguish cavernous-sinus thrombosis from orbital cellulitis, which is normally unilateral. Moreover, cavernous-sinus thrombosis can be life threatening and thus requires admission for intravenous antibiotics or possible surgical drainage.

Orbital cellulitis is typically the result of a superimposed bacterial infection, often following trauma or spread from the ethmoid sinus. However in rare cases, orbital cellulitis can be caused by an orbital pseudotumor. The clinical features of orbital cellulitis included proptosis, swelling of the eyelids, con-

junctival chemosis, and limited ocular motility [7]. Infections can often spread from the ethmoid sinus as it is only separated from the orbit by the thin lamina papyracea. Orbital cellulitis could also lead to cavernous-sinus thrombosis.

Tolosa-Hunt syndrome is a variant of idiopathic orbital inflammation formally pseudotumor syndromes and imaging findings may be nonspecific and need to be reviewed in light of the clinical context. Magnetic resonance with contrast enhancement and fat suppression techniques are the best imaging tools for a patient with painful ophthalmoplegia. It often detects inflammatory changes and mass-like lesions in the anterior cavernous sinus with or without extension of the changes into the superior orbital fissure and orbital apex. Associated inflammatory tissue has an isointense signal intensity relative to skeletal muscle on T1 weighted imaging with contrast uptake during the active phase of disease. The involved areas are usually isointense to fat on T2 weighted imaging.

Alternatively or additionally, magnetic resonance studies will often reveal an asymmetrically enlarged cavernous sinus with a convex outer margin or signal changes reflecting thrombosis. Secondary criteria, which prior to the advent of MR, were findings of direct catheter angiography include luminal narrowing of the cavernous segment of the internal carotid artery.

Computed tomography will show asymmetric enlargement of the cavernous sinus on the affected side with variable contrast enhancement. Similar to magnetic resonance studies, may also present with abnormal soft tissue density in the cavernous sinus. Prior to the use of high-resolution computed tomography and advanced magnetic resonance techniques, patients often underwent direct angiography to exclude other pathology. Numerous studies in which Tolosa-Hunt syndrome was biopsy proven revealed by catheter direct angiograph a narrowed caliber of the cavernous segment of the affected internal carotid artery secondary to periarteritis, occlusion of the superior ophthalmic vein, thrombosis or non-visualization of the cavernous sinus on the side of the painful ophthalmoplegia.

4. Conclusion

Tolosa-Hunt syndrome is a rare, reversible and painful ophthalmoplegia characterized by recurrent unilateral orbital pain, ipsilateral oculomotor paralysis and prompt response to steroids. While the differential diagnosis of both sudden vision loss and eye pain is broad, there are few specific causes of unilateral painful vision loss. Prompt recognition of the disease through appropriate diagnostic imaging and laboratory studies can allow for immediate intervention and thus decrease the length and severity of symptoms including vision loss. Patients should see an ophthalmologist as soon as possible and be started on high dose corticosteroids immediately.

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