

Documentation of CHD risk factors also showed an increased trend from 18% to 37% but this difference did not achieve statistical significance (p value 0.07). Importantly, the percentage of primary prevention patients who underwent lipid monitoring increased significantly from 59% to 90% (p value <0.001). Percentage of patients with LDL at goal increased to 78% and appropriate aspirin prophylaxis increased to 76% but neither result achieved statistical significance.

CONCLUSIONS:

A quality improvement process to improve the primary prevention of CHD at the UMHC outpatient internal medicine resident clinic achieved a significant increase in FRS documentation through resident education and quick reference postings. This improvement significantly increased incidence of lipid monitoring and showed a trend towards increasing the percentage of patients with LDL at goal and on appropriate aspirin prophylaxis. Repeated cycles of quality improvement and hard changes to the electronic medical record are needed to achieve the stated goal of FRS documentation and significantly increase the adherence to ATP III and USPSTF guidelines for CHD prevention.

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Case Report

65-year-old male patient with left sided headache and orbital pain of 2-3 months duration

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Introduction:

Despite advancement of neurotechnology and neuroimaging, detailed history and examination remain the most important tools for diagnosis of unilateral headache and orbital pain. Headache is a common symptom among all age groups with a considerable array of differential diagnoses. Tolosa

Hunt syndrome is a rare cause of unilateral headache and orbital pain. High clinical suspicion based on clinical presentation, thorough history and physical examination is crucial for diagnosis.

Case presentation:

A 65-year-old male patient presented with 2-3 month history of excruciating, sharp, left-sided headache and orbital pain involving the ipsilateral forehead, eye and cheek above the upper jaw, which did not cross the midline. It had a gradual onset, starting as mild intermittent pain and progressing to a continuous pain with frequent spikes lasting 4-6 hours each. These attacks became more frequent and intense during the two weeks prior to presentation. The pain was not affected by posture and did not radiate. It was, however, associated with photophobia, phonophobia, ipsilateral conjunctival redness and tearing, nasal discharge and hypersensitivity to touch over the distribution of pain. There were no clear relieving factors. There was no history of recurrent headaches, fever, neck rigidity, jaw claudication, scalp necrosis, skin rash, blurring of vision, double vision, facial asymmetry, limb weakness or numbness or other localizing symptoms.

Physical examination revealed mild left upper eyelid ptosis, eyelid swelling, conjunctival erythema, and tearing. There was mild weakness of the lateral rectus muscle on abduction suggesting mild left abducens nerve palsy and hyperesthesia over the left ophthalmic and maxillary nerve distribution. The pupils were symmetric in size and reactivity. The examination was otherwise unremarkable, including fundoscopic examination and remaining extraocular motility. Anhidrosis was not appreciated.

The differential diagnoses initially considered were daily persistent headache, ophthalmoplegic migraine, cluster headache, hemicrania continua, trigeminal neuralgia, temporal arthritis, early herpes zoster (HZV), diabetic neuropathy, Horner's syndrome secondary to mass or carotid dissection, and cavernous sinus thrombosis or tumor.

Laboratory studies including Complete Blood Count, Comprehensive Metabolic Panel, Thyroid Stimulating Hormone, Angiotensin-Converting Enzyme level, Hemoglobin A1C, HZV serology, C-Reactive Protein, and vasculitis screen including ANA were normal. The Westergren Erythrocyte Sedimentation Rate (ESR) was minimally elevated at 40 mm/hr (normal 0-20 mm/hr). Chest X-Ray, Head and Neck CT scan, CT angiography with venous phase and MRI also were normal. Temporal artery biopsy was declined by the patient.

The patient was treated with numerous analgesics including narcotics and Non-Steroidal Anti-Inflammatory Drugs, and additionally he received 100% oxygen which did not alleviate his pain.

Based on distribution of the pain, duration, evidence of involvement of cavernous sinus structures including hyperesthesia over left ophthalmic and maxillary nerve distribution, left abducens nerve palsy and ptosis likely secondary to involvement of oculomotor/sympathetic fibers around carotid artery and exclusion of other causes, Tolosa Hunt syndrome was proposed. High dose intravenous glucocorticoids were initiated and the patient improved dramatically within 12 hours of treatment.

Discussion:

Tolosa Hunt Syndrome (THS) is a rare cause of painful ophthalmoplegia caused by idiopathic noncaseating granulomatous or nongranulomatous inflammation of the cavernous sinus or superior

orbital fissure.^{1,2} It is a part of a continuum of idiopathic orbital inflammation, also known as idiopathic orbital pseudotumor, with which it shares histopathological and clinical features, and is distinguished only by its unique anatomic localization to the cavernous sinus. THS has an estimated incidence of 1 per million per year, affecting any age group, but is rare before the age of 20.^{1,2}

Clinically, THS is characterized by acute onset unilateral, rarely bilateral, periorbital pain that is described as “severe,” “intense,” or “lancinating.” It often resolves spontaneously but tends to have episodes of relapse and remission.³

The pain frequently extends into retro-orbital, frontal and temporal regions and features of cavernous sinus structure involvement may provide clues to diagnosis. Key signs include ophthalmic and maxillary nerve involvement manifesting as facial paresthesia and loss of corneal reflex, cranial nerves III, IV, VI involvement evidenced by ophthalmoplegia, diplopia, miosis and ptosis, sympathetic fiber involvement appearing as ptosis with or without features of orbital involvement such as lid swelling, proptosis, orbital pain and vision loss. There is no pathognomonic feature of THS and all these signs can be seen with other cavernous sinus pathology such as thrombosis, tumor, fistula or infections. Furthermore, THS can mimic temporal arteritis especially if the pain occurs before cranial nerve involvement and ESR is elevated (which is seen in 45% of THS cases). On the other hand, eye pain, diplopia and cranial nerve involvement are rare in temporal arteritis.⁹ Accordingly, THS is a diagnosis of exclusion.^{1,4} Extracavernous extension of inflammation has been infrequently reported in the form of mandibular and facial nerve involvement, but no systemic involvement has been reported.^{2,3,5}

While THS is considered a benign condition, permanent neurologic deficits like vision loss and cranial nerve palsies do occur, and relapses are common, often requiring prolonged immunosuppressive therapy.^{1,2,3}

The International Journal of Headache/International Classification of Headache Disorders 2nd edition (ICHD-2) criteria for THS include:⁴

- One or more episodes of unilateral orbital pain persisting for weeks if left untreated.
- Paresis of one or more of the third, fourth, and/or sixth cranial nerves and/or demonstration of granuloma by MRI or biopsy.
- Paresis coincides with the onset of pain or follows it within 2 weeks.
- Pain and paresis resolve within 72 hours when treated adequately with glucocorticoid.
- Other causes have been excluded by appropriate investigations.

Although painful ophthalmoplegia is a feature of THS, most patients (over 75 percent) who present with painful ophthalmoplegia do not have THS.² Diagnostic testing, including neuroimaging by angiography and MRI brain and orbit should be performed to rule out other causes.^{1,2} Thin-slice high-magnetic field MRI of the cavernous sinus with fat-suppressed cuts of the orbits is the modality of choice looking for typical inflammatory changes in the cavernous sinus, superior orbital fissure, and/or orbital apex. MRI findings of THS include enlargement of the cavernous sinus with abnormal tissue, abnormal convexity of the wall of the cavernous sinus and focal narrowing of the intracavernous internal carotid artery.² However, these findings are not specific to THS and normal images do not exclude the diagnosis.^{1,2,3} Based on MRI findings, THS can be classified as benign with normal MRI scan, and inflammatory with classic inflammatory features on MRI scans.⁶ In a meta-

analysis, approximately one-third of clinically defined THS had normal MRI findings, but a defined MR protocol has yet to be determined.⁷ Reliable detection is complicated by the fact that differentiation of the normally enhancing venous space in the sinus from the contrast enhancement of granulomas may be limited with the conventional spin echo MRI and thus requires specific imaging modalities.⁸

Biopsy of the lesion may be required to confirm the diagnosis; however, the technical difficulty of cavernous sinus region biopsies limits its usefulness. Instead, a trial of glucocorticoids is usually performed and rapid response with dramatic decrease in pain occurs. More aggressive testing, including biopsy and CSF evaluation, to exclude other causes is recommended if symptoms are progressing, atypical or recurrent. This is particularly the case if the patient has failed treatment with glucocorticoids or if glucocorticoid efficacy is lost soon after an initial response.^{1,2} Even with careful adherence to clinical criteria and diagnostic evaluation, misdiagnosis can still occur; consequently, follow-up is required to exclude other causes of painful ophthalmoplegia.^{2,4}

Glucocorticoids have altered the course of the disease by providing significant pain relief within 24-72 hours of therapy initiation. However, there are no clinical data as to whether glucocorticoids hasten recovery of associated cranial nerve palsies.^{1,3} Additionally, no standard dose or duration has been indicated in literature. A dose of 1mg/kg/day of methylprednisone tapered slowly was well received.⁵

Although the glucocorticoid trial is instructive, an initial clinical or MRI response is not diagnostic since other entities, such as lymphoma and vasculitis, also may respond clinically and radiographically to glucocorticoid therapy.^{2,3}

Ophthalmoparesis usually requires weeks to months for resolution.⁶ In some cases, the ophthalmoparesis may not completely resolve depending on the degree of inflammation and the aggressiveness of therapy. For refractory cases, azathioprine, methotrexate, or radiation therapy has been employed.¹

Recurrences occur in about one-half of reported patients over an interval of months to years.² Ipsilateral, contralateral, and bilateral relapses have been reported. Relapses require repeated investigations to rule out inflammatory and neoplastic disorders such as sarcoidosis, Wegener's granulomatosis, and lymphoma.²

Conclusion:

THS is a rare cause of relapsing remitting painful ophthalmoplegia and unilateral headache secondary to idiopathic inflammation of cavernous sinus, superior orbital fissure, or both. THS can mimic many other conditions. A dramatic response to systemic glucocorticoids is helpful in the diagnosis. An MRI scan is the modality of choice for investigation, but the absence of MRI findings does not exclude THS. High index of suspicion and close follow up are important for accurate diagnosis.

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High Vitamin B12 Level

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Vitamin B12/cobalamin functions as an important co-enzyme in the human body and is essential for purine and pyrimidine synthesis. Vitamin B12 deficiency is a very well recognized clinical entity but the conditions leading to elevated levels of vitamin B12 are generally not; hence the purpose of this article is to discuss such etiologies. Understanding the mechanisms will necessitate a brief review of vitamin B12 metabolism, presented below.

Under normal physiological conditions, dietary cobalamin binds to haptocorrin (HC) in saliva to be transported to the duodenum where free cobalamin is released. The free cobalamin in the duodenum binds to intrinsic factor (IF) forming a complex which is taken up by the intestinal mucosa to be ultimately released into the circulation. The majority of cobalamin in circulation is bound to haptocorrin (HC) and only a small portion (5-20%) is bound to transcobalamin (TC II). The plasma half-life ($t_{1/2}$) of TC II is short, only 40min-5hrs, whereas it is a long, 6-9 days for HC. When transcobalamin passes through enterohepatic circulation it is taken up by the liver for storage and is later released into bile.

Bound protein/form	Transcobalamin (TCII)	Haptocorrin (HC)
Plasma $t_{1/2}$	40min-5hrs	6-9 days
Site of synthesis	Liver, intestine, endothelium	Salivary glands, gastric mucosa

The reference range for vitamin B12 levels is 200-900 pg/mL (picograms per milliliter) and elevated cobalamin levels can be seen in various malignancies including hematological conditions like myeloproliferative disorders, renal and liver disorders.