



Squamous Cell Carcinoma Presenting as Tolosa-Hunt Syndrome

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Learning Objectives

1. Demonstrate that Tolosa-Hunt syndrome is a diagnosis of exclusion
2. Evaluate the relative risks and benefits of invasive biopsy compared to imaging studies in diagnosis of a soft-tissue mass
3. Recognize perineural invasion as a potential route of invasive skin cancer

Case Description

A 65-year-old right-handed man with a history of right trigeminal neuralgia and basal cell carcinoma presented to the ED with one week of right ptosis and diplopia. He reported right-sided headache but denied trauma, nausea, or vomiting. Surgical history was significant for Mohs micrographic excision of squamous cell carcinoma of the right cheek in 2004, basal cell carcinoma of the mid forehead in 2004 and right forehead in 2016, right rhizotomy in 2018 and microvascular decompression 6 months prior to presentation. The decompression improved his trigeminal neuralgia symptoms, but left him with chronic sinusitis and anosmia, for which he received multiple CT scans and antibiotic courses. He reported a poor appetite and 30-lb. weight loss due to anosmia. Motor strength, sensation, coordination, and speech were intact on neurological exam. He displayed right-sided ophthalmoplegia with limited abduction, upward and downward gaze consistent with an oculomotor nerve palsy.

Non-contrast head CT scan revealed no intra-cranial hemorrhage. CT angiogram and venogram showed no vascular abnormalities but revealed an enhancing mass along the right cavernous sinus, measuring ~2.1x1.1cm. MRI confirmed the presence of enhancing soft tissue in the right cavernous sinus, extending into the foramen ovale (Figure 1).

Chest-abdomen-pelvis CT found no evidence of malignancy. CBC, serum chemistry, and CSF were unremarkable. Serologic and CSF screening for VDRL, HIV, Lyme, VZV, CMV, and HSV were negative. CSF cultures

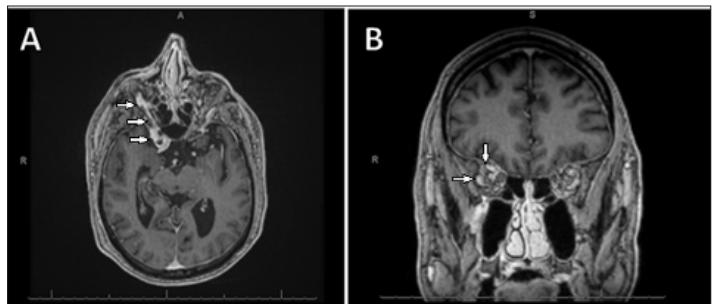


Figure 1. T1 weighted 3D MRI of the orbits demonstrating a contrast-enhancing soft tissue mass in the right cavernous sinus, extending into the right orbital apex, obliterating Meckel's cave and ranging into the foramen ovale.

A = axial view. B = coronal view.

grew no organisms. ANA, serum and CSF ACE, anti-TPO, ESR and CRP screening revealed only mild CRP elevation. Biopsy was initially deferred due to patient's preference to avoid brain biopsy. Tolosa-Hunt syndrome was suspected, and the patient was given high-dose IV dexamethasone. After 3 days the eye pain resolved, but diplopia remained. He was discharged on a 2-week dexamethasone taper.

One month after dexamethasone completion, the patient reported minimal improvement. He underwent fine needle aspiration of the right pterygopalatine fossa, revealing atypical squamous cells and keratin pearls consistent with squamous cell carcinoma. Treatment with radiation and systemic chemotherapy was initiated.

Discussion

Tolosa-Hunt is a rare syndrome with symptoms of unilateral headache with ipsilateral ophthalmoplegia.¹⁻² The annual incidence is estimated at one case per million.³ MRI with contrast is highly sensitive for diagnosis. Glucocorticoids are considered the first-line treatment.⁴⁻⁵ Our patient appeared to meet the criteria for Tolosa-Hunt and was discharged on glucocorticoids (Figure 2).

Other causes of cranial neuropathy including malignancy, autoimmune or vascular disease must be eliminated to diagnose Tolosa-Hunt.⁶ Considering the cost-effectiveness of successful dexamethasone treatment, and the inherent risks of accessing the cavernous sinus, a shared decision was made to initiate dexamethasone before attempting



Criteria for the diagnosis of Tolosa-Hunt syndrome

All the following criteria must be met:

1. Presence of granulomatous inflammation of cavernous sinus, superior orbital fissure, or orbit, seen on MRI or biopsy
2. Unilateral palsies of one or more of cranial nerves III, IV, or VI
3. Ipsilateral and unilateral headache which preceded the cranial neuropathy by two weeks or less
4. Not better explained by another etiology

Figure 2. Criteria for diagnosis of Tolosa-Hunt syndrome, as described by the Headache Classification Committee of the International Headache Society (IHS). All the above criteria must be met for diagnosis.

the biopsy. However, other case reports have suggested prioritizing tissue biopsy before considering a diagnosis of Tolosa-Hunt.⁷

With failure of dexamethasone treatment, biopsy became necessary. Ultimately, he was found to have squamous cell carcinoma imitating Tolosa-Hunt. No other primary lesions were found, but the patient had a history of multiple skin cancers including a squamous cell carcinoma in 2004. Metastasis of skin cancer, particularly squamous cell carcinoma, may occur via perineural spread.⁷⁻⁹ It is important for physicians to recognize cranial neuropathies as a potential sign of perineural invasion in patients with a history of facial skin cancer. This case reinforces Tolosa-Hunt syndrome as a diagnosis of exclusion. Tissue biopsy is a necessary measure to rule out malignancy when differentiating an orbital mass.

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