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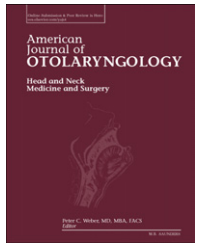

Atypical culture-negative skull base osteomyelitis masquerading as advanced nasopharyngeal carcinoma☆,☆☆

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ABSTRACT

Skull base osteomyelitis typically arises as a complication of otogenic or sinonasal infections in immunocompromised patients. A much rarer entity, atypical skull base osteomyelitis is not associated with an obvious infective source. Atypical and culture-negative skull base osteomyelitis is even rarer and hampers diagnosis, as its clinical presentation is remarkably similar to skull base neoplasms. We report a case of extensive skull base osteomyelitis with orbital apex syndrome and multiple lower cranial nerve palsies which initially masqueraded as possible advanced nasopharyngeal carcinoma. Extensive investigations and consult with an infectious diseases specialist aided in elucidation of the correct diagnosis. Through this article, we emphasize that skull base osteomyelitis must be considered in the setting of headache, cranial neuropathies, elevated inflammatory markers and abnormal imaging findings. Early tissue sampling for histology, stainings and cultures and prompt appropriate treatment may prevent or arrest further complications.

1. Introduction

Skull base osteomyelitis (SBO) is an infection of the bone and/or bone marrow of the calvarium, typically caused by bacteria or fungal invasion from sinonasal and otological sources [1]. Most commonly seen in immunocompromised individuals and usually associated with malignant otitis externa, SBO is a rare but potentially fatal condition. Mortality from SBO complications ranges from 20 to 40% but early diagnosis and appropriate treatment of SBO can prevent or arrest neurologic deficits and reduce morbidity and mortality significantly [2]. In this article, we describe a rare case of extensive atypical culture-negative skull base osteomyelitis with orbital apex syndrome and multiple cranial nerve palsies which initially masqueraded as nasopharyngeal carcinoma. The diagnostic, management and therapeutic options are discussed.

2. Case report

A 54-year old Chinese gentleman presented with left-sided headache of several months' duration and a sudden loss of vision in his left eye 2 days prior to his presentation to our clinic. There was no history of fever and ear or sinonasal infection. Apart from hypertension, dyslipidemia and well-controlled type II diabetes mellitus, he had no significant personal or family medical history.

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Physical examination revealed no perception to light and a grade 3 relative afferent pupillary defect in his left eye. While the patient had denied any other symptoms, he was noted to have left eye ptosis, proptosis, dense ophthalmoplegia of left cranial nerves III, IV and VI, voice hoarseness and slurring of speech. Ipsilateral left hypoglossal nerve palsy was present with absent gag reflex (Fig. 1). Fibreoptic nasoendoscopy showed a left vocal cord palsy and a slight bulge in the left nasopharynx with a normal looking mucosa. There was no evidence of sinusitis. Further complete neurological examination revealed sparing of the left cranial nerves V, VII, VIII and XI. All right-sided cranial nerves were intact. Otoscopy was unremarkable.

Computed tomography (CT) and magnetic resonance imaging (MRI) scans demonstrated a left nasopharyngeal mass that extended into the left cavernous sinus and orbital apex, highly suspicious for nasopharyngeal carcinoma. There was also involvement of the left Meckel's cave as well as dural thickening and enhancement along the floor of the left middle cranial fossa, with destruction of the underlying clivus and petrous apex and encasement of the left major vessels. Interestingly, however, there was no definite architectural distortion of the nasopharyngeal soft tissue and preservation of the smooth nasopharyngeal mucosa was noted (Fig. 2).

In view of the nasopharyngeal bulge and imaging findings, the patient underwent post-nasal space biopsy and histology returned as lymphoid hyperplasia and inflammatory granulation tissue admixed with histiocytes, with no evidence of malignancy. The biopsy was repeated and yielded similar results.

The incongruent histology and imaging results prompted an endoscopic left orbital apex biopsy under image guidance. To access the lesion, a left-sided endoscopic middle meatal antrostomy, anterior and posterior ethmoidectomy and wide sphenoidotomy were performed. Intra-operative findings revealed a polypoidal mass with overlying smooth mucosa just anterolateral to anterior face of sphenoid (Fig. 3). Histology from the orbital apex lesion showed inflammatory granulation tissue admixed with histiocytes and covered with purulent exudate.

Blood investigations returned, suggesting an inflammatory state (white cell count of 10,700 cells per microliter, C-reactive protein level of 89.2 mg per liter and erythrocyte sedimentation rate (ESR) of 115 mm per hour). In view of the inflammatory state on blood investigations and prior non-diagnostic histology, the infectious diseases specialist was consulted, following which, apart from histology, bacterial cultures and fungal stains were sent. Unfortunately, all microbiological results returned as negative. After multidisciplinary discussion, despite the negative cultures, the infectious disease specialist opined that an inflammatory condition such as culture-negative skull base osteomyelitis was likely, given the imaging findings, repeated non-malignant biopsy results and raised inflammatory markers.

Intravenous ceftazidime and vancomycin were commenced for 6 weeks under infectious disease recommendations and significant downtrending of the patient's inflammatory markers followed. Remarkably, his left eye ptosis and vocal cord paralysis improved while unfortunately the rest of cranial nerves deficits, including left eye blindness remained (Fig. 4). An interval scan performed at 6 weeks post-microbial therapy also confirmed significant resolution of his skull base lesions. He currently remains well on infectious diseases specialist follow-up.

3. Discussion

Typical cases of SBO are initiated by otogenic or sinonasal infections in immunocompromised individuals with *Pseudomonas aeruginosa* as the usual pathogen [1]. Lower cranial nerves are commonly affected and may present in a myriad of syndromes such as Vernet's (paresis of 9th to 11th cranial nerves) and Collet Sicard's (paresis of 9th to 12th cranial nerves) [3]. Atypical SBO, which refers to SBO without preceding or associated sinonasal or otogenic infections, is a much rarer entity. These patients may have headache as the only initial symptom, followed by cranial neuropathies much later, thus delaying presentation and diagnosis [4].

Apart from *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Klebsiella* spp and fungi such as *Aspergillus* spp are common microbials found in usual SBO cultures [5,6]. In 2006, Djalilian et al. reported the emerging phenomenon of culture-negative SBO due to increasing prevalence of antibiotic administration by primary care physicians prior to presentation [7]. However, our patient had denied a history of seeking prior medical attention. This, accompanied by a lack of fever and an obvious infective source, and extensive cranial nerve involvement prompted consideration of differential diagnoses such as carcinomas, lymphomas and inflammatory pseudotumor.

Inflammatory pseudotumors of the skull base is a well-reported phenomenon characterized by a benign but locally destructive fibroinflammatory lesion [8]. Imaging findings are

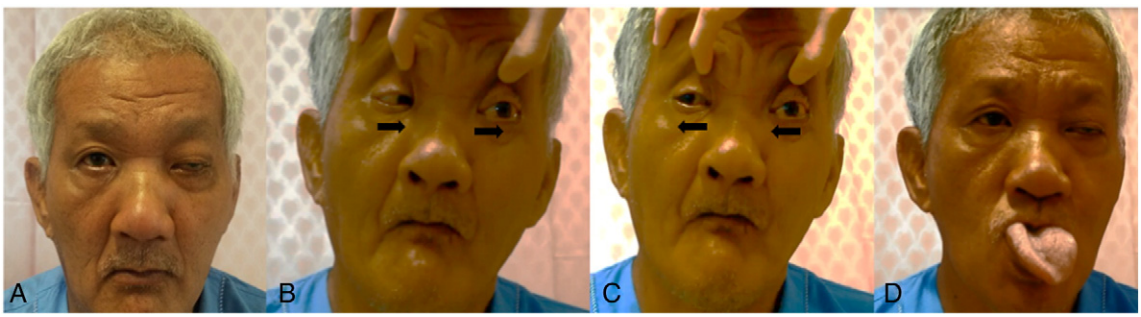

Fig. 1 – Cranial nerves examination at presentation demonstrating (A) left proptosis and ptosis, and palsy of left cranial nerves (B) VI, (C) III and (D) XII.