Diagnostic dilemma between skull base osteomyelitis and nasopharyngeal carcinoma: a case series

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Case reports

Skull base osteomyelitis (SBO) is a rare and life-threatening complication of otorhinological infection. The anatomical location of the disease and clinical features allow it to mimic nasopharyngeal carcinoma (NPC): a malignancy that is endemic in Southeast Asia. Suspicious clinical or radiological findings warrant prompt histological investigation for confirmation. Misdiagnosis of either entity can lead to devastating consequences of late treatment and disease progression. Our centre identified four cases of SBO between 2019 and 2020, all of which mimicked NPC at presentation. The caveats encountered during the diagnostic process are highlighted here.

Case 1

An 81-year-old diabetic man presented to our department with left middle ear effusion. Endoscopy revealed vague bulging over the left nasopharynx with obliteration of the left fossa of Rosenmuller. Gadolinium-enhanced magnetic resonance imaging (MRI) showed enhancing signal intensities in the left nasopharynx involving multiple skull base structures (Fig). Multiple biopsies yielded only benign results. Tissue culture grew methicillin-sensitive Staphylococcus aureus. Blood test results revealed elevated inflammatory markers including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). His plasma Epstein–Barr virus (EBV) DNA level was 0 copies/mL. The final diagnosis was SBO and the patient was treated accordingly with a good response.

Case 2

A 76-year-old man presented with left-sided headache and left jaw pain with a recent history of lower molar tooth extraction. Physical examination revealed left otitis media with effusion, and tongue and uvula deviation. Endoscopy showed a vague swelling over the left nasopharynx. The MRI images indicated locally invasive NPC, involving the clivus and ipsilateral skull base foramina. The patient underwent multiple biopsies including under general anaesthesia with computed tomography (CT) navigation. Blood ESR and CRP levels were elevated and tissue cultures grew Candida, Pichia, and Lactobacillus. All results indicated inflammation only. The patient was treated with a prolonged course of meropenem and antifungal medication with a favourable clinical response. His headache and inflammatory markers improved, and interval MRI showed reduced signal intensities at the skull base.
Case 3
A 71-year-old man was referred to our clinic for persistent left otalgia, headache, and facial pain. Initial endoscopy demonstrated bulging of the left nasopharynx and left cord palsy. Computed tomography and subsequent MRI revealed a neoplastic process in the left nasopharynx with invasion of the parapharyngeal space and skull base. Prominent retropharyngeal lymph nodes were suggestive of nodal spread. Multiple biopsies were carried out, once with MRI navigation via a transsphenoidal approach towards the clivus. Results were all benign. His plasma EBV DNA level was 0 copies/mL. Cultures grew methicillin-resistant S. aureus and Corynebacterium. White cell count and blood ESR and CRP levels were elevated. A prolonged course of meropenem was prescribed with consequent improvement of symptoms and reducing trend of inflammatory markers. The 3-month interval MRI demonstrated reduced enhancement of skull base structures.

Case 4
A 59-year-old man with poorly controlled diabetes underwent left mastoidectomy for malignant otitis externa. After surgery, he complained of persistent left temporal headache and dysphagia. Pathology from the operation was suggestive of inflammation only. Endoscopy revealed bulging of the left nasopharynx and left cord palsy. Computed tomography showed left otomastoiditis whilst MRI demonstrated an aggressive process with extensive involvement of skull base structures. Nasopharynx biopsies failed to confirm malignancy. Cultures were positive for methicillin-resistant S. aureus, Staphylococcus spp, and Klebsiella. His plasma EBV DNA was 0 copies/mL. White cell count and blood ESR and CRP levels were elevated. After 6 weeks of treatment with meropenem and vancomycin, his headache resolved, inflammatory markers normalised, and tissue culture results from a new biopsy were negative.

Despite the apparent clinical resolution, interval MRI 8 weeks after cessation of treatment showed disease progression. There was new right-sided contrast enhancement in the nasopharynx with extension to the right carotid space, hypoglossal canal, and petrous apex. The patient was soon re-hospitalised with right temporal headache and bilateral vocal cord palsy. Transphenoidal CT-guided biopsy was performed on the clivus and overlying mucosa and results were still benign. Culture results were similar to those previously and inflammatory markers were again elevated. He was given a second course of antibiotics and had a prompt clinical response.

Discussion
Three patients were referred to our department with intractable headache, facial pain, or otalgia, some of the most common presenting complaints of SBO along with cranial nerve deficits.1 These differ markedly to those of NPC: blood-stained nasal discharge, unilateral conductive hearing loss, and cervical lymphadenopathy. Cranial nerve palsies suggest local invasion. Singh et al2 recommend that SBO be suspected if patients with treated malignant otitis externa present with persistent headache, otitis media with effusion, and cranial nerve deficits without a mucosal lesion in the nasopharynx, but there are no internationally recognised diagnostic criteria and recommendations differ.

The diagnostic dilemma occurs in the physical findings on initial examination. A unilateral otitis media with effusion in Southeast Asian adults (Cases 1 and 2) is presumed to be NPC until proven otherwise. Endoscopic findings of a bulging nasopharynx further raise the alarm, even in the absence of an obvious mucosal lesion. At this point, regardless of co-morbidities, symptoms, presence or absence of nerve palsies, efforts should be made to confirm or exclude mucosal or submucosal malignancy before settling on a diagnosis of SBO.

The key to differentiating malignancy from infection is the result of tissue biopsy. Simple bedside punch biopsies of the visibly abnormal mucosa are usually adequate to obtain histological confirmation of NPC. In our cases, only vague bulging of the nasopharynx was evident. Negative results led to more invasive procedures to obtain deeper samples or down to the clivus. There is no established recommendation for use of intraoperative image-guided biopsy in this regard. This method attempted to maximise the yield of abnormal tissue to exclude with certainty any presence of malignancy.

Negative plasma EBV DNA level, in view of its high negative predictive value for endemic NPC, is another reason to exclude NPC. Inflammatory markers were raised in all our patients. Serial blood ESR level is also a useful marker for disease monitoring as it rapidly normalises with disease resolution3 but rises again with disease relapse.

Imaging played a key diagnostic role. Although CT can detect osseous destruction, these bony changes are a rather late phenomenon. In comparison, MRI offers higher soft tissue resolution, allowing delineation of anatomical location and soft tissue involvement.4 The MRI images in our cases typically showed gadolinium-enhanced signals at the nasopharynx, involving the clivus, petrous apex, skull base foramina, and parapharyngeal spaces on T1-weighted images. Images were suggestive of neoplasm, described by radiologists as “space occupying lesions”...
and “aggressive lesions with erosion/invasion of surrounding structures”. This further highlights the importance of histological correlation.

In conclusion, SBO is a rare disease that can masquerade as NPC. Although the two diseases warrant entirely different treatment modalities, it remains difficult to confidently differentiate one from the other during diagnosis. A holistic consideration of the patient’s clinical picture, and histological and microbiological results are essential for correct diagnosis.

Author contributions
All authors contributed to the design, acquisition of data, analysis of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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All patients were treated in accordance with the Declaration of Helsinki. All patients provided informed consent for all procedures and for the publication of non-identifiable information.

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