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Letter to the Editor: New Observation

Differential Diagnosis of a Cystic Notochordal Skull Base Lesion: A Case Report

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Notochordal tumours are rare neoplasms arising from remnants of the primitive notochord. They can be located anywhere across the bony neuro-axis but are most commonly found at the clivus or coccyx. We report a 62-year-old male who presented with cerebrospinal fluid leak and intracranial pneumocephalus secondary to a clival cystic notochordal lesion. Although we favoured the diagnosis of cystic chordoma, the clinical, radiological and histological differential diagnosis in our case included other notochordal neoplasms.

A 62-year-old male patient presented with a seven-week history of severe postural headaches, left nostril rhinorrhea and photophobia, but no focal neurological deficits. Computed tomography (CT) scan of the head demonstrated pneumocephalus with a large bony defect along the dorsum of the clivus, with mixed fluid density within the contiguous left sphenoid sinus (Figure 1A/B). The defect measured about 12 mm by 10 mm in anteroposterior and transverse dimensions, respectively. Magnetic resonance imaging (MRI) of the brain demonstrated a heterogenous, but predominantly cystic, multilobulated lesion partially extending into the posterior aspect of the left sphenoid sinus. The lesion was hypointense on T1-weighted images (Figure 1C), hyperintense on T2-weighted images (Figure 1D) and showed linear peripheral enhancement with gadolinium. Imaging performed a decade previously also demonstrated the lesion and was thought to represent a ruptured sphenoidal meningocele.

An endoscopic endonasal transsphenoidal approach was used to expose the sella for reconstruction of the skull base defect. The lateral walls of the sphenoid sinus were exposed via drilling such that the lateral extent was the vertical segment of the internal carotid artery. The sella was drilled laterally and rostrally to facilitate pituitary transposition in order to remove the posterior clinoids and access the rostral part of the clivus. The defect was reconstructed with intracranial duroplasty followed by fascia lata graft. The right pedicled nasoseptal flap was swung into the sphenoid sinus to cover the clival dural defect and the posterior wall of the sphenoid sinus, over the carotid arteries and up to planum. Debulking surgery was completed. On follow-up 1 month after surgery, the patient had complete resolution of headaches and rhinorrhea, with imaging showing a small cystic cavity that was equivocal for residual versus post-operative changes. Close follow-up with post-operative radiation therapy is being planned.

Microscopic inspection of the resected tissue revealed a small amount of dense fibrous connective tissue intermixed with cellular tissue showing features of a notochordal neoplasm. The latter contained medium-sized cells with clear-to-vacuolated (physaliferous) cytoplasm disposed in sheets and chord-like arrangements on a focally myxoid background (Figure 2A). The constituent cells showed positive membranous immunostaining for S100 (Figure 2B), epithelial membrane antigen (Figure 2C) and nuclear staining for brachyury (Figure 2D), confirming the diagnosis of a notochordal lesion. The cells retained nuclear expression of SMARCB1 and were also positive for vimentin and broad-spectrum cytokeratin (not shown).

The differential diagnosis in this case included chordoma, or benign notochordal proliferation such as ecchordosis physaliphora or benign notochordal cell tumour. Histological features consistent with chordoma included the presence of chord-like arrangements of cells on a myxoid background and evidence for proliferation, albeit low, as revealed by Ki67 staining. Radiologically, it demonstrated the typical characteristics of chordoma on MRI: hypointensity on T1-weighted images (Figure 1C), hyperintensity on T2-weighted images (Figure 1D), areas of enhancement with gadolinium and bony destruction.[1]

Chordomas are rare, locally invasive tumours that arise from embryonic remnants of the notochord along the bony neuro-axis. The distribution of chordomas is almost equal across the sacrum, mobile spine and skull base.[1] They account for approximately 1-4% of bone neoplasms, mostly occurring between the fourth and sixth decades of life from the clival region with extensive bone lysis.[1,2] Chordomas can be sub-classified into four types based on their histology and behaviour: classical (conventional) chordoma, chondroid chordoma, dedifferentiated chordoma and poorly differentiated chordoma.[2] Of these, our case is most in keeping with conventional chordoma. These appear as soft, grey-white

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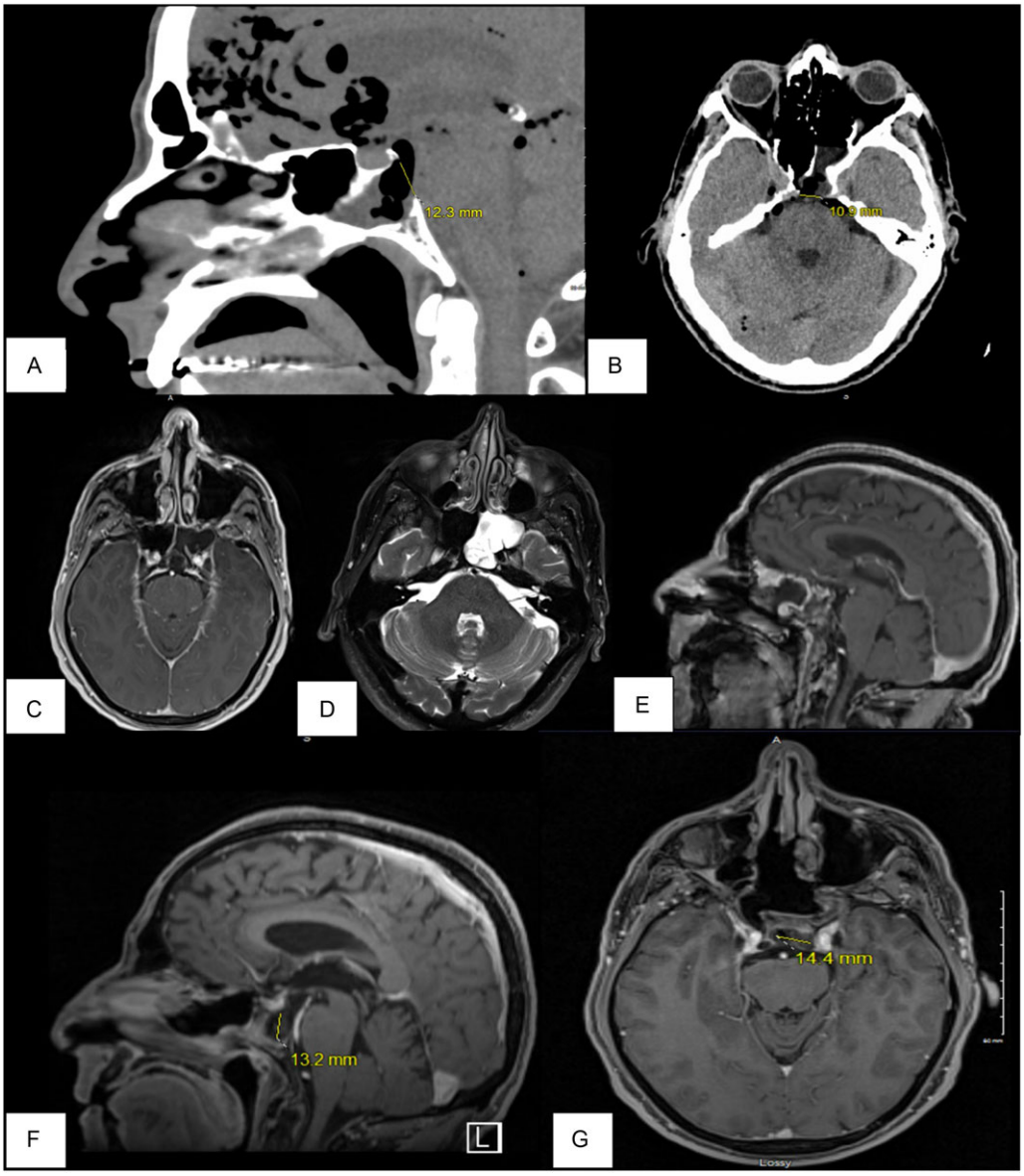

Figure 1. Pre-operative sagittal (A) and axial (B) computed tomography head demonstrating pneumocephalus with a lytic bone lesion along the dorsum of the clivus, and a mixed fluid density extending into the left sphenoid sinus. Pre-operatively, the lesion demonstrated (C) hypointensity on T1 axial magnetic resonance imaging (MRI) and (D) hyperintensity on T2 axial MRI. (E) demonstrates the same hypointense lesion on pre-operative T1 sagittal MRI. (F) and (G) demonstrate post-operative sagittal and axial T1 MRI, respectively.

tumours defined by physaliferous cells with bubble-like vacuoles within their cytoplasm, within a myxoid stroma.[1] They are immunoreactive for epithelial membrane antigen (EMA), cytokeratin, S100 protein, vimentin and show nuclear immunoreactivity for brachyury.[2] Although they are slow growing, histologically benign tumours, conventional chordomas are locally invasive and notoriously recurrent, rendering the nature of their clinical progression similar to malignant tumours.[1,2] Median overall survival times are reported as 155 months.[3] Chondroid chordomas show foci of cartilaginous differentiation and behave similarly to conventional chordomas. Dedifferentiated and poorly differentiated chordomas are aggressive neoplasms showing high-grade histological features and, in the latter case, loss of SMARCB1 expression. Unlike conventional and chondroid chordomas, these two types have poor prognoses with median overall survivals of 20 and 51 months, respectively.[3,4]

In light of these considerations, combined with the cystic nature of the lesion on imaging, we favoured a diagnosis of cystic (conventional) chordoma. However, the amount of tissue available for histological analysis was limited, and alternative low-grade notochordal lesions could not be excluded on histological grounds. The lengthy clinical history was also consistent with a more benign notochordal lesion. Finally, whether the bony involvement detected on imaging reflected true bony destruction, versus remodelling by the adjacent mass, was uncertain. Benign notochordal cell tumours (BNCT) are intraosseous benign lesions of notochordal cell origin that have an identical anatomical distribution to chordomas.[2] Due to the nature of the specimen, BNCT could not be excluded in this case. However, BNCTs typically do not possess intercellular regions of myxoid matrix.[5] Moreover, it has been suggested that the presence of bone destruction on CT is a significant discriminator between chordomas and BNCT.[5] Ecchordosis physaliphora (EP) is an ectopic notochordal remnant, also included in the differential diagnosis, as it is histopathologically indistinguishable from chordoma.[6] However, EPs typically lack bone destruction on

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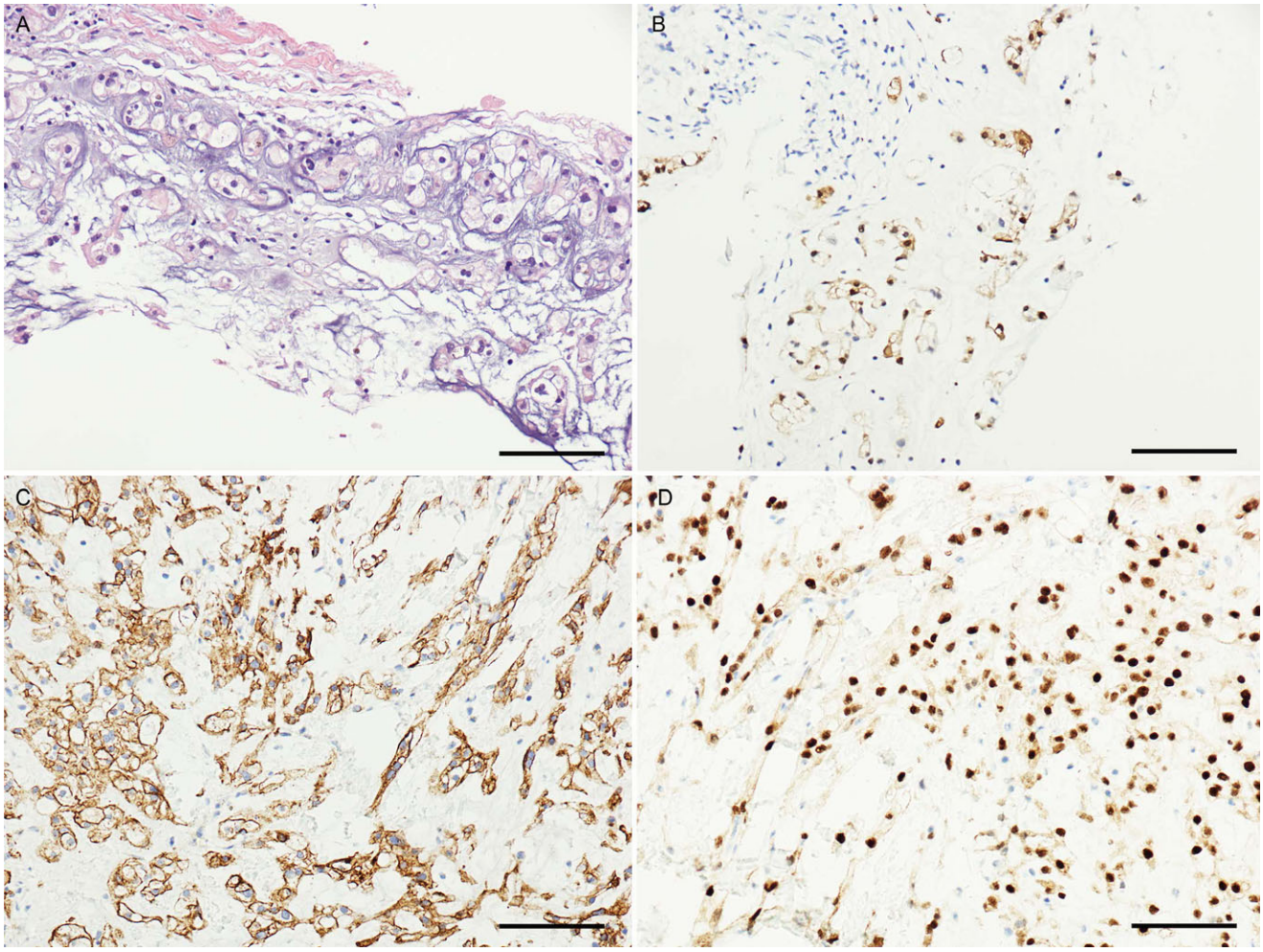

Figure 2. (A) Proliferation of epithelioid cells with eosinophilic, vacuolated cytoplasm disposed in lobules and ill-defined chord-like arrangements on a myxoid background. Haematoxylin and eosin. (B-D) Positive immunostaining for S100 (B), epithelial membrane antigen (C) and brachyury (D). Scale bars = 100 microns.

CT, and contrast enhancement on T2-weighted images on MRI.[6,7] On the other hand, there are case reports of symptomatic EP presenting with bone erosion. Consequently, EP could not be definitively ruled out based on imaging characteristics alone.[8]

In summary, our case highlights the challenges involved in definitively classifying notochordal lesions in the setting of a limited tissue sample, unconventional imaging characteristics and an atypical (prolonged) clinical history.

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