Clinico-Pathologic Conference: Case 3

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Clinical Presentation

A 17-year old male was referred to the otolaryngology clinic with a history of nasal obstruction for 3 years. Physical examination uncovered mild asymmetry and proptosis of the left eye; palpation revealed softness of the posterior left hard palate and anterior maxilla, with no erosion. Nasal endoscopy, using a 4 mm, 30-degree sinus telescope, revealed complete obstruction of both nostrils.

Computed tomography (CT) without contrast revealed a nearly 6 cm sharply margined unilocular expansile radiolucent lesion appearing to arise from the left maxillary alveolar ridge. The lesion eroded the apices of teeth and extended from tooth #13 through unerupted tooth #16. It expanded into the left maxillary sinus and left nasal cavity and elevated the left orbital floor, with a thinned but intact eggshell-like margin. No definite calcifications were evident within the lesion on CT (Fig. 1a, b, c, d).

Differential Diagnosis

The radiological features were interpreted to be consistent with a slowly growing lesion rather than an aggressive

process. The pathology was thought to arise from either a traumatic, infectious, nonneoplastic or neoplastic process. Within the neoplastic category, benign, locally aggressive or low-grade malignant lesions were considered.

The epicenter of the lesion was thought to originate, in order of decreasing likelihood, from the maxillary sinus, the maxilla or the nose or, least likely, to represent a metastasis or to be of intracranial origin. When evaluating an origin from the maxillary sinus or nasal cavity several conditions were included in the differential diagnosis. The possibility of a deep mycosis was considered. Most of these patients are immunosuppressed. The patient's medical and travel history would be therefore important factors in progressing towards a more definite diagnosis. Radiographically, chronic fungal lesions may have calcifications. Nonneoplastic lesions considered also included allergic fungal sinusitis, a response to fungal allergens which is more common in warmer climates and may cause bone erosion. This occurs more commonly in the 3rd–7th decade and identification of peripheral eosinophilia with an elevated anti-fungal IgE aids in the diagnosis [1]. It was felt that a diagnosis of a sinonasal polyp was unlikely given the extensive size of the lesion. Consideration was given to the possibility of a sinus mucocele, a benign mucus-filled lesion which can occur at any age. Mucoceles arise from initial obstruction of the mucous glands which may occur due to trauma, surgery, allergies, inflammatory disease or infections but often no cause is identified. There is often a long history of symptoms. About 90% of mucoceles involve the frontal or the ethmoid sinuses and 10% involve the maxillary sinus. Signs and symptoms include facial deformity, proptosis or enophthalmos, loss of vision or diplopia, facial pain, headache or nasal obstruction [2].

A locally aggressive lesion considered within the differential diagnosis was a nasopharyngeal angiofibroma.

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Fig. 1 Computed tomography (CT) without contrast. **a** Axial; **b** Coronal; **c** Sagittal; **d** 3D reconstruction

This lesion affects boys and adolescent young men and commonly they are fair-skinned and red-haired. The highest incidence occurs in the second decade of life. The lesions arise in the posterolateral nasal wall or nasopharynx and infiltrate extensively into surrounding tissues [1]. However, it was considered that the site of the current case was not consistent with a diagnosis of a nasopharyngeal angiofibroma. Another indolent tumor considered within the differential diagnosis was a sinonasal glomangiopericytoma [1]. An olfactory neuroblastoma [1], a tumor which often originates in upper nasal cavity, but which can also originate in maxillary sinus, was also considered. Calcifications may be seen on CT scans with this tumor. Salivary gland tumors are rare and generally occur in an older age group, but an adenoid cystic carcinoma could not be entirely excluded as a possible diagnosis. These tumors have a wide age range. The paranasal sinus is the most common site of these tumors outside of the salivary glands [3]. They are insidious and infiltrate extensively through bone. Most other malignancies in this region arise in an older age group and the history in the given case is too long. However, two lesions which were considered included a botryoid rhabdomyosarcoma [1] a slow-growing variant of rhabdomyosarcoma, as well as Ewing's sarcoma [1]. Both these tumors occur in a younger age group and can occur in the sinonasal tract.

Odontogenic lesions of aggressive behavior, arising in the maxilla, that were considered within the differential diagnosis included an odontogenic keratocyst/keratocystic odontogenic tumor, an ameloblastoma, a squamous odontogenic tumor, and an odontogenic myxoma. Although a calcifying epithelial odontogenic tumor and dentinogenic ghost cell tumor were considered, it was felt that there was insufficient evidence of calcification within the CT images provided to propose either of these diagnoses. Malignant odontogenic lesions and a metastasis were discounted on account of the long history provided. Lastly, extension of an intracranial lesion, such as a meningioma [1], was also discredited as a potential diagnosis due to a lack of convincing radiological evidence.

It was felt that in order to narrow the differential diagnosis, a plain film such as a dental panoramic radiograph would have been invaluable. Additional CT scan slices should also be examined. In addition, supplementary investigations recommended would include an aspiration or fine needle biopsy and/or an MRI film with and without gadolinium to identify if the mass contained fluid, and an incisional biopsy.

The differential diagnosis arrived at from the information provided was wide and included, in decreasing order of likelihood, a maxillary sinus mucocele, allergic fungal rhinitis, a nasopharyngeal angiofibroma, a sinonasal

Fig. 2 Microscopic features of calcifying cystic odontogenic tumor (CCOT). Low power magnification (**a** at 4× and **b** at 10×) shows fibrous connective tissue lined by ameloblastic epithelium and calcifications. **c** and **d** (at 20× and 40×) show the characteristic ghost cells of CCOT

glomangiopericytoma, an odontogenic myxoma, an ameloblastoma, an odontogenic keratocyst/keratocystic odontogenic tumor, a rhabdomyosarcoma or an adenoid cystic carcinoma.

Diagnosis and Discussion

A medial maxillectomy was performed by the surgeon, using 0, 30 and 70 degree nasal endoscopes. The specimen submitted consisted of several fragments of soft tissue with membranous appearance and also fragments of flat bony tissue.

The histologic examination showed the presence of fibrous connective tissue partially lined by ameloblastic epithelium exhibiting the presence of ghost cells on the upper layers (Fig. 2a, b, c, d). Small calcifications were embedded within the connective tissue. These features are characteristic of calcifying cystic odontogenic tumor [4, 5], also known as calcifying odontogenic cyst, prior to the publication of the 2005 World Health Organization (WHO) Histologic Classification of Odontogenic Tumors [6]. It was first reported in 1962 by Gorlin et al., describing calcifying odontogenic cyst as a possible analogue of the cutaneous calcifying epithelioma of Malherbe [7].

The molecular changes underlying the development of calcifying cystic odontogenic tumor (CCOT) include mutations and overexpression of b-catenin gene, which regulates Wnt signaling. Aberrations of the Wnt signaling

pathway may play a crucial role in the differentiation of the odontogenic epithelium in CCOT via the deregulation of cell proliferation [8].

Positive staining for MMP-9 protein has been detected in stromal cells of CCOT and it may be linked with invasive ability of this tumor [9].

Cases of association of CCOT with other tumors such as keratocystic odontogenic tumor and orthokeratinized odontogenic cyst have been documented [10]. The most frequently reported association has been that of CCOT with odontoma [11]. The presence of another tumor within the same lesion does not appear to influence the favorable prognosis and low recurrence rate of CCOT [12].

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