Case Report

Pigmented Pindborg tumor of the maxilla: A case report

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Abstract

The calcifying epithelial odontogenic tumor (CEOT), also known as the Pindborg tumor, is a benign locally invasive neoplasm. Common variants of CEOT include noncalcifying, Langerhans cell, bone and cementum forming and clear cell, which have a prognostic significance. Pigmented variants are known to occur in other odontogenic tumors. However, a definitive pigmented variant of CEOT has not been reported in literature so far. Here, we report the first case of pigmented Pindborg tumor arising from the maxilla in a young female. The pigment was demonstrated as melanin by staining and confirmed by immunohistochemistry. The pigmented variant of CEOT did not recur within 18 months postsurgery. Our report indicates that it is essential to recognize the pigmented variant. We discuss the common variants of CEOT and potential histogenesis of the pigmented variant. Further studies are required to reveal the histogenesis of melanocytes and their pathological significance in the odontogenic tumors.

Key Words: Calcifying epithelial odontogenic tumor, melanin, odontogenic tumors, pigmented Pindborg tumor

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INTRODUCTION

The calcifying epithelial odontogenic tumor (CEOT) is also known as Pindborg tumor. The Dutch Pathologist, Dr. Jens Jorgen Pindborg, described and designated CEOT as a distinct pathologic entity in 1955.[1] It is a benign, locally invasive neoplasm that constitutes about 1% of all odontogenic neoplasms.[1] CEOT usually presents in patients aged between 30 and 50 years and both sexes are equally affected. Molar and premolar regions of the posterior mandible are the most common sites of intraosseous occurrence. Ten percent of CEOTs occur extraosseously, with a predilection to the anterior gingival region. More than half (53%) of these tumors are associated with an unerupted teeth, most commonly, mandibular molars.[1] Clear cell,[2] noncalcifying,[3] bone and cementum forming[4] and Langerhans cell[5] variants have been reported. Pigmented variants of odontogenic tumors are extremely rare and only 47 cases have been reported, of which 20 cases were reported in calcifying cystic odontogenic tumors (CCOT) and one case was described as unclassifiable.[6] However, no definitive case of pigmented CEOT has been reported in literature so far.[6] The histogenesis of Pindborg tumor has not been established conclusively; however, most authors accept that intraosseous tumors arise from the stratum intermedium of the enamel organ whereas extraosseous tumors originate from the epithelial rests of the dental lamina or from the basal cells of gingiva.[7] CEOT is usually benign and has a local recurrence rate of 10–15%.[8]

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Tumors which arise in the maxilla tend to be more locally aggressive than those which arise in the mandible.[9]

CASE REPORT

A 28-year-old female patient visited the Dental Outpatient Department of our institute with a complaint of swelling in the left maxillary region for the past 6 months. Intraoral examination revealed a 3.5 cm × 3 cm swelling, extending from the left molar to the left incisor region. Radiograph revealed a mixed pattern revealing a radiolucent mass with scattered radiopaque areas associated with an unerupted tooth fragment. Computerized tomography (CT) scan revealed a heterogeneous soft-tissue mass, epicentering the alveolar margin of the left maxilla around the root of the first molar tooth and measuring 3.6 cm × 3.3 cm × 3.2 cm, causing expansion with resultant thinning of the bony wall and a thin rim of calcification in the periphery [Figure 1a and b]. An eccentrically located small, unerupted tooth fragment measuring 8 mm × 6 mm × 6 mm was also identified [Figure 1a]. The mass was enucleated and was immediately fixed in 10% neutral buffered formalin. Paraffin-embedded tissues were cut into 4-mm sections, stained with hematoxylin and eosin (H and E), Congo Red and Masson-Fontana. Melanin bleach using potassium permanganate was performed. Immunohistochemistry with monoclonal mouse anti-S100 antibody (DAKO Carpenteria, CA, USA) and monoclonal mouse anti-melanoma (HMB45) antibody (Biogenex, San Ramon, CA, USA) was performed. The postoperative course was uneventful. The patient was asymptomatic without recurrence for 18 months following the procedure.

Histopathologic findings

Microscopic examination of H and E-stained sections demonstrated a tumor composed of epithelial cells arranged in sheets, nests, plexiform and occasional pseudoglandular pattern. These epithelial cells were polyhedral with abundant dark staining eosinophilic cytoplasm, large vesicular nuclei with smooth nuclear margins and fine chromatin, separated by loose connective tissue stroma [Figure 2a]. Epithelial cells were admixed with cells containing abundant brownish black pigment [Figure 2b]. Homogeneous eosinophilic material, which is pathognomonic of CEOT, was found in the intercellular areas [Figure 2c and f]. Numerous foci of calcification and calcific spherules forming Liesegang rings [Figure 2d and g], ossification [Figure 2e] and acanthomatous areas were also observed. Atypical mitotic figures were not detected. Homogeneous eosinophilic material stained positive with Congo Red and therefore is an amyloid-like material [Figure 3a]. Melanin bleach using potassium permanganate and Masson-Fontana staining [Figure 3b] demonstrated that the pigmented cells contained melanin. Immunohistochemistry revealed strong positivity for S100 [Figure 3c] and HMB45 [Figure 3d] in all pigment-containing cells.

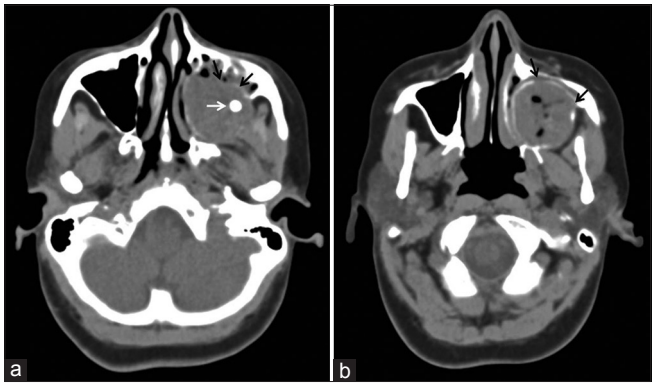

Figure 1: Computerized tomography images. (a) Axial section reveals a heterogeneous soft-tissue density lesion (black arrows), filling the left maxillary antrum. The lesion contains an eccentrically located tooth (white arrow). (b) Axial section shows the lesion (black arrows) in the left maxillary antrum, causing expansion with resultant thinning of the bony wall and thin rim of calcification in the periphery

DISCUSSION

Classically, CEOT is comprised of polygonal epithelial cells with eosinophilic cytoplasm, well-defined cellular borders and vesicular nuclei with conspicuous nucleoli. Epithelial cells are typically arranged in sheets, nests, cribriform or pseudoglandular pattern. Mild to moderate pleomorphism can be found, but atypical mitotic figures are usually absent. Intercellular areas contain homogeneous pale eosinophilic material that resembles amyloid. This amyloid-like material, proposed to be derived from degradation of keratin filaments secreted by the epithelial cells, stains positive with Congo red and is characteristic of Pindborg tumor.[7] Another important distinguishing feature of CEOT is the presence of calcifications ranging from small to large aggregates or in the form calcific spherules forming concentric laminations known as Liesegang rings.

Five histopathologic patterns have been described in Pindborg tumor: Sheets and islands of polyhedral cells with well-defined cell outlines and intercellular bridges; a cribriform pattern with the presence of eosinophilic substance resembling amyloid within the spaces, which undergoes calcification to form Liesegang rings; abundant polyhedral neoplastic cells admixed with many multinucleated giant cells; polyhedral cells in nests resembling salivary gland tumors; and predominantly pseudoglandular pattern composed of clear cells.

In general, CEOTs are benign with an indolent biological behavior and a local recurrence rate of 10%–15%.[10] It is important to recognize the variants of Pindborg tumor

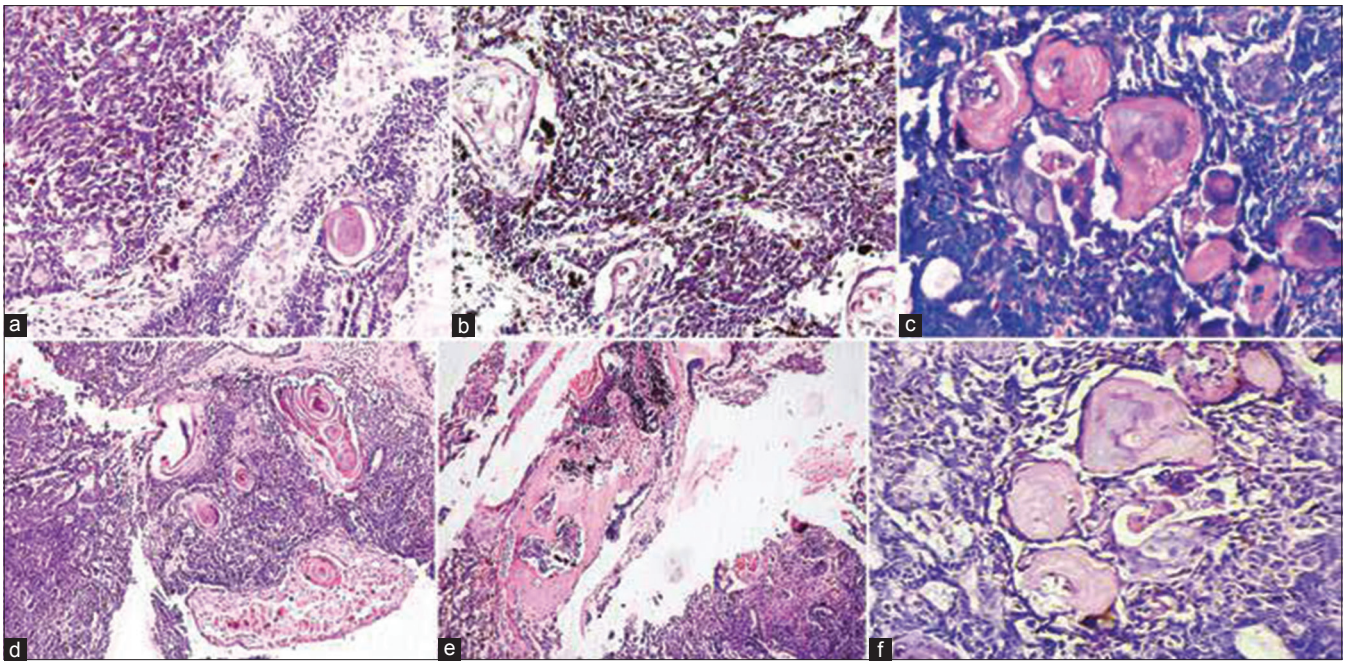

Figure 2(a-f): Histopathology findings. (a) Polyhedral epithelial cells in sheets, plexiform and occasional pseudoglandular arrangement having abundant dark staining eosinophilic cytoplasm are separated by loose connective tissue stroma (H&E, ×100). (b) Abundant brownish black pigment containing cells admixed among tumor cells (H&E, ×200). (c) Tumor cells with intercellular areas showing homogeneous eosinophilic material undergoing calcification (H&E, ×100). (d) Foci of calcific spherules forming Liesegang rings (H&E, ×40). (e) Foci of ossification (H&E, ×40). (f) Polyhedral cells with acellular material undergoing calcification (H&E, ×100)

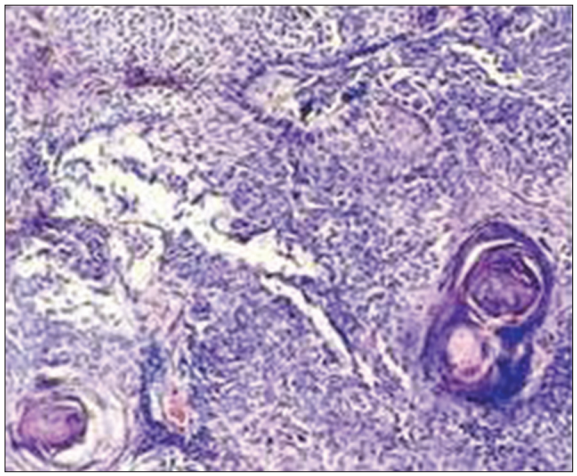

Figure 2g: Globular calcifications with onion skinning (Liesegang rings) (H&E, ×40)

because of their varied clinical course, aggressiveness, recurrence potential and malignant behavior. Clear cell variant is characterized by the presence of abundant clear cells in the pseudoglandular pattern. The origin of clear cells is not clear and may arise from degenerated epithelial cells with glycogen, Langerhans cells or odontogenic epithelium. The presence of clear cells indicates an aggressive behavior.[2] The absence of calcification in the noncalcifying variant is a sign of poor tumor differentiation and is associated with greater chances of recurrence. Pindborg has reported that even cases with minimal calcification can recur.[3] Bone and cementum forming variant shows extensive mineralized areas, either cellular resembling bone or acellular areas resembling cementum and composed of collagen. Collagen is most likely deposited by stimulated stromal cells of the tumor on any calcified nidus.[4] Langerhans cell variant is distinguished by its occurrence in the Asian population, involvement of anterior part of the maxilla, few nests and islands of clear tumor cells exhibiting positivity with S100 and CD1a, lack of calcification, excess of amyloid-like substance and presence of chronic inflammatory cells. This variant does not recur and hence resembles conventional CEOT in behavior. Langerhans cells are claimed to play a major role in antigen presentation and regression of the tumor.[5]

The pigmented odontogenic tumors are rare and cases of pigmentation are reported in CCOT.[6] The origin of melanocytes in these tumors is controversial. Some authors suggest that the lesional odontogenic tissue has the potential to undergo neuroectodermal differentiation under certain situations and could give rise to melanocytes.[6] Others propose that the process of odontogenesis is multifarious and occurs as a result of close and mutual interactions involving oral epithelium and ectomesenchyme, which in turn is derived from cranial neural crest. Hence, melanocytes which are also derived from neural crest might be present in odontogenic lesions.[6] A few other authors identified the presence of melanocytes in outer enamel epithelium and dental lamina in fetuses during early gestation (12–18 weeks)[8] and hence stated that

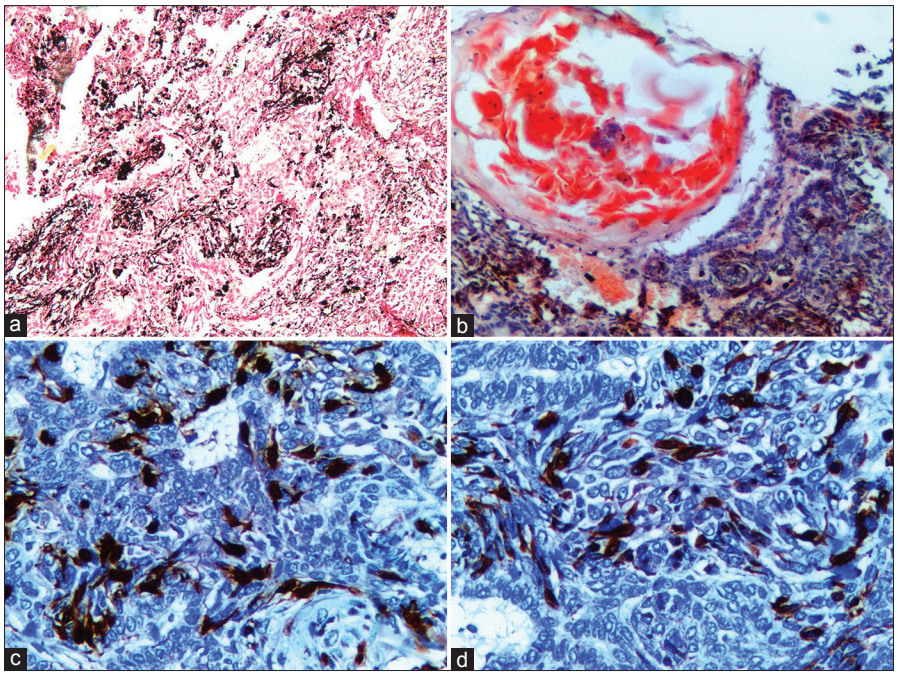

Figure 3: Special stains and immunohistochemistry. (a) Masson-Fontanna stain showing strong positivity in the pigments, demonstrating the presence of melanin (Masson-Fontanna stain, ×100). (b) Congo Red stain showing positivity in the homogeneous eosinophilic amyloid-like material (Congo red stain, ×100). (c) Anti-S100 antibody showing positivity in round and spindled pigment-containing cells (IHC stain, ×200). (d) Anti-HMB45 antibodies showing positivity in pigment-containing cells (IHC stain, ×200)

melanocytes could be seen in odontogenic lesions. The same authors observed that the occurrence of pigmented lesions and melanocytes is common in pigmented races and suggested a strong racial predilection for these lesions.[11]

An additional speculation for the presence of melanocytes in odontogenic lesions includes the migration of melanocytes through the mesenchyme. In dog fetuses, the melanocytes were seen surrounding mesenchymal tissue in the dental anlage.[12] It is observed that most of the pigmented odontogenic lesions have a prominent mesenchymal component either as in the form of dentin or in the form of calcification suggesting that the presence of calcification or dentin may activate the melanocytes previously present there, to form pigment. Takeda *et al*. demonstrated two types of pigment-containing cells: S100-positive spindle or round cells and HMB45-positive dentritic and spindle cells derived from melanocytes.[13]

While pigmented variants of CCOT have been reported, it is not known if pigmented variants of CEOT occur. Here, we report the first case of pigmented variant of CEOT in the jaw. The tumor was found in a young Asian female in the left maxilla and was associated with an unerupted tooth. The tumor was extensively calcified, and it is possible that ossification could have triggered melanocytes to produce melanin. The patient was asymptomatic for 18 months after surgery, indicating that the pigmented variant could be similar to conventional CEOT in progression. However, prospective studies on a larger patient population are required to ascertain the prognosis of patients diagnosed with pigmented variant of Pindborg tumor described in this case report. Since this variant possesses unique histologic and uncommon clinical features, it may possibly create problems for differential diagnosis. Therefore, it is important to recognize the occurrence of a pigmented variant of CEOT. Further investigation is required to unravel the biological behavior of this variant, precise origin of melanocytes and the pathological implication of their presence in the odontogenic tumors.

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Conflicts of interest

There are no conflicts of interest.

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