

A pigmented calcifying cystic odontogenic tumor

Pigmentli kalsifiye kistik odontojenik tümör

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ABSTRACT

A case of a pigmented calcifying cystic odontogenic tumor (CCOT) localized in the mandible occurring in a 16-year-old white female - is reported, and the characteristic histomorphologic features of CCOT and the pathogenesis of melanin and melanocytes present in the pigmented type is discussed under the light of histochemical and immunohistochemical data.

Key words: Odontogenic tumor, calcifying odontogenic cyst, pigment, melanin, melanocytes

ÖZET

On altı yaşında bir kadın hastada mandibula yerleşimli pigmentli tipte kalsifiye kistik odontojenik tümör olgusu sunulmaktadır. Kalsifiye kistik odontojenik tümör için tanımlanmış karakteristik histomorfolojik özellikler ve ayrıca pigmentli tipte mevcut melanin ve melanositlerin patogenezi histokimyasal ve immünohistokimyasal veriler eşliğinde tartışılmaktadır.

Anahtar sözcükler: Odontojenik tümör, kalsifiye odontojenik kist, pigment, melanin, melanosit

INTRODUCTION

The calcifying odontogenic cyst, renamed as calcifying cystic odontogenic tumor (CCOT) (1) was first described by Gorlin et al. (2) as a distinct entity, which has a histologic resemblance to cutaneous calcifying epithelioma of Malherbe. In an analysis of 392 odontogenic tumors, Daley et al. (3) found that CCOT forms 4.6% of all odontogenic tumors. The characteristic histology of CCOT includes an epithelial lining showing a well-defined basal layer of columnar cells, a zone of loose edematous cells bearing some resemblance to stellate reticulum, abnormal keratinization producing ghost cells and a few small calcifications (1,4). A rare variant of CCOT, in which melanin is present in the epithelium, can also be seen in literature (2,5-8).

A pigmented variant of CCOT is described here with its histomorphologic, histochemical and immunohistochemical features.

CASE REPORT

Clinical Summary

A 16 year-old white female was referred to Istanbul University, Istanbul Faculty of Dentistry because of a painless swelling in her left half of the mandible. Panoramic radiograms demonstrated a well-defined unilocular radiolucent liquid containing cyst localised between left canine and the second premolar in the mandible (Figure 1). The lesion was enucleated and the postoperative course was uneventful.

Pathological Findings

A well-demarcated, 2x1x1 cm cystic mass was seen in gross examination. The cut surface was dark-brown in color. Light microscopic

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Figure 1. Radiographically, a well-defined radiolucent cystic lesion in the left half of the mandible is defined.

examination demonstrated a cyst displaying characteristic features for the CCOT, such as a well-defined basal cell layer, an epithelial component in varying thickness resembling stellate reticulum of enamel organ, eosinophilic ghost cells protruding into cystic cavity and small calcifications (Figure 2).

Abundant deposition of a dark-brown pig-

ment was seen in the cytoplasm of spindle/dendritic cells and also in the swollen round cells localised between the epithelial cells. The cell detail was obscured by this pigmentation. Histochemically, positivity for Masson Fontana (Figure 3) and negativity for Prussian blue stains demonstrated that the dark-brown pigment within the lesion was melanin.

Immunohistochemically antibodies for pancytokeratin (NeoMarkers, 1/200 dilution, 1 h incubation), S-100 (NeoMarkers, 1/100 dilution, 1 h incubation) and HMB-45 (NeoMarkers, 1/40 dilution, 1 h incubation) were performed. The epithelial cells lining the cyst wall and ghost cells protruding to the lumen displayed immunopositivity for pancytokeratin. Although S-100 displayed strong immunopositivity in all melanin pigment-containing cells (Figure 4),

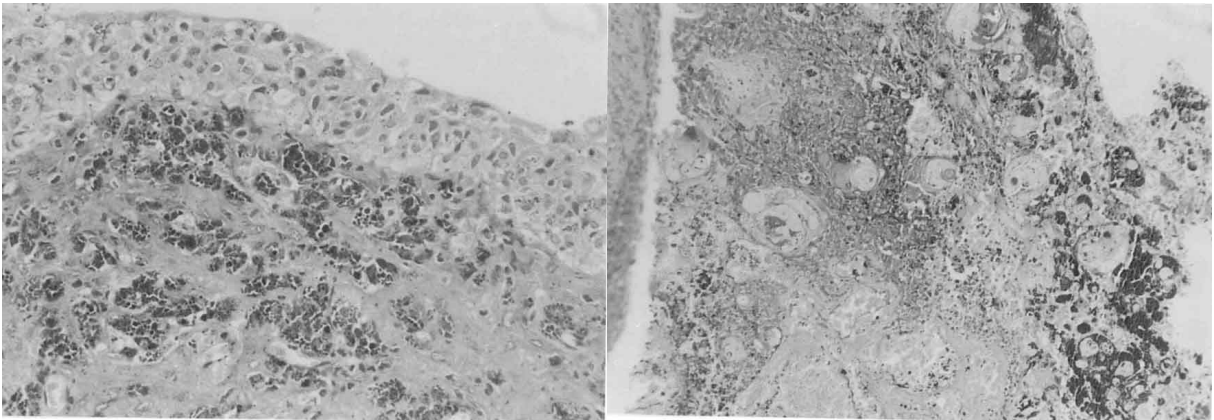


Figure 2. The epithelial lining in varying thickness with a basal cell layer, abnormal keratinization producing eosinophilic ghost cells protruding into the lumen and abundant pigmentation in the cyst wall (HE, $\times 125$, $\times 310$).

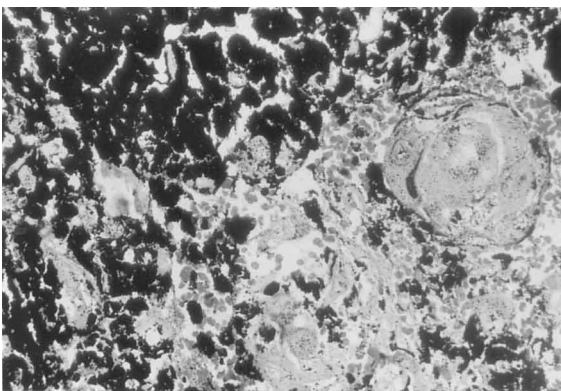


Figure 3. The melanin pigment between the ghost cells stained with Masson-Fontana stain ($\times 310$).

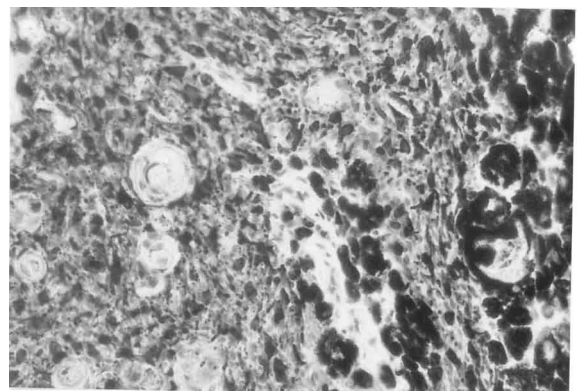


Figure 4. Diffuse and strong immunopositivity with anti-S-100 protein in all pigmented cells between the epithelial cells ($\times 310$).

HMB-45 was positive only in spindle/dendritic cells (Figure 5). This finding suggested that the pigmented cells were in two types such as, melanophages and melanocytes. Both antibodies indicated the presence of a coarse granular pattern of cytoplasmic immunopositivity.

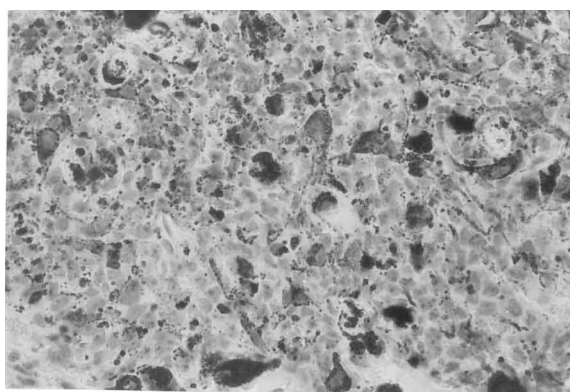


Figure 5. Positive anti-HMB-45 immunoreactivity only in dendritic cells (x500).

DISCUSSION

Calcifying cystic odontogenic tumor is a benign cystic odontogenic neoplasm with well defined characteristic histologic features which constitutes only 4.6% of all odontogenic tumors (1,3). Although World Health Organization (WHO) defined CCOT as a benign odontogenic neoplasm (1), CCOT has heterogenous histologic spectrum including both cystic and solid forms, and also displays various clinicopathological features with diverse clinical behaviour (9-11).

Pigmented odontogenic lesions are rare, with only 47 cases, 20 of which formed by CCOT reported in English literature (12-15). Most of these patients having pigmented odontogenic lesions are Asians (6-8,15) followed by blacks (13,16-18). White CCOT patients are exceedingly rare (19,20). The limited number of reported cases does not lead to any statistical value as for racial predisposition (6-8,12,13,15-18). Our patient being a white female is a rare example of an infrequently seen race in CCOT cases presented in the literature.

Our review of the literature revealed a total of 21 cases of pigmented CCOT (12,13). The mean age of those patients were detected to be 22.8, and 12 of the patients were female. The localization of the tumors, whether to the mandible or maxilla, did not differ significantly. Six of the cases were associated with odontomas (12,13). Other pigmented odontogenic lesions including cysts are lateral periodontal cyst (13), ameloblastic fibrodentinomas (14), adenomatoid odontogenic tumors (21,22), odontogenic keratocysts (23) and a few other types. Although the lesion type differs, histochemical, immunohistochemical and ultrastructural methods used in studies demonstrated that the pigment is always melanin.

Takeda et al. (14) showed the presence of positive immunoreactivity for S-100 in spindle and dendritic cells, and no immunostaining for CD68, in a case of a pigmented ameloblastic fibrodentinoma, which is an odontogenic tumor with epithelial and mesenchymal components like CCOT. Their results suggested that the spindle and dendritic cells were melanocytes. In accordance with their results S-100 was immunoreactive in both spindle/dendritic cells and swollen round cells, whereas HMB-45 was reactive in only spindle/dendritic cells in our case of CCOT. This result may lead to a conclusion that in pigmented odontogenic lesions there should be two kinds of melanin pigmented cells, one of which is of melanocytic origin.

To our knowledge two ultrastructural studies were reported in English literature which support our immunohistochemical findings for the cells of probable melanocytic origin. One of these studies is from Soames (7) who reported a pigmented calcifying odontogenic cyst occurring in a 15-year-old female. The other ultrastructural study was related to a pigmented odontogenic keratocyst from Macleod et al. (19). In both studies melanocytes were demonstrated within two different tumors by electron microscopic examination, associated with the absence of desmosomes and tonofilaments and the presen-

ce of melanised melanosomes and/or premelanosomes in various stages of development in cytoplasm and cytoplasmic processes between surrounding cells (7,19).

The origin of melanocytes present in odontogenic lesions is not known and their pathological significance is still of interest. An interesting observation is that melanin containing intra-osseous lesions, except malignant melanoma metastases, are all localized in the jaw bone. The probable pathogenesis of this localization is speculative. It is generally known that melanocytes are normally present in clinically non-pigmented oral mucosa, therefore the presence of melanocytes can be anticipated in odontogenic lesions since the dental lamina originates from the primitive oral lining. Lawson et al. (24) have discovered melanocytes in the dental lamina and outer enamel epithelium during 12-18 weeks of gestation which were apparently more common in blacks than in whites, suggesting a racial predisposition for pigmented odontogenic lesions.

Another theory of melanocytic origin in odontogenic lesions is the migration of melanocytes through the mesenchyme rather than the ectoderm (25). Takeda et al. (25) displayed melanocytes in mesenchymal tissue around the dental anlage in dog fetuses. They could not show any melanocytes both in the oral epithelium and in the epithelial element of the dental anlage.

It is a striking feature that all pigmented odontogenic lesions, but not cysts, have an epithelial component accompanied by a mesenchymal component with dentin formation and calcification. Some factors such as the presence of mesenchymal component or the hard tissue formation, that can activate the melanocytes already present in the epithelium might have played a role. More future investigations must be performed to illuminate the origin of melanocytes in odontogenic lesions.

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