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CLINICAL PATHOLOGIC CONFERENCE CASE 6: A RADIOLUCENCY WITH MILD SWELLING OF THE RIGHT MANDIBLE

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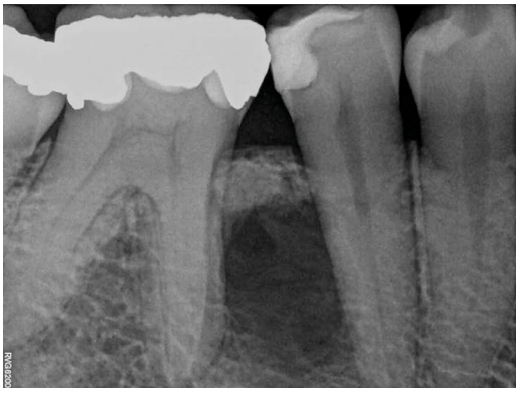

Fig. 1. Periapical radiograph showing relatively well-defined unilocular radiolucency.

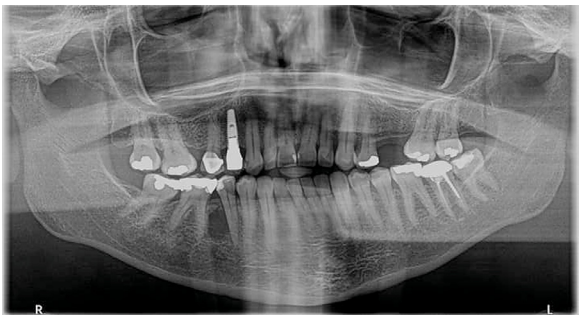

Fig. 2. Panoramic radiograph showing well-defined unilocular radiolucency in the right posterior mandible.

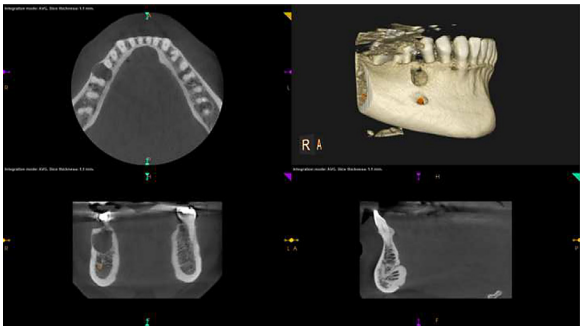

Fig. 3. Computed tomography images of the lesion in the right posterior mandible showing buccal expansion and thinning of the buccal cortex.

Clinical Presentation: A 58-year-old female presented with an asymptomatic mild buccal cortical expansion between teeth #29 and #30. Her medical history was unremarkable. A periapical x-ray, panoramic radiograph, and computed tomography scan were taken (Figures 1-3). Upon surgical excision, a solid mass was removed and submitted for microscopic examination.

Differential Diagnosis: After reviewing the clinical and radiographic features, this disease process is likely benign. The radiographs exhibit a well-circumscribed, unilocular radiolucency; disruption of the overlying alveolar bone; and resorption of the buccal cortical plate. The differential diagnoses include central odontogenic fibroma, lateral periodontal cyst, ameloblastoma, squamous odontogenic tumor, and cemento-ossifying fibroma.

Central odontogenic fibroma (COF) is a benign tumor that is more commonly found in the posterior mandible, but it can also be seen in the anterior maxilla. Clinically, it presents as a nontender swelling and painless expansion of the cortical bone. Radiographically, central odontogenic fibromas may be unilocular or multilocular radiolucencies. Occasionally, some of the lesions have a mixed radiopaque/radiolucent appearance. A wide age range of patients can be affected. COF has a slight predilection for female patients.[1] COF is the top differential diagnosis because the patient is a female with a radiolucent, painless, and slightly expansile lesion of the posterior mandible. Grossly, COF is a benign and solid mass, much like the lesion in this case.

Lateral periodontal cyst (LPC) is an asymptomatic odontogenic cyst commonly seen in the premolar, canine, and lateral incisor regions of the mandible. Most LPCs occur in the fifth to seventh decades of life and have a male predilection. Radiographically, LPC usually presents as a well-circumscribed, unilocular radiolucency adjacent to a vital tooth.[2] LPC is in the differential diagnosis because it is consistent with the clinical and radiographic presentation of this case. The patient falls in the correct age range. She had an asymptomatic, radiolucent lesion that was located adjacent to a vital premolar. However, the gross specimen in this case was described as a solid mass, whereas an LPC would have a cystic appearance.

Ameloblastoma is a benign odontogenic tumor commonly found in the posterior mandible. It can appear as an unilocular or multilocular radiolucency. Ameloblastoma is locally aggressive and can exhibit extensive growth. Displacement of adjacent teeth along with perforation of the cortical plate may occur.[3] The peak age of incidence is in the fourth to fifth decades of life. There is no gender predilection.[4] Ameloblastoma is in the differential diagnosis because of its radiographic appearance and clinical age range. However, the lesion in this case appears to be more stable in growth when compared to an ameloblastoma, which tends to be a more expansive tumor.

Squamous odontogenic tumor (SOT) is benign and often located in the anterior maxilla or posterior mandible.[4] It presents as a slow-growing, asymptomatic swelling. Some cases of SOT may present with swelling of the alveolar process. Radiographically, SOT is unilocular and may have a triangle or semicircular shape. Diagnosis occurs in the fourth decade of life and there is a slight male predilection.[5] Like SOT, the lesion in our case exhibits disruption of the overlying alveolar process, it is radiolucent, and it presents as a solid mass upon removal. However, the shape of the radiolucency in this case is circular versus the triangular shape typically associated with SOT.

Finally, Central Ossifying Fibroma (COsF) is found in the posterior mandible. Like most benign fibro-osseous lesions, COsF ranges from radiolucent to radiopaque radiographically. There is a significant female predilection in the second and fourth decades of life.[6] COsF in its early stages may mimic the lesion discovered in this patient and has a consistent location and radiographic appearance. However, COsF usually occurs in younger female patients and becomes more expansive over a long period of time.[4]

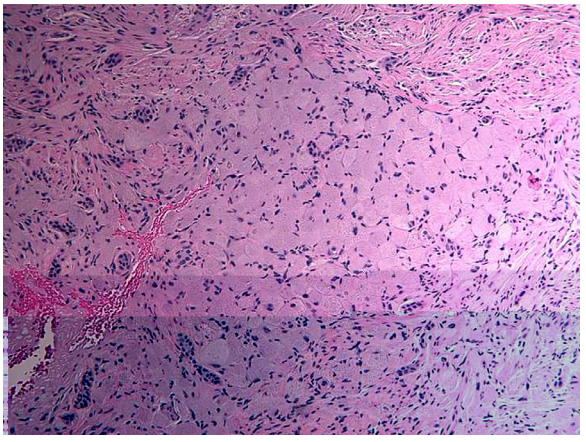

Fig. 4. Low-power photomicrograph showing abundant granular cells with interspersed islands and cords of cells (hematoxylin and eosin, 10 × original magnification).

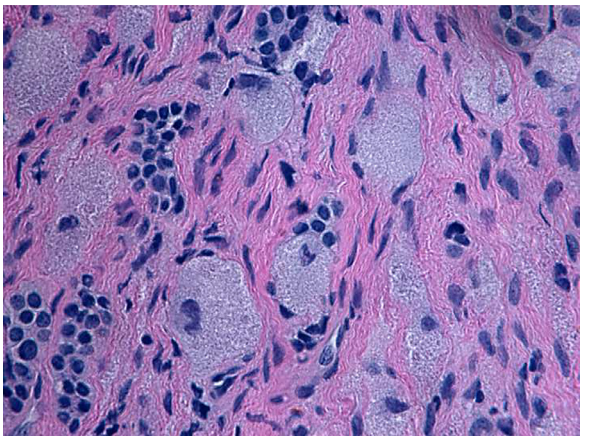

Fig. 5. High-power photomicrograph showing granular cells with eccentric nuclei and admixed islands and cords of cells with central round nuclei (hematoxylin and eosin, 40 × original magnification).

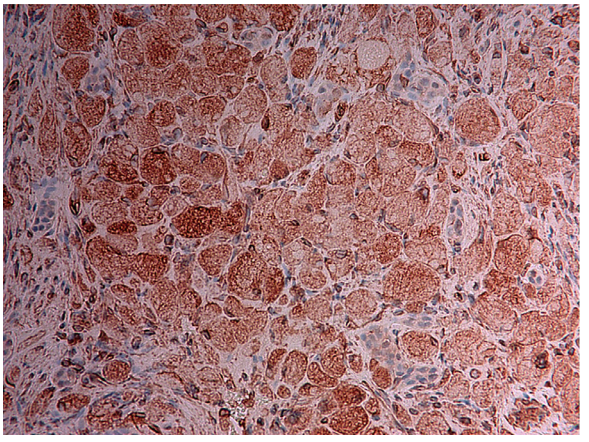

Fig. 6. Granular cells showing strong reactivity with vimentin immunostain.

Diagnosis and Management: Microscopic examination of the excisional biopsy specimen revealed individual and collections of large oval cells with abundant eosinophilic granular cytoplasm and eccentrically placed nuclei. Cords, nests, and islands of cells with central round nuclei were interspersed within the granular cells (Figures 4 and 5). Some of these cells exhibited clear cytoplasm. Tissue was sent for immunohistochemistry to determine the nature of the granular cells and islands of cells with central round nuclei. The granular cells were strongly positive for vimentin (Figure 6). The islands of cells with central round nuclei were strongly positive for cytokeratin (Figure 7). The granular cells and islands were both negative for S100 (Figure 8). Based on all of these findings, the final diagnosis rendered was central granular cell odontogenic tumor (CGCOT).

Discussion: CGCOT has a long history of nomenclature from its identification to current name, as summarized in Table I.[7-14] CGCOT is exceedingly rare, with only 38 cases reported in the literature.[7] This tumor appears to comprise approximately 0.2% to 0.3% of all odontogenic tumors.[7] CGCOT occurs in patients with a broad age range of 16 to 77

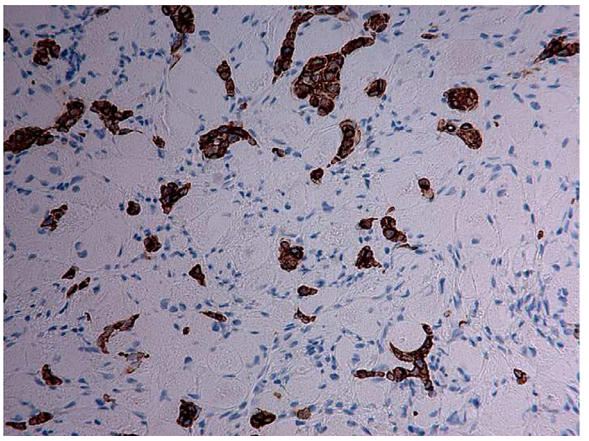

Fig. 7. Islands and cords of cells showing strong reactivity with CK5/6 immunostain.

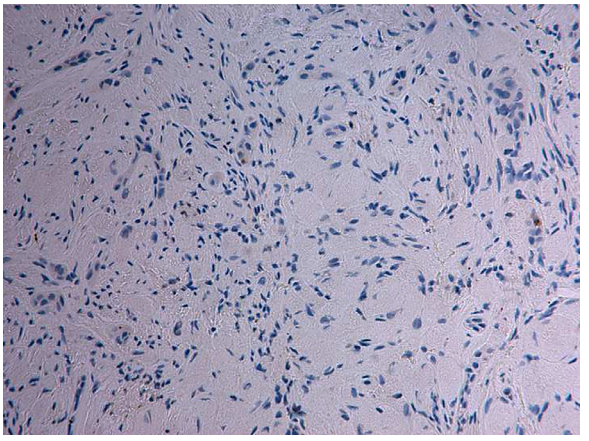

Fig. 8. Granular cells and islands showing no reactivity to S100 immunostain.

with a mean age of 45.21.[7] However, 53.3% of tumors occur in the sixth to eighth decades of life.[15] A definite female predilection of 3.1:1 is reported.[16,17] The posterior mandible is the most common location but posterior maxillary tumors have also been identified in a 3:1 ratio as well.[18] Though this tumor is typically centrally located in the jaw, 3 peripheral lesions have been documented.[15]

Table I. History of nomenclature of CGCOT[7]

Author	Year	Terminology
Werthemann[8]	1950	Spongiocytic adamantinoma
Couch et al.[9]	1962	Granular cell ameloblastic fibroma
Dalforno and Donna[10]	1970	Ameloblastic fibroma with stroma of granular cells
White et al.[11]	1978	Central granular cell tumor of the jaws
Vincent et al.[12]	1987	Central granular cell odontogenic fibroma
Shiro et al.[13]	1989	Central granular cell odontogenic fibroma
World Health Organization[14]	2005	Central granular cell odontogenic tumor

CGCOT, central granular cell odontogenic tumor.

Table II. Microscopic features

Granular cells	Epithelial islands	Stroma/other
Large oval **cells with abundant eosinophilic granular cytoplasm**	Cords and nests of **inactive odontogenic epithelial islands**	Thin, **fibrous connective tissue septae** containing small, thin-walled vessels
Eccentrically placed nuclei	May be surrounded by hyalinized acellular eosinophilic zone	Small, oval, basophilic **calcifications** resembling cementum can be present
Often in sheets or lobular arrangement	Cells may exhibit **clear cytoplasm**	Periphery frequently well demarcated and often shows evidence of a thin fibrous connective tissue "capsule"

Table III. Immunohistochemistry profile

	CGCOT Granular cells	CGCOT Islands	Our case Granular cells	Our case Islands
Vimentin	+++	−	+++	−
CK	−	+++	−	+++
S100	−	−	−	−
CD68	+ (Weak)	Focally + dendritic cells	−	Focally + dendritic cells

CGCOT, central granular cell odontogenic tumor.

Clinically, CGCOT usually presents as a slow-growing swelling of the involved jaw bone. Tooth displacement and cortical perforation are occasionally seen. CGCOT most commonly presents radiographically as a unilocular radiolucency, often with a sclerotic border. However, a few mixed radiolucent and radiopaque lesions have been reported.[7,16] On microscopic examination, CGCOT shows large cells with abundant eosinophilic granular cytoplasm admixed with islands of odontogenic epithelium. The characteristic microscopic features of the granular cells, epithelial islands, and stromal component of CGCOT are highlighted in Table II. However, immunohistochemistry is necessary to rule out other tumors in the differential diagnosis, including granular cell tumor and granular cell ameloblastoma. The immunohistochemical profile of CGCOT along with comparison to our case is summarized in Table III.

The etiology of the granular cells in CGCOT is an important topic. Ultrastructural study of the granular cells shows numerous electron-dense intracytoplasmic lysosome-like particles.[15] Phagocytic activity suggests that the granular cells are derived from a histiocytic cell line. Transmission electron microscopy study of the granular cells conducted by Shiro et al. showed mesenchymal differentiation, with some fibroblastic characteristics.[13] In summary, the granular cells of CGCOT appear to be mesenchymal in origin, with a potential for histiocytic or fibroblastic differentiation.[15]

Most cases of CGCOT are treated by conservative surgical removal, often enucleation or curettage, with additional extraction of teeth if necessary.[19] Surgical removal with reconstruction is performed in some cases. The prognosis is good, with 22 cases in the literature reporting no evidence of recurrence with follow-up periods ranging from 2 months to 180 months.[7] Only one case showed recurrence 13 years after it was initially removed by curettage.[7] Piatelli et al. reported a single case of a maxillary tumor that exhibited features of malignancy.[19,20] Overall, CGCOT is a rare, benign odontogenic tumor with a good prognosis and negligible recurrence rate.

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