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Odontogenic Carcinoma with Dentinoid: A New Odontogenic Carcinoma

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Abstract Dentinoid is an integral part of some odontogenic tumors. This article describes the clinico-pathological features of three cases of odontogenic carcinomas with dentinoid (OCD). A comparison of these with previously reported cases of dentinoid-producing epithelial odontogenic tumors allowed us to identify another six cases that may be considered as examples of OCD. Six cases occurred in the mandible and three in the maxilla, all developing behind the canines. There was no sex predilection (five men and four women; age range 14–61 years, mean 38.1). Pain or discomfort was mentioned in five cases, four of which showed tooth resorption. All cases appeared initially as well-defined radiolucencies, five of which showed variable amounts of calcified material. Recurrences were recorded in three instances, but no evidence of metastasis has been found. Seven cases were composed predominantly or entirely of clear cells, usually with minimal cellular atypia and variable mitotic activity; however, in all cases there was evidence of tumor infiltration into adjacent tissues, including the presence of perineural invasion in two tumors. Those cases in which no reference was made to the presence of clear cells exhibited evident mitotic activity and cellular pleomorphism. The epithelium in OCD does not produce buds or enamel organ-like structures such as those found in ameloblastic fibro-dentinoma and this tumor does not contain a mesenchyme-like connective tissue resembling dental papilla as observed in several mixed odontogenic tumors. Based on the existing data and the present series of cases, OCD appears to represent a distinct entity.

Keywords Carcinoma · Dentinoid · Jaw neoplasms · Odontogenic tumors

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Introduction

Dentinoid was defined by Gardner and Farquhar as a collagenous tissue, generally non-mineralized, which resembles dentin, but which neither contains tubules nor fulfils the criteria for atubular dentin, and which is located in a close anatomical relationship to odontogenic epithelium [1]. It may or may not exhibit cellular inclusions. It is frequently recognized as a component of a number of benign odontogenic tumors, especially complex odontoma, dentinogenic ghost cell tumor and ameloblastic fibrodentinoma, but it may also be found in some cases of adenomatoid odontogenic tumor (AOT), calcifying cystic odontogenic tumor (CCOT) and ameloblastic fibro-odontoma [2]. The recognition of most of these entities is based on specific cellular and histomorphological features, and

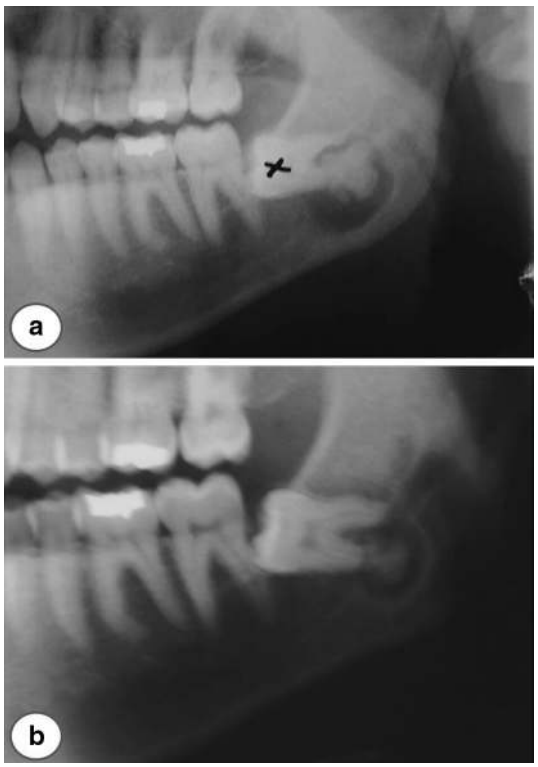

Fig. 1 Case 1. **a** A circumscribed radiolucency with central radiopacity is associated with the roots of the impacted left mandibular third molar. **b** A panoramic radiograph taken 4 years earlier showed the presence of a slightly smaller and less calcified lesion

some do not require the presence of dentinoid to establish their diagnosis. There are, however, some very rare dentinoid-producing odontogenic tumors, with microscopic features that are not recognized in the current W.H.O. Histological Classification of Tumors [2]. Among these unusual lesions are the so-called "dentinoma" (immature and mature types) [3–7], "dentinoameloblastoma" [8], "adenoid ameloblastoma with dentinoid" [9–12], "adenomatoid dentinoma" [13, 14], and the very rare examples of "odontogenic carcinomas with dentinoid" [11, 15–19].

The purpose of this study is to describe and characterize the clinical and histopathologic features of three cases of odontogenic carcinoma with dentinoid induction, and to review and compare them with the previously reported cases of malignant dentinoid-producing epithelial odontogenic tumors and the currently recognized subtypes of odontogenic carcinomas.

Case Reports

Case 1

A 34-year-old man presented with a chief complaint of mild pain in the left posterior mandible. A panoramic radiograph revealed a 2 × 2 cm circumscribed radiolucency with central calcification at the apex of the impacted third molar (Fig. 1a). Evaluation of a previous radiograph taken 4 years earlier showed the presence of a similar smaller lesion at this same site (Fig. 1b). In both films, the radiopaque component appeared to be attached to the mesial root apex, which showed evidence of resorption. The tooth and the attached mass were removed and submitted with a provisional clinical diagnosis of cementoblastoma. At the time of surgery, the growth had perforated the mandibular buccal cortex at the inferior aspect of the lesion.

Microscopic examination showed a mass of acellular, eosinophilic dentinoid product, which was attached to the tooth roots (Fig. 2a). This dentinoid material surrounded narrow cords and sheets of ovoid to polygonal epithelial cells (Fig. 2b). These cells demonstrated fairly uniform, vesicular nuclei, although occasional mitotic figures could be identified (Fig. 2c). In some areas, these cells had a clear cytoplasm, whereas other areas demonstrated a vague squamoid appearance (Fig. 2d). In focal areas, the cords of cells exhibited eosinophilic cytoplasm. The epithelial cells were positive for pancytokeratin (AE1/AE3). A final diagnosis of "epithelial odontogenic tumor with prominent dentinoid production" was made, including a comment that the biologic behavior of this lesion was uncertain.

Three and one-half years later, recurrence of the lesion was noted. Radiographic examination at that time revealed an irregular, destructive radiolucent mass, measuring approximately 3.5 cm in greatest dimension, in the left mandibular ramus. A mandibular resection was performed in combination with a lymph node dissection of the left neck. Microscopic examination of the recurrent tumor revealed sheets of polygonal cells with relatively uniform vesicular nuclei, although these cells appeared slightly more pleomorphic than those seen in the previous specimen. The tumor cells often demonstrated a clear cytoplasm, and occasional mitotic figures could be identified (Fig. 3a). Focal deposits of an eosinophilic dentinoid product were present, some of which were surrounded by columnar cells with evidence of palisading (Fig. 3b). In one area, the tumor consisted of larger cells with eosinophilic cytoplasm and squamoid features (Fig. 3c). These cells were somewhat reminiscent of the pattern found in a calcifying epithelial odontogenic tumor, but no amyloid could be identified with Congo red staining. One area of the lesion showed destruction of cortical bone with perineural and intraneural invasion by tumor cells, which demonstrated some peripheral palisading and central looser cells reminiscent of stellate reticulum (Fig. 3d). A total of 29 lymph nodes were examined, all of which were negative for metastatic tumor. A final diagnosis of "odontogenic carcinoma with dentinoid production" was made.

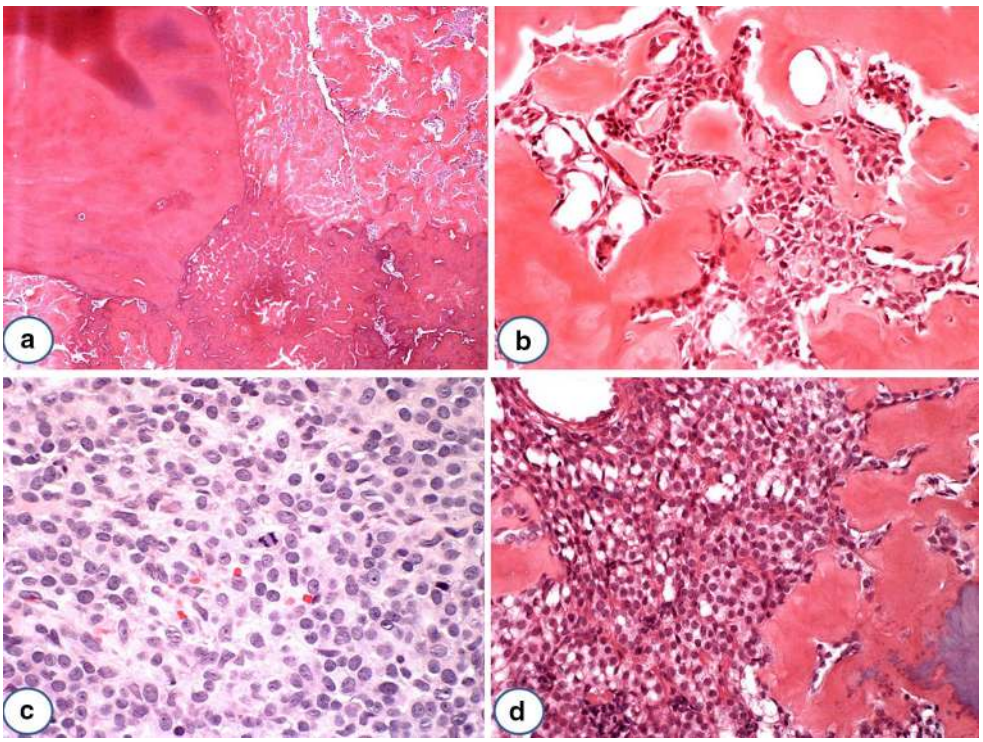

Fig. 2 **a** Case 1. Low-power view showing the tooth root (*left*) with attached eosinophilic dentinoid material. **b** Medium-power view showing deposits of dentinoid product associated with sheets of ovoid and polygonal tumor cells. **c** The tumor cells exhibit relatively uniform, vesicular nuclei with occasional mitotic figures (*center*). **d** In this field, the tumor cells exhibit a clear cytoplasm and adjacent dentinoid material (*right*)

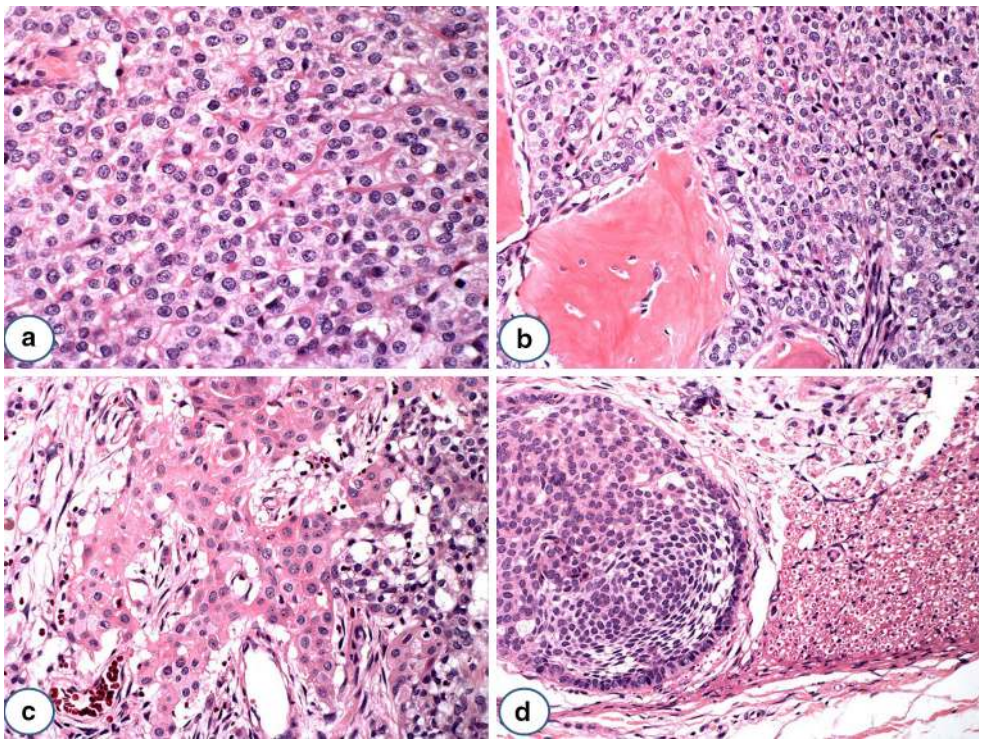

Fig. 3 Case 1. **a** Sheets of ovoid to polygonal cells with clear cytoplasm. **b** The tumor cells are focally associated with a dentinoid product (*lower left*). Note the palisaded arrangement of columnar cells adjacent to the dentinoid material. **c** Focal collection of eosinophilic squamoid cells, reminiscent of calcifying epithelial odontogenic tumor. **d** An island of tumor cells with some peripheral palisading and central looser cells reminiscent of stellate reticulum is seen invading a large nerve bundle, located on the *right side*

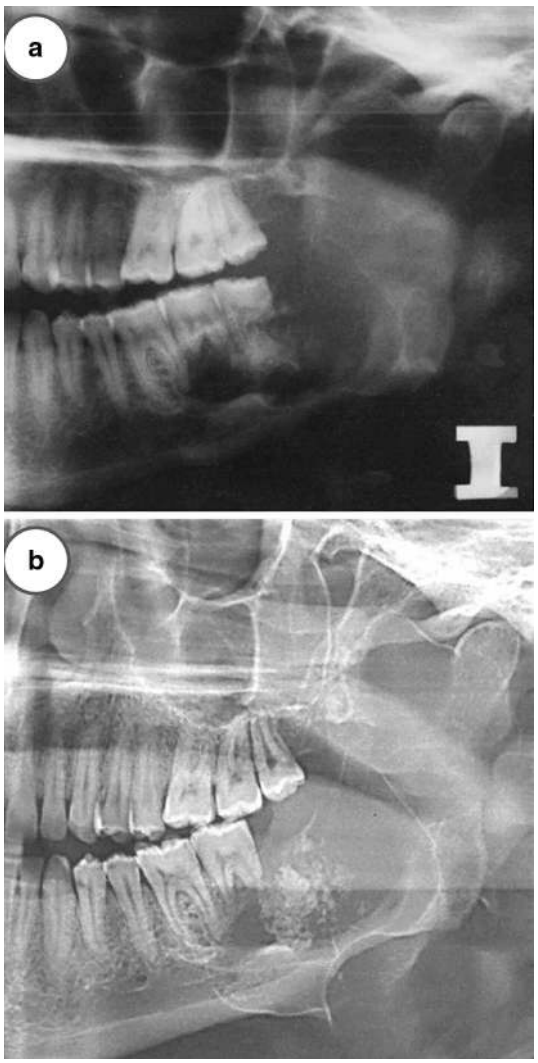

Fig. 4 Case 2. **a** A well-defined, multilocular radiolucency with a central focus of radiopacity extending from the *left lower* first molar up to the midportion of ascending ramus. Note root resorption of second and third molars. **b** A panoramic radiograph taken 3 months later demonstrates an increase in size with marked buccal expansion

Case 2

A 31-year-old man presented with a slightly-tender, gradually increasing tumoral mass in the posterior region of the left mandible, which had been clinically evident for the last 5 months. The patient denied a history of previous trauma, surgery or infections in that area. Clinical examination revealed a significant bony expansion of the left ramus that produced marked extraoral asymmetry. Three months before admission a panoramic radiograph had been taken because of the asymmetry, which showed a complete dentition and a large, well-defined multilocular radiolucency with a sclerotic margin and some radiopaque foci scattered in the lower and central areas of the lesion. The radiolucent component extended from the mesial aspect of the first molar up to the midportion of the ascending ramus and produced marked root resorption of second and third molars (Fig. 4a). The third molar was extracted because of mobility. A new radiograph revealed an increase in the size of the lesion, with marked buccal expansion (Fig. 4b). The lesion was aspirated but no fluid was obtained, and an incisional biopsy was interpreted as "dentinoid-producing odontogenic tumor of uncertain behavior". The patient was admitted soon afterwards and underwent surgical segmental resection of the lesion. Macroscopically, the tumor was predominantly solid, with occasional cystic areas. The lesion appeared well-defined but not encapsulated, and it was surrounded by normal-appearing bone. The patient was followed for 24 months with no signs of recurrence.

Microscopically, the lesion was composed of sheets and strands of round to ovoid epithelial cells surrounding masses of dentinoid (Fig. 5a). These cells exhibited scant pale eosinophilic to clear cytoplasm, minimal nuclear pleomorphism, occasional mitoses, and in some areas there were small droplets of eosinophilic intercellular substance (Fig. 5b). Although there were circular holes or microcysts, no true duct-like spaces could be found within the epithelial sheets. The eosinophilic masses of dentinoid had occasional cell inclusions (Fig. 5c), and irregular tubules were identified in some areas (Fig. 5d). In addition, some of these dentinoid masses showed evidence of globular foci of mineralization. The periphery of the tumor was composed of extensive areas of mature and myxoid fibrous connective tissue stroma, which was in direct continuity with adjacent cancellous bone with no evidence of capsule formation. These findings were consistent with the diagnosis of "odontogenic carcinoma with dentinoid".

Immunoreactions in this case showed that the tumor mesenchymal cells were strongly positive for vimentin and focally positive for alpha smooth muscle actin in the more cellular regions. Desmin, S-100 protein, and CD34 were negative. Ki-67 expression was low (<2 %) and the epithelial component was strongly positive for pan-cytokeratins (AE1/AE3) and cytokeratins 8, 14, and 19.

Case 3

A 32-year-old woman visited her dentist with a chief complaint of an uncomfortable feeling in the right upper premolar region, which had been present for 6 months. The patient was referred to Kochi Health Sciences Center for further examination and treatment of the lesion.

Clinical examination revealed bone expansion in the right maxillary premolar region, with mobility of the first and second premolars (Fig. 6a). Panoramic and periapical radiographs showed a relatively well-demarcated radiolucent lesion at the apical area of the 1st and 2nd premolars.

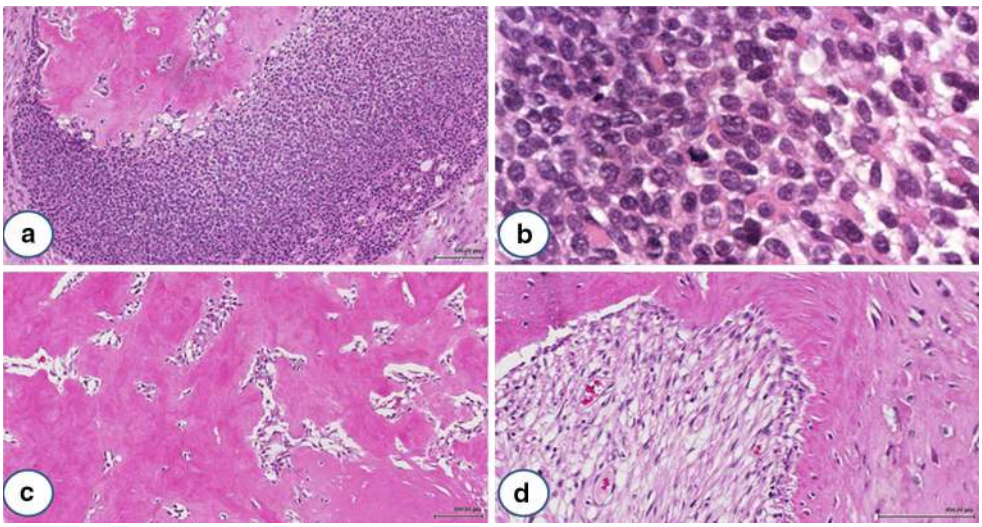

Fig. 5 Case 2. **a** Dentinoid associated with sheets of ovoid and polygonal tumor cells. **b** Higher power view of the tumor cells, which exhibit discrete pleomorphism and some mitotic figures (*center*). **c** The eosinophilic masses of dentinoid had occasional nests of tumor cell included. **d** Irregular tubules were identified in some areas at the periphery of the dentinoid material

The roots of the premolars were resorbed by the lesion, which also extended into the floor of the maxillary sinus (Fig. 6b). CT examination revealed destruction of the buccal cortical bone, palatal plate, and floor of the maxillary sinus (Fig. 6c). Highly calcified tissue was noted in the lesion on the CT study. PET-CT showed accumulation of fluorodeoxyglucose (FDG) in the lesion (Fig. 6d).

Under the clinical diagnosis of a maxillary tumor, a biopsy was performed. Tumor cells with clear cytoplasm proliferated in solid nests or in a trabecular fashion (Fig. 7a). There was no prominent cellular atypia (Fig. 7b). In the tumor tissue, a large amount of eosinophilic dentinoid or osteodentin matrix-like tissue with calcification was observed (Fig. 7c). Tumor cells were scattered in the dentinoid matrix individually or in a small nest-like fashion. The tumor cells showed relatively high p53 immunoreactivity (42 %) and Ki-67 was expressed in <5 %, but the positive rates were not considered high enough to indicate its frank malignancy; however, based on both the clinical and pathological features, a diagnosis of odontogenic carcinoma with dentinoid formation was favored. With the diagnosis of a low-grade malignancy, a partial maxillectomy was done. The surgical specimen showed cortical bone destruction on the buccal, palatal and antral sides of the tumor, with protrusion of the tumor into the maxillary sinus. Microscopic examination confirmed destruction of the cortical alveolar bone and the floor of maxillary sinus. Tumor tissue also destroyed the alveolar bone proper and invaded into the periodontal ligament space. Invasion into the antral mucosa was also observed. Furthermore, perinural invasion was seen in one place (Fig. 7d).

The tumor tissues could be characterized by two patterns. One part consisted of a solid proliferation of tumor cells, whereas other areas showed production of eosinophilic dentinoid or osteodentin-like matrix. The solid tumor zones were composed of clear cells arranged in strands or solid tumor nests. The surgical material contained solid proliferations of basaloid cells as well (Fig. 8). In the other areas, abundant eosinophilic dentinoid or osteodentin-like matrix was formed, which also included strands and small nests of tumor cells. Based on the findings of the surgical specimen, a diagnosis of odontogenic carcinoma with dentinoid formation was made.

Discussion

The presence of dentinoid has been identified as an integral part of some odontogenic tumors. Malignant odontogenic tumors include nine types of carcinomas and two variants of sarcomas. Excluding the dentinogenic ghost cell carcinoma and the odontogenic fibrodentino- and fibro-odontosarcomas, the W.H.O. Histological Classification of Tumors [2] does not recognize other malignant odontogenic neoplasms that may produce this extracellular substance.

According to our review of the literature and the present series, there are nine cases with histopathological criteria that could be considered as odontogenic carcinomas with dentinoid (OCD), whose clinical and microscopic features are summarized in Tables 1 and 2. Six cases occurred in the mandible and three in the maxilla. All developed behind the canines, five affecting the premolar region and four located

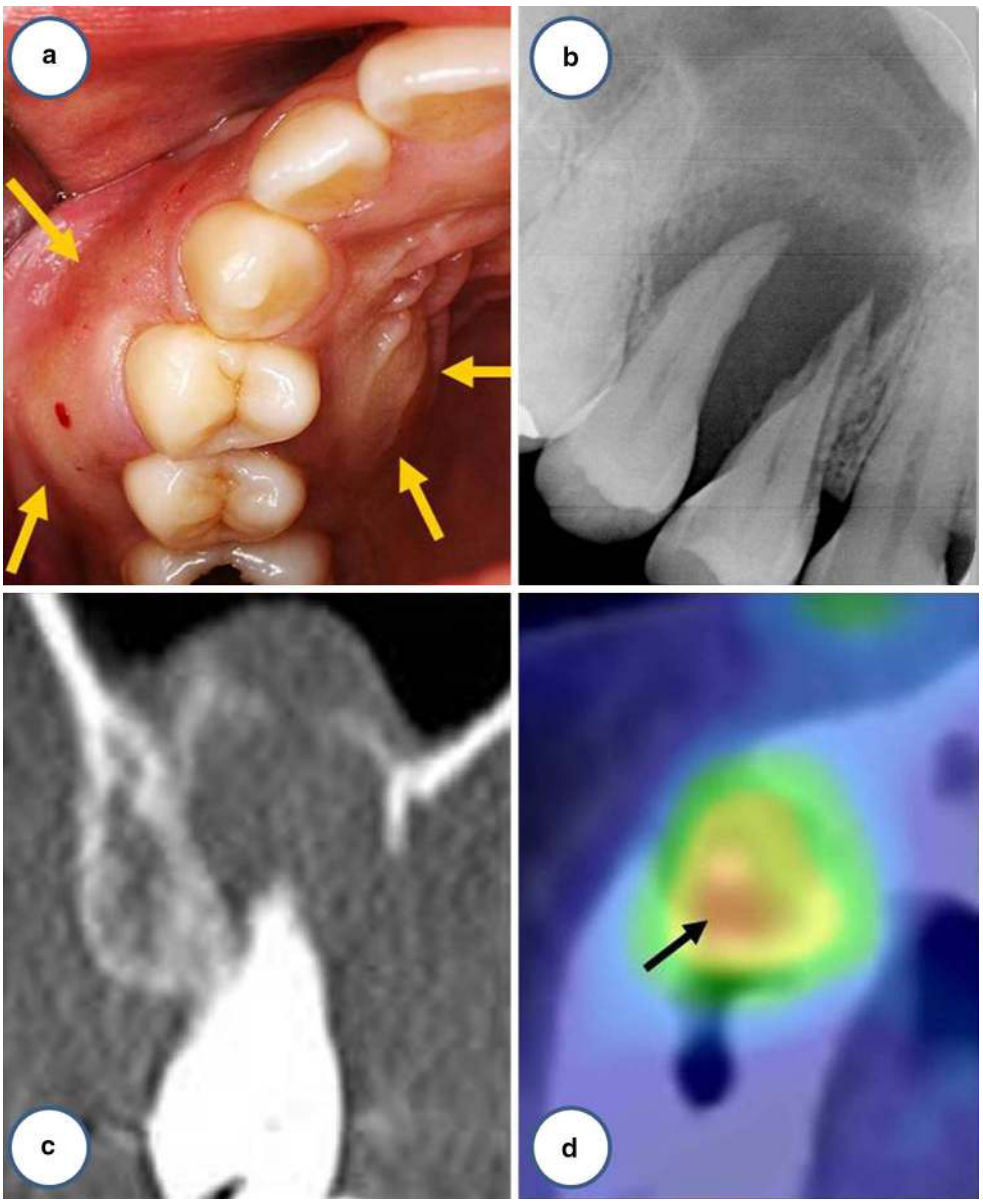

Fig. 6 Case 3. **a** Buccal and palatal expansion in the right premolar region. **b** Relatively well-demarcated radiolucent lesion at the apical area of the 1st and 2nd premolars. Roots of the premolars are resorbed by the lesion. The floor of the maxillary sinus is invaded by the tumor. **c** CT revealed destruction of the buccal cortical bone, palatal plate, and floor of the maxillary sinus. **d** PET-CT showed accumulation of fluorodeoxyglucose (FDG) at the lesion

in the molar area, with two of them extending into the ascending ramus of the mandible. No sex predilection was found, as there were five men and four women, whose ages ranged from 14 to 61 years (mean 38.1). The most frequent clinical complaint was swelling, which was recorded in eight cases. Pain or uncomfortable feeling was mentioned in five cases, four of which showed tooth resorption. Information on how long the lesions had been clinically or radiographically evident was known in 8 cases, which ranged from 2 to 50 months (mean 15 months).

All cases appeared initially as well-defined radiolucencies, five of which contained variable amounts of calcified material, either in the form of small patchy areas or as more defined larger radiopaque foci. Two lesions were described as multilocular. Presumptive clinical diagnoses included: dentigerous cyst, ameloblastoma, cementoblastoma and benign tumor or cyst, but no preoperative diagnosis was mentioned in three cases. Recurrences were recorded in three instances, but after wide excision there was no evidence of disease in any of them. Cervical lymph node

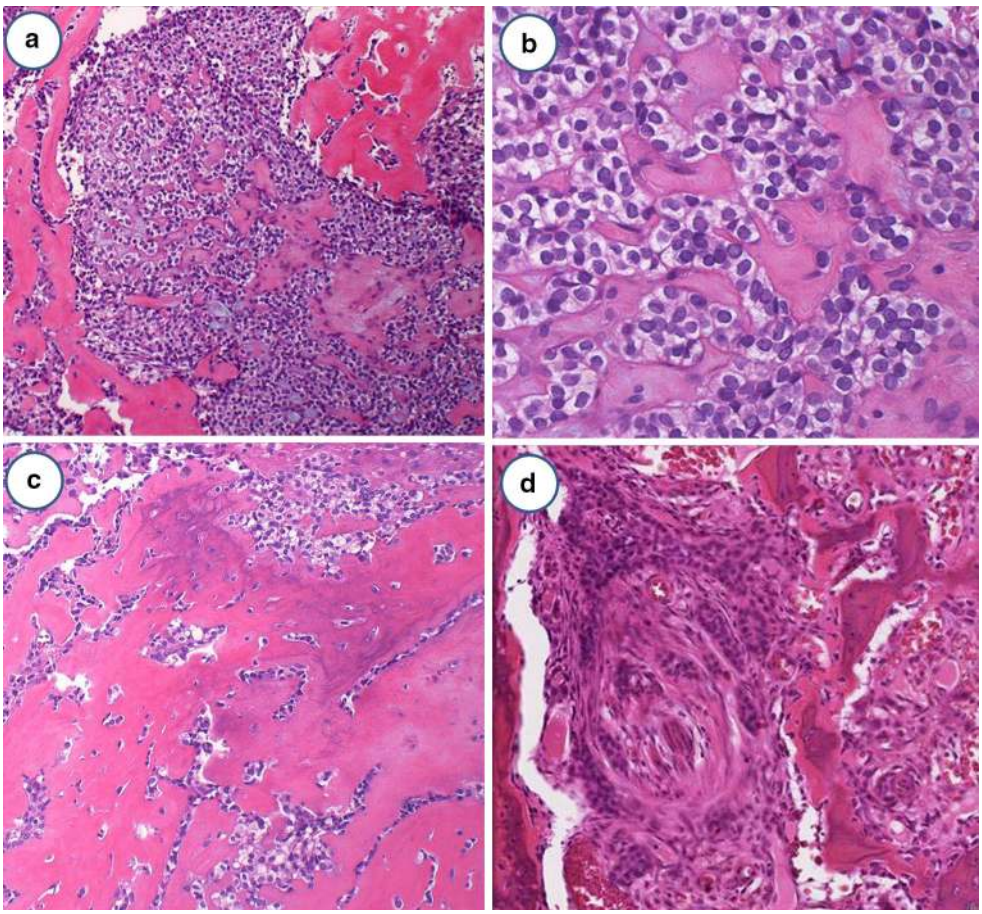

Fig. 7 Case 3. Biopsy specimen. **a** Tumor cells with clear cytoplasm proliferate in solid nests or in a trabecular fashion. **b** Tumor cells show no prominent cellular atypia. **c** A massive amount of eosinophilic dentinoid or osteodentin matrix-like tissue with calcification is observed in the tumor. **d** Perineural invasion of tumor cells

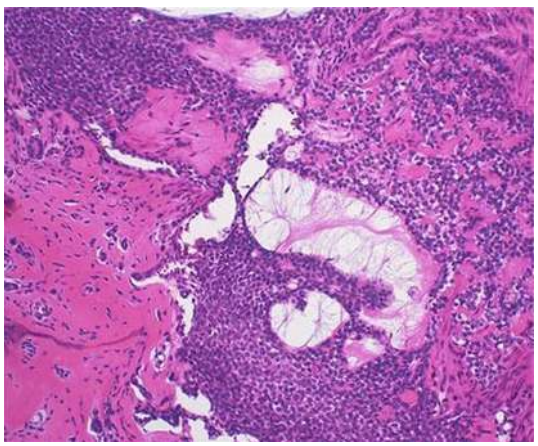

Fig. 8 Case 3. Area of tumor composed of solid proliferations of clear and basaloid cells. Eosinophilic dentinoid or osteodentin-like matrix is formed in the tumor

dissection was performed in two cases, with no evidence of metastasis.

With respect to the histopathological findings, seven cases were composed predominantly or entirely of clear cells. One case also exhibited clusters of ghost cells interspersed among the clear cell component, which exhibited frequent mitotic figures and mild cellular and nuclear atypia [18]. However, the authors discarded the possibility of a dentinogenic ghost cell carcinoma because no epithelial lining compatible with CCOT was found and because there are no reported cases of this tumor with a clear cell component.

The other clear cell examples showed minimal cellular atypia and variable mitotic activity; however, in all cases there was evidence of tumor infiltration into adjacent tissues, including the presence of perineural invasion in two tumors. These findings, in spite of the

Table 1 Main clinical features of cases reported as odontogenic carcinoma with "dentinoid" or "inductive dentin formation"

References	Age (years)	Sex	Location	Unerupted teeth	Clinical findings and presumptive diagnosis	Radiographic findings	Treatment	Recurrences	Follow-up and outcome
Sawyer et al. [15]	14	M	Right maxilla (molar region)	Third molar	Swelling and pain. Clinically evident 3 months. Odontogenic cyst	WD, RL with patchy areas of radiopacity	Enucleation (1) Marginal resection (2)	One (at 1 year)	18 months NED
Miyauchi et al. [16]	56	F	Left mandible (premolar-molar region)	None	Painless swelling. Clinically evident 2 years	WD, RL with scalloped margin	Surgical resection	No	Monthly (time NS) NED
Kumamoto et al. [17]	61	M	Left mandible (premolar-molar region)	None	Painless swelling. Evolution time NS. Ameloblastoma	WD, ML, RL. CT shows irregular margins	Tumor excision with extraction of six teeth and curettage	No	11 months NED
Ariyoshi et al. [18]	50	M	Left mandible (molar region And ramus)	None	Painless swelling. Clinically evident 2 months. Benign tumor or cyst	WD, UL, RL without sclerotic margin	Enucleation (1) Segmental resection (2)	One (at 4 months)	NS
Punnya et al. [19]	18	F	Right maxilla (premolar region)	None	Painful swelling. Clinically evident 6 months. Odontogenic cyst	WD, RL with small radiopaque foci and root resorption	Enucleation	No	16 months NED
Ide et al. [11]	47	F	Left mandible (premolar-molar region)	None	2-cm mass on lingual gingival. Clinically evident 2 years	WD, UL, RL with sclerotic inferior border	Resection with cervical lymph node dissection	No	6 years NED
Present case 1	34	M	Left mandible (third molar and Ramus)	Third molar	Mild pain in the left posterior mandible	WD, RL with central radiopacity at the apex of impacted third molar	Tumor excision with extraction of third molar	One (at 3 and a half years)	LFU
Present case 2	31	M	Left mandible (molar region and ramus)	None	Slightly tender, slowly growing tumor. Clinically evident 5 months. Benign odontogenic tumor	WD, ML, RL with large radiopaque foci	Segmental resection	No	2 years NED
Present case 3	32	F	Right maxilla (premolar region)	None	2 × 1.5-cm mass clinically evident for 6 months. Looseness of first and second premolars	WD, UL, RL with small radiopaque foci noted on CT	Partial maxillectomy	No	3 years NED

WD well-defined, *RL* radiolucent, *ML* multilocular, *UL* unilocular, *NED* no evidence of disease, *NS* not specified, *LFU* lost to follow-up

lack of metastasis, suggest that these cases may possess at least low-grade malignant potential [17]. In the cases reported by Sawyer et al. [15] and Punnya et al. [19], no reference was made to the presence of clear cells, and it is interesting to note that both cases exhibited high or evident mitotic activity and cellular pleomorphism.

Many malignant odontogenic tumors are considered the counterparts of benign odontogenic tumors, and some may derive from previously benign, usually long-lasting or

Table 2 Salient histopathological findings of cases reported as odontogenic carcinoma with "dentinoid" or "inductive dentin formation"

References	General arrangement	Epithelial components	Mesenchymal soft tissue components	Dentinoid material
Sawyer et al. [15]	Thick-walled cystic lesion. Cyst lumen was a third of the size of the lesion. Neoplastic mass lined the cavity. Recurrent lesion solid.	Odontogenic epithelium with tall columnar cells at the periphery and some evidence of palisading. Pleomorphism and high mitotic index. No clear cells described	Thick fibrous connective tissue wall	Closely associated with the epithelial cells. Few cells trapped in this collagenous matrix (dentinoid). Ill-formed tubules were observed
Miyauchi et al. [16]	Solid mass	Sheets and nests separated by thin mature fibrous septae. Two cell types: large clear oval and eosinophilic polygonal. Mitotic figures evident but cellular and nuclear atypism not prominent. Tumor nests invading adjacent muscle	Mature fibrous connective tissue stroma	Eosinophilic fibrillar dentin-like structures (dentinoid) between epithelial nests and stromal connective tissue
Kumamoto et al. [17]	Non-encapsulated tumor mass	Proliferative nests of odontogenic epithelium composed by large clear vacuolated cells and small eosinophilic basaloid cells. Some nests with peripheral columnar cells with nuclear palisading. No atypia and few or no mitoses. Occasional cysts within the tumor. Duct-like structures with eosinophilic deposits. Tumor infiltrates adjacent muscle	Scant cellular fibrous connective tissue stroma	Eosinophilic dentin-like structures containing numerous cells without a tubular pattern, closely adjacent to and entrapping small tumor cell nests
Ariyoshi et al. [18]	Tumor mass (on first enucleation). Non encapsulated cystic mass (on resected specimen)	Sheets and small islands of clear cells admixed with hyaline deposits and separated by thin fibrous stroma. Some nests infiltrating adjacent tissues. Frequent mitosis and mild atypia. Clusters of "ghost cells" among clear cells	Fibrous connective tissue stroma	Hyaline material reminiscent of dysplastic dentin in direct contact with the tumor cells. Irregular dentinal tubules were observed
Punnya et al. [19]	Ovoid mass filled with granular material of sandy consistency	Sheets of pleomorphic round to ovoid cells with vesicular and hyperchromatic nuclei and minimal cytoplasm. Several mitotic figures also evident. Tumor cells invading the surrounding fibrous capsule. No cyst lining	Mature fibrous connective tissue capsule	Multiple eosinophilic masses with occasional cell inclusions adjacent to and within sheets of tumor cells. Globular type of mineralization was seen in some of these structures
Ide et al. [11]	Solid mass	Islands of large clear and small round Cells and double stranded cords of basaloid cells diffusely infiltrating the cancellous bone. Minimal pleomorphism and scant mitosis. Focal duct-like spaces and fusion with gingival epithelium	Not described	Juxtaepithelial mass of dentinoid in the deeper portion of the tumor
Present case 1	Unencapsulated, solid mass	Sheets of ovoid to polygonal cells; scant eosinophilic to clear cytoplasm; minimal pleomorphism; occasional mitoses; focal columnar cells bordering dentinoid product; focal eosinophilic squamoid cells; neural invasion	Scant connective tissue stroma	Amorphous eosinophilic dentinoid product attached to the tooth root; Occasional tumor cells entrapped within the dentinoid

Table 2 continued

References	General arrangement	Epithelial components	Mesenchymal soft tissue components	Dentinoid material
Present case 2	Unencapsulated and macroscopically ill-defined, partly cystic tumoral mass	Sheets and strands of round to ovoid cells with minimal pleomorphism, scant pale eosinophilic to clear cytoplasm. Occasional mitoses. Some eosinophillic intercellular substance and occasional cyst-like spaces. Tumor cells invading surrounding tissues	Extensive fibrous and slightly myxoid connective tissue stroma. No capsule	Large eosinophilic masses with occasional cell inclusions adjacent to and within sheets of tumor cells. Irregular dentinal tubules in some areas
Present case 3	Unencapsulated solid mass with cortical bone destruction	Strands and solid proliferation of clear and basaloid cells admixed with eosinophilic hyaline materials. Invasion into adjacent tissues and periphery of nerve fiber. Cellular atypia and mitosis not prominent, but p53 overexpression	Mature fibrous connective tissue. No capsule	Eosinophilic hyaline materials with calcification containing strands and small nests of tumor cells

recurrent lesions (e.g. ameloblastic carcinoma, ameloblastic fibrosarcoma) [2]. The existence of some very rare, locally aggressive epithelial tumors that induce the production of dentinoid in a mature or slightly myxoid connective tissue stroma, different from ameloblastic fibrodentinoma, would open the possibility of considering them as potential sources or examples of OCD, in a similar way that CCOC was once considered a clear cell variant of ameloblastoma [20] or as a benign neoplasm called "clear cell odontogenic tumor" [21, 22]. On one hand are those lesions designated as "dentinomas", whose existence dates back to the 1930s. However, it is questionable whether all such reported cases represent a single diagnostic entity, since some examples showed the presence of enamel, enamel organ-like structures of the epithelial component or loose connective tissue resembling the dental papilla, and may, therefore, be better classified as ameloblastic fibrodentinoma or related tumors [3–7]. However, the case reported by Takeda [6] as "immature dentinoma" describes an encapsulated tumor that acted in a benign fashion, although it showed a very similar appearance to our OCD cases, as it was composed of masses of dentinoid intermixed with epithelium (part of which had clear cytoplasm and there was no histodifferentiation toward an enamel organ-like structure). In addition, there are other apparently benign entities that are characterized by variable amounts of dentinoid production associated with an epithelial proliferation suggestive either of ameloblastoma ("dentinoameloblastoma"), AOT ("adenomatoid dentinoma"), or both ameloblastoma and AOT ("adenoid ameloblastoma with dentinoid") [8–14], which need to be included in the differential diagnosis of OCD.

We suggest that OCD may present a spectrum of histopathological features composed predominantly of clear cells with variable amounts of small round to basaloid cells with more accentuated pleomorphism. In some cases, there may be duct-like or pseudocystic structures, peripheral columnar cells with evidence of palisading and, as described in one case above, scattered ghost cells. The common feature of this tumor is the induction by these epithelial cells of production of variable amounts of dentinoid in a mature fibrous connective stroma. Unlike the currently defined odontogenic tumors, the epithelium in these cases may be relatively undifferentiated or it may exhibit some ameloblastic-type of differentiation in a few cases, although it does not produce buds or enamel organ-like structures such as those found in ameloblastic fibrodentinoma. In addition, these tumors do not contain a mesenchyme-like connective tissue resembling dental papilla as observed in several mixed odontogenic tumors. As clear cells may appear in diverse primary and metastatic tumors in the jaws, including those from squamous epithelium, salivary glands, renal epithelium, cutaneous adnexa, odontogenic epithelium, melanocytes and some types of mesenchymal tissues, it is necessary to rule out these origins, particularly on incisional biopsy specimens, which may not contain dentinoid material.

Based on the existing data and the present series of cases, OCD seems to represent a distinct entity. According to the classification of odontogenic carcinomas included in the current W.H.O. Classification of Tumors [2], this neoplasm and the ghost cell carcinoma may be considered a particular subgroup of odontogenic carcinomas in which dentinoid is a prominent feature. Although the described

cases have presented a wide variability regarding cytological evidence of malignancy, all examples have demonstrated an aggressive behavior and absence of encapsulation, and some have shown infiltration into the surrounding tissues and even perineural invasion, which suggests that such tumors have at least the potential of being low-grade malignancies; however, because no cases of metastasis have been reported thus far, there is some uncertainty regarding the most appropriate classification of this unusual lesion.

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Conflict of interest None.

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