
Cheriyanthalth Sisupalan Jayapalan, Anthony George*, Ahammed Noufal, Meera Kunjumon Pynadath and Ummar Mangalath

Department of Oral Pathology and Microbiology, MES Dental College, Perinthalmanna, India

*Corresponding author: Anthony George, Department of Oral Pathology and Microbiology, MES Dental College, Perinthalmanna, India, E-mail: drantgeo@gmail.com

Received date: October 27, 2016; Accepted date: November 23, 2016; Published date: November 29, 2016

Abstract

A 17-year girl reported with painful right lower posterior teeth. Orthopantomogram showed unilocular radiolucency with scalloped non-sclerotic border at apical area of non-caries right mandibular molars and premolar. A provisional radiological diagnosis of ameloblastoma or odontogenic keratocyst was given. Histopathological examination revealed follicular areas of peripheral palisaded hyperchromatic basaloid cells and central round-polygonal clear cells. A diagnosis of clear cell odontogenic carcinoma (CCOC)-ameloblastomatous variant was made after assessing the provisional diagnoses. A nosological dilemma arose as many authors opined that the terms ‘clear cell ameloblastoma’ and ‘clear cell odontogenic tumor’ should be invalidated and CCOC should be the preferred diagnosis because of the reported aggressive nature of clear cell odontogenic neoplasms. The scientific literature gave variable biological behavior and prognosis with diverse therapeutic approaches leading to therapeutic dilemma in management of the case. The authors have attempted to resolve the diagnostic and therapeutic challenges by presenting the clinical, radiological and histological aspects of the case and discussing the differential diagnoses of clear cell lesions involving the maxillofacial region along with the therapeutic approaches and prognosis of CCOC.

Keywords: Clear cell; Odontogenic; Carcinoma; Tumor; Ameloblastoma; Metastatic; Salivary gland; CCOC, CCOT

Case

A 17-year girl reported to the Department of Oral Medicine and Radiology with dull aching right lower posterior teeth since 1 month. Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.

Routine intraoral examination revealed a good oral hygiene with no carious, missing, filled, or mobile teeth. Vertical percussion of FDI tooth number 45, 46 and 47 elicited a painful response. Palpation of the associated cortical area revealed a firm symptomatic bony buccal expansion, without ulceration, paresthesia or discoloration of the overlying mucosa. She had no known systemic disease, was not on any medications, and gave no history of trauma.
features as of incisional biopsy (Figure 3). Nuclear pleomorphism was scanty and mitotic activity was absent or <1 mitosis per high-power field. Focal areas of the associated stroma showed animal-like arrangement of compressed darkly staining odontogenic epithelium with the adjoining fibrovascular connective tissue showing hyalinization, desmoplasia, and increased vascularity (Figure 4). The resected bony margins and soft tissue appeared to be free from the lesional tissue, and hence the patient was not referred for adjuvant radiotherapy or chemotherapy. The tissue sections stained negative for periodic acid-Schiff (PAS), Congo-red, mucicarmine, and human melanoma antigen (HMB-45); indicating negativity for glycogen, amyloid, mucin, and melanocyte. The case is under quarterly follow-up and has been disease-free over 1.4 years.

Discussion

A literature review showed that the most common age of clinical presentation of CCOC were 53-56 yr. (17-89 yr.), with female predilection (1.8:1), and the mandible (62.5%) being more commonly involved than the maxilla, with preponderance for the posterior segment [1-11]. Some early reviews found preponderance for the anterior segment of the jaws [10]. The most commonly reported clinical symptoms were pain, localized jaw enlargement, and mobility of the involved teeth [5-7]. Most of the cases reported as painless slow growing swelling of several months or years [6]. Bleeding, paresthesia of lower lip, trismus, proptosis, and non-healing ulcer were rare complaints [6,7]. Radiographically CCOC are not distinguishable from other osteolytic lesions of the jaws. They appeared as non-specific radiolucent lesions with irregular margins, often associated with root resorption and cortical bone perforation, and not associated with unerupted teeth [1,5-7]. Histopathologically the CCOC is composed
predominantly of sheets, solid islands, nests or trabeculae of round-polygonal cells with cytoplasmic clearing, separated by hyalinized fibrous septa, and often admixed with basoaid-polygonal cells having granular eosinophilic cytoplasm [4]. Three histopathological patterns or variants have been described based on the relative proportions of these cells: (1) Monophasic – islands and nests of monomorphic clear cells with well-defined cell membrane and centrally placed round nucleus; (2) Biphasic – characterized by oval and linear nests of clear cells intermixed with islands of smaller hyper-chromic polygonal-basaloid cells with scanty eosinophilic granular cytoplasm and well-defined cell membrane. Sometimes the eosinophilic polygonal cells are arranged in double layers centrally within the clear cell cluster and appeared as duct-like structures (gland-like pseudolumina), indicating their odontogenic origin; (3) Ameloblastomatous – characterized by islands of clear cells having peripheral layer of ameloblastoid palisaded hyperchromatic cuboidal cells [1-6]. A systematic review of 67 cases by Loyaola AM, et al. in 2015 reported that 79.2% demonstrated biphasic pattern, 16.9% ameloblastomatous pattern, and 3.9% monophasic pattern [7]. Mild-moderate pleomorphism, anacrotosis, anisokaryosis; gland-like pseudolumina and squamous metaplasia were observed in most cases [4,6]. Abnormal mitotic figures, necrosis, neural/vascular invasion, keratin pearl, hemorrhage, increased vascularity, and osteodentin deposition were rare [6]. Occasionally mild-moderate chronic inflammatory infiltrate of lymphocyte and plasma cells with or without giant cells were identified [6]. Rarely regional metastasis (19%) to level IB (submandibular) lymph nodes and distant metastasis (11.9%) to the lungs has been reported [6,7]. Without giant cells were polygonal cells with cytoplasmic clearing, separated by hyalinized granular eosinophilic cytoplasm [4]. Usually were PAS positive and diastase sensitive (indicating glycogen), stained negatively for Congo-red (amyloid) and mucicarmine. Positivity for cytokeratins (CK) 8, 13, 14, 18, 19, AE1/AE3, epithelial membrane antigen (EMA), S-100, p53, p16, antiameloblastoma antigen, vimentin and collagen type IV has been reported, while some published cases found that 17 (29%) cases that were primarily diagnosed as ameloblastoma were later classified as CCOC [11]. Most authors believe that immunohistochemical evaluation is a reliable diagnostic criterion to distinguish the two [4,10]. Recent molecular studies have reported that both HCCC and CCOC have EWSR1 rearrangement and 83% of CCOC had EWSR1 rearrangement [14]. Balanced translocations has been observed in approximately one-third of the sarcomas and EWSR1-ATF1 translocation in CCOC could signal the aggressiveness of this lesion [14]. Primary intra-osseous localization, absence of any salivary gland tissue, and desmosplastic ameloblastoma-like areas helped differentiate our case from HCCC. The intra-osseous CCMEC is very rare and the triphasic architecture of mucous, epidermoid and intermediate cells along with...
clear cells gave these lesions a distinctive histopathological appearance [5]. Lack of cystic spaces lined by mucous cells, absence of intermediate cells, squamous differentiation, and mucin (as indicated by mucicarmine negativity) helped exclude CCMEC from our diagnosis. Other rarer salivary gland neoplasms with clear cell histopathological appearance include the clear cell myoepithelial carcinoma, clear cell oncocytoma, and clear cell acinic cell carcinoma [4]. These tumors have distinct morphological, histopathological and immunophenotypic appearances that help pathologists to distinguish them from CCOC [4,5].

The other consideration in our differential diagnoses was to exclude the possibility of metastatic lesions such as renal cell carcinoma, thyroid carcinoma, and clear cell breast carcinoma. Our case had no clinical signs or symptoms of renal, thyroid or breast carcinoma and was negative for any pathology under ultra-sound evaluation of these organs. Lack of prominent intra-tumoral hemorrhage, sinusoidal vascularity, and other histopathological features that characterize these metastatic carcinomas helped in excluding metastatic lesions from our diagnosis. Melanocytic tumor could be excluded from our differential diagnosis by the absence of melanoma associated antigen HMB-45, as well as from the fact that most of these tumors arise in the soft tissues and never occur as a primary intra-osseous lesion.

The clinical and biological behavior of CCOC is complicated by the different prognosis and mortality rate reported in the scientific literature. The aggressiveness of these neoplasms are documented by some authors as extensive invasion of adjacent tissues, regional metastasis to the lymph nodes, less frequent distant metastasis to the lungs, and a recurrence rate of 55% [1,4]. The management of CCOC are a challenge as the most appropriate treatment for a tumor is determined by a definitive diagnosis and adequate understanding of the biologic behavior of the tumor. Because of the insufficiency in the number of cases and the varied prognosis reported, various therapeutic approaches have been applied by the surgeons over the years including curettage, enucleation, en bloc resection, and subtotal mandibulectomy/maxillectomy [1,7,8]. Recurrence (80%) within 2 year and/or metastasis developed in cases, which underwent curetage or enucleation, and hence wide local resection with partial mandibulectomy/maxillectomy with clear margins was the treatment of choice [5-10]. Fatal clinical outcome has been reported in cases with distant metastasis [8-10]. Treatment protocol included lymph node resection and radical surgery if the nodes were positive, and adjuvant chemotherapy and/or radiotherapy for those with tumor positive margins and/or regional/neral/vascular invasion [5-8]. Adjuvant radiotherapy at carcinoma doses of 6600 cGy at 200 cGy per fraction delivered once a day or a total dose of 7440 cGy at 120 cGy per fraction delivered twice daily is advocated by some authors [7,8]. Chemotherapy is usually reserved for palliative care as there is lack of evidence for its efficacy in definitive treatment [8]. Most authors acknowledge that this rare tumour has an aggressive behavior and consider them as low grade malignant odontogenic neoplasm which require a long term follow-up [5]. In the presenting case to maintain the quality of life in the young girl and due to variable prognosis reported in the scientific literature a segmental osteotomy through intraoral approach and iliac bone graft with titanium bone plate reconstruction was performed. Lymph node resection or neck dissection was not performed as there was no clinically palpable lymphadenopathy. No radiotherapy or chemotherapy was provided as the resected margins were tumor free. Recurrence has not been identified in the 1.4 year of follow-up, and the young girl is leading a satisfactorily happy life.

Conclusion

The scientific literature has reported less than 124 cases of CCOC after 30 year of its first reporting. Because of the paucity in CCOC cases that gave varied prognosis the scientific fraternity has limited knowledge about its biological behavior and this complicates establishing a standard criteria for diagnosis and management. The authors hope that the reporting of this additional case contributes to a better characterization of the epidemiology, histopathology, and prognosis of this odontogenic carcinoma, and help the clinicians to arrive at a better informed management option. It is recommended to avoid usage of confusing terms like clear cell ameloblastoma (CCA) and clear cell odontogenic tumor (CCOT), as clear cell dedifferentiation in odontogenic neoplasms is considered as low grade malignancy.

References