International Journal of Oral & Maxillofacial Pathology. 2019;10(1):10-14 ISSN 2231 – 2250
Available online at http://www.journalgateway.com or www.ijomp.org

Case Report

Stromal Digressions Influencing the Diagnosis of Odontogenic Tumours: A Case Report of Calcifying Cystic Odontogenic Tumour

Heera R, Devu Aloka, Padmakumar SK, Sivakumar R, Rajeev R

Abstract

The presence of odontogenic epithelium, ectomesenchyme or sometimes both is imperative for an odontogenic tumour to eventuate. Calcifying cystic odontogenic tumour is presently thought to arise from odontogenic epithelium along with odontogenic ectomesenchyme. The uncertainty regarding its origin has led to mushrooming of nomenclature and classification of this tumour. Atypica histologic presentations often add up to the dubious biologic nature of calcifying cystic odontogenic tumour. The present case is of a 16-year-old boy with a swelling in the mandible, microscopically showing ameloblastomatous epithelial lining, ghost cells, abundant dentinoid and also a primitive dental papilla like stroma.

Key words: Calcifying Cystic; Dental Papilla; Ectomesenchyme; Odontogenic Tumour; Odontogenic Cyst.

Heera R, Devu Aloka, Padmakumar SK, Sivakumar R, Rajeev R. Stromal Digressions Influencing the Diagnosis of Odontogenic Tumors: A Case Report of Calcifying Cystic Odontogenic Tumour. International Journal of Oral & Maxillofacial Pathology; 2019:10(1):10-14.

Introduction

Calcifying cystic odontogenic tumour (CCOT) is a unique odontogenic neoplasm which has generated over the years, a substantial interest and speculation regarding its true biologic nature. According to WHO, it is a cystic neoplasm characterised by an ameloblastomatous epithelial lining and a mature connective tissue capsule and also, aberrant keratinisation may be found in the form of ghost cells in association with varying amounts of dysplastic dentin.[1] It is grouped along with odontogenic lesions arising from odontogenic epithelium with odontogenic ectomesenchyme with or without dental hard tissue formation. But the nomenclature and definite histoarchitecture of this lesion has always been a topic of controversy. Renaming of Calcifying odontogenic cyst (COC) to CCOT and Dentinogenic ghost cell tumour (DGCT) was authoritatively first done in WHO classification in 2005 to refer to the so-called cystic and neoplastic variant of COC respectively.[2] Though the histologic criteria to accept an odontogenic lesion as CCOT or DGCT are apparent, many a times, a plethora of overlapping clinical and histologic features and bounteous terminologies introduced in the past, put even an experienced oral pathologist in a nomenclature dilemma.

The present case is of a 16-year-old boy with a swelling in the mandible, microscopically showing ameloblastomatous epithelial lining, ghost cells, abundant dentinoid and also a primitive dental papilla like stroma. We also attempt to examine and clarify the existing terminologies and points to keep in mind to arrive at apt diagnosis of an odontogenic tumour with aforementioned histologic presentations.

Case Report

A 16-year-old male patient reported to out-patient department in December 2015 with the chief complaint of a swelling in the left side of lower jaw of three months duration. On examination, the swelling was mildly tender, smooth surfaced, skin coloured swelling of approximate size 7 x 5 x 4cm on left side of face extending inferiorly from lower border of mandible superiorly to the zygomatic region with expansion of cheek both intra orally and extra orally. (Figure 1a) The swelling was initially slow growing and grew to the present size in the past three months. Intra orally, the swelling obliterated lower buccal vestibule in the molar and retro molar region and mucosa over the swelling appeared normal. On palpation, swelling was found to be of varying consistency and egg shell crackling sound was elicited. The swelling was afebrile, non-compressible, non-mobile, non-pulsatile and non-translucent. Left submandibular lymph nodes were palpable soft and tender.

Orthopantomograph showed a multilocular radiolucency in the left body of mandible extending from distal aspect of 36 to whole of ramus and coronoid process on left side with irregular border. Developing 38 was pushed

to lower border of mandible and distal and mesial roots of 37 showed resorption. (Figure 1b) Computed Tomography scan showed a well-defined unilocular expansile lytic lesion having discontinuous sclerotic border involving the body ramus and condylar process of mandible on the left side. The lesion was homogenously hypo dense and showed no post contrast enhancement and was suggestive of a cystic lesion. (Figure 1c)

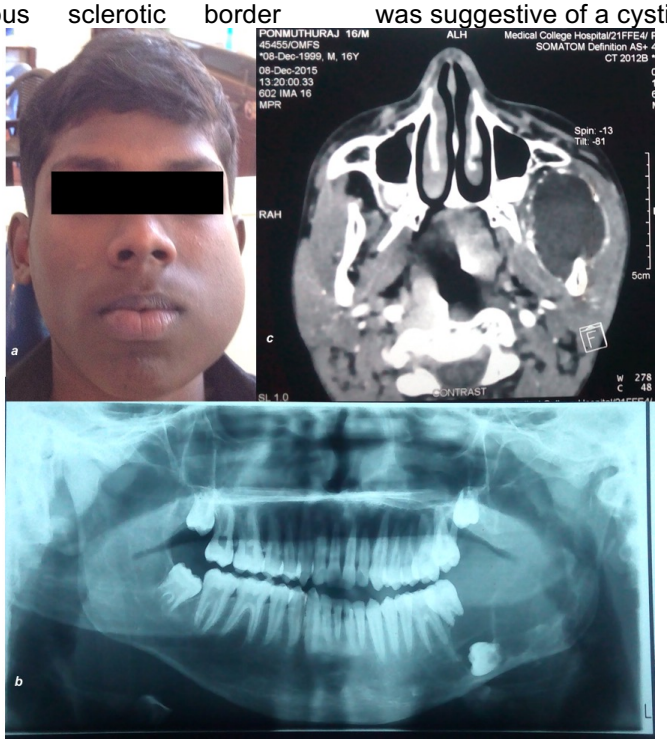

Figure 1: The extra oral photograph (a) showing a unilateral swelling on the left side of the face, Orthopantomograph (b) showing a multilocular radiolucency and computed tomography (c) showing well defined unilocular expansile lytic lesion involving the body, ramus and condylar process of mandible.

Fine needle aspirate was a chocolate coloured fluid. Papanicolaou stained smear of aspirate showed clusters of cells with darkly stained nuclei and scanty cytoplasm suggesting a lesion of odontogenic origin. After routine blood examination, an incision biopsy was done. The incision biopsy constituted six soft tissue bits and extracted second molar. The bits were flesh coloured, smooth surfaced and were soft in consistency. Microscopically, the hematoxylin and eosin stained section of incison biopsy revealed an odontogenic epithelium with hyperchromatic tall columnar basal cell layer showing reversal of polarity and stellate reticulum like cells superior to it, overlying a mature connective tissue capsule. Abundant ghost cells were seen, both within the epithelium and connective tissue stroma, a few of which were calcified. Juxtaposed to epithelium, at many areas, dentinoid like eosinophilic homogenous material was found. Consolidating all these features, diagnosis of CCOT was made. (Figure 2a) Conservative surgical enucleation of the lesion was done two weeks later. Twenty-five soft tissue bits along with first and third mandibular molar teeth were received. The soft tissue bits were flesh colored, soft to firm in consistency and had a nodular surface texture. (Figure 2b). The specimen was sent for processing in separate capsules.

Microscopically, excision specimen was not very different from the incision biopsy. It was compatible with CCOT. In addition to this, numerous odontogenic epithelial cells in the form of small islands and slender strands were seen in a cell rich primitive connective tissue stroma, which was reminiscent of dental papilla. The cells were plump spindle to ovoid in shape, resembling fibroblasts with hyperchromatic nuclei. Mature collagenous stroma was seen only in few areas. (Figure 2c & d) Van-Gieson histochemical stain was also employed to highlight the presence of abundant dentinoid and ghost cells in the lesion. The dentinoid, juxta epithelial, took up bright red colour of acid fuschin while ghost cells were seen in yellow shade of picric acid. (Figure 2e). Postoperatively, the surgical site healed uneventfully and the patient is on follow-up.

ISSN 2231 - 2250

Discussion

The origin of odontogenic lesions have always been an enigma to oral pathologists. The progress of the lesion to become cystic or neoplastic is thought to be determined by complicated interactions among various molecular entities, which also have a definite role in physiological tooth formation.[3] There is no debate on the concept that an odontogenic component- epithelium or ectomesenchyme is imperative to trigger the tumorigenesis. Apart from odontogenic epithelium, the stromal component also has an active role in determining the biological behaviour of the lesion. In odontogenesis, the component tissues undergo differentiation continuously and at any point of time, any of these tissues can contribute to inception of pathology.[3] Thus the histology, morphology and clinical behaviour of odontogenic lesions vary considerably owing to the vast possible interactions among these component tissues.

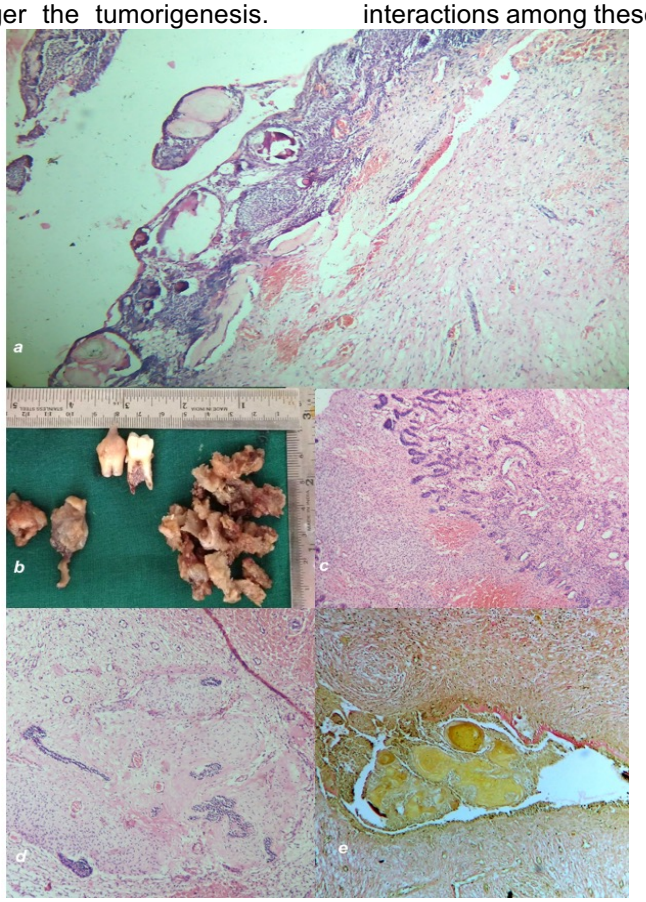

Figure 2: The hematoxylin and eosin stained photomicrograph at scanner view (a) shows odontogenic epithelium with overlying stellate reticulum like cells, ghost cells and underlying globular calcifications & dentinoid-like material. The macroscopic examination of the excision specimen (b) showing numerous soft tissue bits of varying sizes along with first and third mandibular molar teeth. The given photomicrograph in H and E stained section at low power view shows numerous odontogenic epithelial islands in a cell rich primitive connective tissue stroma (c) and stroma reminiscent of dental papilla(d) whereas in Van Gieson staining the dentinoid (stained red) and ghost cells (stained yellow) (e) can be appreciated.

The physiologic ectomesenchyme has been described as to have spindle shaped cells and abundant ground substance.[4] The stroma of odontogenic tumours is thought to be mature collagenous stroma composed of fibrous collagenous matrix with proliferating fibroblasts, exhibiting predominantly type I, III, and type IV collagen fibers along with oxytalan, elastin, and reticulin fibers.[3] Collagen I and IV are the prominent fibres in odontogenic ectomesenchyme.[5]

In 1992, WHO classified odontogenic tumours based on the products of tumour cells.[5] As more light was thrown on to the etiopathogenesis, the classification was modified, later in 2005, to be based on the fundamental component that is neoplastic viz. epithelium or connective tissue.[2,6]

COCs were once thought to be a variant of ameloblastoma with ghost cell keratinisation.[7] In 1940, Kurt Thoma and Henry Goldman reported three cases similar to COC and

reported them as tumors of both ectodermal and mesodermal origin.[8] The calcifying odontogenic cyst was first described as a distinct clinicopathologic entity by Gorlin and his colleagues in 1962.[9] The histologic features comprised of an odontogenic epithelium resembling preameloblasts with overlying stellate reticulum like area and characteristic ghost cell keratinisation within it. Ghost cells, though not pathognomonic, are mandatory for diagnosis. Juxtaepithelially, dentinoid is seen and the nature of dentinoid, though not yet thoroughly confirmed, is believed by some authors, as an induction product of epithelial mesenchymal interactions.[10]

An apt nomenclature for the lesion never came to a consensus and many investigators over a time period suggested many names. In 1971, WHO classification cited the term COC as a lesion consisting of odontogenic epithelium.[5] In addition to the histological features described for COC, they also quoted that it is not uncommon to see enamel, dentine or dentine like material and epithelial strands in the surrounding connective tissue. This can be accommodated as an odontome formation along with COC as was later suggested by Pretorius in 1981.[11] Pretorius and co-workers followed the dualistic concept that the lesion has cystic and neoplastic variants. They divided the cystic variant into three and separated neoplastic variant.[11]

Type I: Cystic variant:

A. Simple Unicystic type
B. Odontome producing type
C. Ameloblastomatous proliferating type

Type II: Neoplastic variant: Dentinogenic ghost cell tumour

Type IA, as the name suggests is composed of a characteristic COC lining with ghost cells but no hard tissue formation. Type IB, apart from the epithelial lining, is quoted to have ameloblastic fibroma like areas in it but along with calcified structures resembling compound or complex odontome. Type IC claims to have odontogenic epithelial proliferations both in the lumen and cyst wall. Type II or the neoplastic type or DGCT histologically has ameloblastoma like strands but in a mature connective tissue stroma. Ghost cell transformation of epithelial cells is notable and dentinoid material can be present juxta epithelial. Though the present case belongs to Type IB, calcified structures resembling odontome were absent in the cyst wall.

In 1992, WHO Classification of odontogenic tumours, COC was grouped in the category of odontogenic epithelium with odontogenic ectomesenchyme, with or without dental hard tissue formation. It was described as a neoplasm of pure epithelial origin but capable of inducing dysplastic enamel and dentin formation. The stroma was described as mature connective tissue. In 2005, WHO cited the terms, CCOT and DGCT. In both these tumours, the stroma has been mentioned as mature collagenous stroma.[2] Reichart and Philipsen[2] questioned the placement of CCOT/COC in the second group by WHO. According to them, the stroma is not characterized by ectomesenchyme but rather by mature, collagenous connective tissue. They also clarified that the presence of dentinoid material is a result of metaplastic process rather than it being a product of reciprocal epithelio-ectomesenchymal interactions.

In the present case, the stroma resembled primitive ectomesenchyme and characteristic strands and islands of odontogenic epithelium were seen scattered in it. Mature collagenous stroma was found only at a few areas.

Through polarised microscopic studies, it has been shown that stroma of COC show well organised and thickly packed collagen fibres.[3] Inflammation has been shown to affect the packing of collagen fibrils, by degrading the collagen and consequent regeneration which can cause haphazard or loose packing of collagen.[12] In the present case focal collections of inflammatory cells were seen but not in all the areas of primitive stroma implying the immature stroma is a part of the tumour de novo.

Similar stromal picture is seen Ameloblastic fibroma (AF), an odontogenic tumour in which both odontogenic epithelium and odontogenic ectomesenchyme are neoplastic. Induction phenomenon may or may not take place in these tumours. It has been hypothesised that epithelial cells of AFs may induce normal mature stroma to form ectomenchyme.[2] Yoon et al in 2004 reported a case of hybrid tumour of COC and AF[13] That lesion was described to have epithelial features of a COC with presence of dentinoid along with odontogenic epithelial islands in a dental papilla like stroma. Propositions that COC arises as a secondary event in a pre-existing odontogenic tumour and vice versa has been put forth in the past. The

mechanism of synchronised occurrence of these lesions has not been proved yet.[14]

Conclusion

Though, Reichart and Philipsen hypothesised that the dentinoid is a result of metaplastic process; the fact that, in lesions where dental papilla like ectomesenchyme is present, it can be formed by true epithelial-ectomesenchyme induction is to be deliberated further. Based on the above discussion, various conclusions can be drawn regarding the presence of ectomesenchyme in a case of CCOT. The dental papilla like area can be a part of one of the diverse histo-architectures of this particular tumour, validating its presence in the second group of odontogenic tumours. The epithelial cells of CCOT might be in an active state, evidenced by the formation of dentinoid, to induce the formation of ectomesenchyme. The present case can be one of the rare examples of a hybrid tumour of CCOT and AF. It might be the residuum of dental apparatus in the posterior mandibular area, (considering the age of the patient who is still in the tooth developing age), which might have been infiltrated by an aggressive CCOT.

Author Affiliations

1.Dr.Heera R, Professor and Head, 2.Dr.Devu Aloka, Senior Resident, 3.Dr.Padmakumar SK, Assistant Professor, 4.Dr.Sivakumar R, Assistant Professor, 5.Dr.Rajeev R, Associate Professor, Oral Pathology and Microbiology, Kerala University of Health Sciences, Government Dental College, Thiruvananthapuram, Kerala, India.

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Corresponding Author

Dr. Devu Aloka,
Senior Resident,
Oral Pathology and Microbiology,
Government Dental College,
Thiruvananthapuram, Kerala-695011
Ph: +91 9496734344
E-mail: devualoka@gmail.com

Source of Support: Nil, Conflict of Interest: None Declared.