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DESMOPLASTIC AMELOBLASTOMA: A REPORT OF THREE CASES FROM A SINGLE INSTITUTE WITH REVIEW OF LITERATURE.

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Abstract:

Desmoplastic ameloblastoma (DA) a rare type of ameloblastoma, arises from the rests of dental lamina, developing enamel organ, epithelial lining of odontogenic cyst or from the basal cells of the oral mucosa. Clinically, DA develops as a slow growing, painless, bony hard swelling resulting in facial asymmetry. Histologically, it represents stromal collagenization or desmoplasia with small nests and strands of odontogenic epithelium. But the true biologic profile of DA is not well understood as they mimic fibro-osseous lesions clinico-radiographically. As DA is a rare entity,we aim to discuss three case reports of DA from a single institution which deserves pre-eminence owing to its distinct site, radiological and histological features, local aggressiveness and high chance of false clinical appearance. Desmoplasia is an inductive phenomenon occurring in the mesenchymal tissue of the head and neck region. The pathologist and the clinician should be aware of the concepts and the association with malignant transformation and spread of the lesion in order to deliver appropriate treatment.

Key words: odontogenic tumors,desmoplastic, ameloblastoma, fibrosis, jaw, maxilla, mandible

Introduction:

Ameloblastoma is a true neoplasm of odontogenic originthat may arise either from the rests of dental lamina, the developing enamel organ, the epithelium lining of an odontogenic cyst, or from the basal cells of the oral mucosa.[1]

The three common clinico-radiographic presentations of the tumour include conventional solid/multicystic ameloblastoma (75-85%), Unicystic ameloblastoma (13-21%), and Peripheral (extraosseous) ameloblastoma (1-4%).Among the histological variants of ameloblastoma, desmoplastic ameloblastoma (DA) is rareand accounts for approximately 4-13% of all ameloblastomas. It was first described by Eversole in 1984 and was included in the classification by World Health Organization (WHO) in the year 1992.[2,3]

Clinically DA may develop as a slow growing, painless, bony hard swelling resulting in facial asymmetry. Pain, paraesthesia and mobility of teeth may be present incase of large lesions. These lesions are locally invasive and can infiltrate the medullary spaces causing erosion of the cortical bone.[4]Radiographically, DA may present asa diffuse, mixed radiolucent-radiopaque lesion.Histologically, DA is characterized by stromal collagenisation or desmoplasia with small nests and strands of odontogenic epithelium.[2]But the true biologic profile of DA is still not well understood due to paucity of adequate samples.[5]Various treatment modalities have been used for DA. Resection is the preferred modality of treatment due to the infiltrative behaviour of the tumour. Enucleation along with curettage and enucleation alone has also been used in some cases. [6]The purpose of this article is to describe the unique nature of this tumour through a series of three cases, review the existing literature and provide a better understanding of this rare tumour.

MATERIALS AND METHODS: Histopathological reports were retrieved from the archives of Department of Oral Pathology and Microbiology, MCODS, Mangalore. We evaluated three cases of desmoplastic ameloblastomawhich clinico-radiographically presented asFibro-Osseous lesions. The first case occurred in a 34-year-old woman in relation to mandibular anterior region, the second in a 55-year-old man in the maxillary anterior region and the third in a 32-year-old female in the maxillary anterior region.

Case Report: 1

A 34-year-old woman visited the Departmentof Oral and Maxillofacial Surgery with a chief complaint of swelling in the lower front teeth region of three and a half years' duration.History revealed that there was a gradual increase in the size of the swelling without any loss of sensation or pain. Patient was a known diabetic.On extra-oral examination,a swelling was seen on the left lower lip region measuring approximately about 2 x 2 cm. There was no discharge associated with the swelling and the lymph nodes were not palpable. There was no associated caries or periodontal disease in relation to the teeth involved. Teeth 31 and 41 exhibited grade I mobility.

Intraoral examination showed the presence of a single hard, non-tender swelling with no discharge and measuring approximately 3 x 5 cm on the labial aspect of gingiva in relation to 31, 32, 33, 34 and extending superiorly till the marginal gingiva and interdental region (Figure 1A). Lingually it extended to the region of the attached gingiva of 32 and 33. Inferiorly it was seen to obliterate the labial sulcus.

Cone beam computed tomography images of the jaws showed the presence of a well-defined mixed radio-lucent radiopaque lesionextending across the midline fromteeth 31 to 42. The lesion was seen to extend superiorly till the alveolar crest and measured aproximately 25 ×37 mm in the greatest dimension. Mesial displacement of tooth 32 was also observed.(Figure 1B) Sagittal sections showed evidence of loss of labial cortical plate from mesial aspect of 34 to distal aspect of 42. Loss of lingual cortical plate from cervical third to middle third in relation to roots of 31,32 and 41 was also noted.

Based on the clinical features and radiological appearance a provisional diagnosis of a fibro-osseous lesion was made. Histologicallythe tissue sections showed the presence of numerous odontogenic follicles in a desmoplastic stroma along with trabeculae of woven bone intermixed with marrow spaces. (Figure 1C) The follicles exhibited predominantly hyperchromatic cells with focal areas showing peripheral and central cellular differentiation.Few peripheral cells showed Vickers and Gorlin criteria. Based on these histological findings a diagnosis of Desmoplastic ameloblastoma was given.

Case Report: 2

A 55-year-old, malevisited the Department of Oral and Maxillofacial Surgery, with a chief complaint of rapidly growing swelling of four months' duration in the upper right front teeth region. The patient reported of pain associated with the swelling and enlargement subsequent to the extraction of 13 and 14 which were mobile. She had a habit of smoking forthe past 20 years.

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Intra-oral examination disclosed a round and smooth mass approximately 2 cm in size extending from 12 to 16 involving alveolus, buccal and lingual cortical plates of approximately. On palpation, the swelling was found to be of bony hard consistency.

The OPG revealed mixed radiopaque-radiolucent lesion in the region of extracted teeth 13,14 and 15 and trabeculae of bone exhibiting small septae with a cloudy appearance. (Figure 2 A)The lesion was seen to extend superiorly till the alveolar crest. Occusal view revealedthe expansion of cortical plates. Based on the radiological appearance a provisional diagnosis of fibro-osseous lesion was given. Histopathologicallythe tissue sections showed odontogenic islands and few follicles in a densely collagenous hyalinized stroma and invading the trabeculae of woven bone. (Figure 2 B). Most of the peripheral cells of follicles showed Vickers and Gorlin criteria. Based on the histological features, the diagnosis was given as desmoplastic ameloblastoma.

Case Report 3: A 32-year-old female patient visited the Department of Oral and Maxillofacial Surgery, with a chief complaint of swelling in the upper front teeth region which was present since one year. The onset of the swelling was gradual however it had increased rapidly since one month. Intra- oral examination revealed the presence of a growth measuring approximately 3 x 3 cm, involving the teeth 12,13,and 14. Based on the clinical findings a provisional diagnosis of giant cell granuloma or osteosarcomawas given. The patient then underwent an incisional biopsy.

Histologically, the tissue sections showed odontogenic follicles in dense collagenous fibrous connective tissue stroma. The follicles showed central and peripheral differentiation. Central cells showed scant epithelial proliferation and focal areas of peripheral cells exhibited Vickers and Gorlin criteria. (Figure 3)

DISCUSSION:

The data from different geographical regions suggest that the frequency of Desmoplastic Ameloblastoma (DA) is more among the Asian populationswith ageranges from 17 to 83 years with a mean age of 41.9 years andan equal occurrence among males and females.[2,7,8]Desmoplastic ameloblastoma occurs frequently in anterior premolars with tooth displacement as a common finding.[9]Reports vary among the frequency of site distribution with authors variably reporting higher incidence in either the maxilla or mandible.According to Philipsen *et al.*, desmoplastic ameloblastoma occurring in maxilla is more aggressive than in mandible.In our case series, 2 out of the 3 cases were seen in the maxilla and in case 2 we could even appreciate the tumour invading the bony trabeculae. This perceived aggression may be attributed to certain factors such as thethin cortical bone in maxilla being a weak barrierwhich in turn favors the dissemination of tumors. Therefore, maxillary ameloblastoma can spread more rapidly than in the mandible.[5]

Radiographically,DAfrequently presents as a mixed radiolucent-radiopaque lesion with diffuse borders.Thismixed RO-RL appearance fails to unequivocally provide a radiographic differentiation between desmoplastic ameloblastoma and fibro-osseous lesions.[10]

However, what is intriguing is the fact that the DA gives this RO-RL appearance while histologically it presents with a dense fibrous/scirrhous stroma.Yazdi *et al.* (2009) suggested that it is the osseous metaplasia occurring within the dense fibrous septae which characterizes the lesion and the mixed appearance is not due to any mineralized product generated by the tumor. [10]Takata *et al.* suggested that the infiltrative behavior of the tumour is responsible for the characteristic appearance whereas Thompson *et al.* correlated the mixed radio-opaque lucent areas and ill-defined borders histologically to bone remodelling in response to expansion of the lesion in bony trabeculae and infiltration of the collagenous stroma.[6]

The density of a tissue greatly influences the radiographic appearance. The greater the density within the region of interest the greater is the attenuation of the X-ray beam leading to a lighter radiographic image (perceived as radiopaque structure). Desmoplastic areas are denser than the normal loose/ myxoid connective tissue thus showing higher degree of radiopacity owing to the property of attenuation.[11]Luo *et al.*from their study on 7cases observed thatthe honeycomb-like appearance formed by coarse trabecular septaewas seen in more than half of theircases.[9]Besides the honey-comb appearance, some cases of DA have been reported to show plenty of radiopaque flecks scattered around a radiolucent cystic lesion without a radiopaque area.Additionally, in a CBCT, DA shows an apparent expansion in the labial or buccal side with partial cortical erosion, while a classicalintra-osseous ameloblastoma may exhibit buccolingual expansion with perforation.[9]

The three radiological presentations of DA are described in literature. They are,

Type I (Osteo-fibrosis type): radiolucent as well as radiopaque appearance;

Type II (Radiolucent type): completely radiolucent appearance; and

Type III (Compound type): radiolucent as well as radiopaque combined with large radiolucent change.[12]

Radiographically the differential diagnoses would include ossifying fibroma, osteoblastoma, desmoplastic fibroma, fibrous dysplasia and osteosarcoma.[1]DA can also mimic chronic sclerosing osteomyelitis, central giant cell granuloma, aneurysmal bone cyst, primary intraosseous squamous cell carcinoma.[7,12]All these cases radiologically exhibit a unilocular or multilocular radiolucent and radiopaque appearance and the final diagnosis can be made with certainty upon microscopic evaluation.

Histopathologically, DA shows dense collagenous stroma that may appear as hyalinized as well as hypocellular.The epithelium of the lesion has greater tendency to grow in thin strands and cords rather than island-like patterndue to the dense connective tissue stroma. Central stellate reticulum-like cells are often scant in the epithelial proliferation, and the peripheral cells making strands and cords are often flattened or cuboidal rather than tall columnar in appearance. Reversal of polarity of nuclei and subnuclear vacuole formation may be difficult to recognize. Sometimes DA can also present with classic islands of follicular ameloblastoma. [4,13]

Effiom OA and Odukoya O groupedDA into two histologicalvariants:

(i) Asimple desmoplastic variant showing extensive stromal desmoplasia.

(ii) desmoplastic variant with osteoplasia showing characteristics of desmoplastic variant with additional calcific structures.[14]Cases 1 and 3 reported by us can be

categorized as the first variant while case 2 belongs to the second group.

Rarely, DA may present as a "Hybrid Lesion" in association with follicular or plexiform solid/multicystic ameloblastoma.[15]

Though the diagnosis is straight forward histologically,ameloblastic fibroma, odontogenic fibroma and squamous odontogenic tumour may be considered in the histological differentials. In DA, the compressed appearance of the odontogenic follicles, the extremely dense collagenous stroma and the occasional presence of Vickers and Gorlin criteria might be helpful in distinguishing this tumor.[16]

The reported rates of recurrence of DA are varied as the WHO classification of odontogenic tumours states a lower recurrence rate like unicystic ameloblastoma and peripheral ameloblastomas. However, Sun JZ *et al.* [2]mention similar recurrence rate of DA as other types of ameloblastomas (15.9%).

Keszler *et al.* (1996) reported higher recurrence rate (21.4%) for DA than the other type of ameloblastoma (10.1%)and suggested the following:

DA's can be diagnosed radiographically asfibro-osseous lesions. They frequently present with ill-defined borders making it difficult to gauge the exact interface of the lesion with normal bone resulting inincomplete surgical enucleation leading to recurrence.Additionally, the loose architecture of the maxillary bone offers less resistance to the infiltration of the tumour leading to more chances of recurrence. [17]DA that radiographically presents with ill-defined borders suggests an infiltrative process and has a higher propensity to recur.[18]

Lamichhane *et al.* suggested that the recurrence of DA could be due to the nature of the tumour (lack of capsule and precise limit) or due to incomplete surgery. [5]

The currently preferred treatment modalities for DA include resection and enucleation. The average relapse time reported by Sun *et al.*in a series of 115 patients was 36.9 months suggesting that the follow-up period of DA must be more than 3 years.[2]The recurrent cases should always be treated by complete resection.[7]

Recently a case of malignant transformation of desmoplastic ameloblastoma to squamous cell carcinoma in a 49-year-old African American man has been put forth by Rais and El-Mofty. Though the exact mechanism of the malignant transformation cannot be explained, the authors suggest that a p53 mutation could have played a role. The authors further state the morphological, clinical and radiographic differences between ameloblastoma and desmoplastic ameloblastoma have tempted them to consider desmoplastic ameloblastoma as separate odontogenic tumour rather than a true ameloblastoma. The malignant counterpart of ameloblastoma is ameloblastic carcinoma, however in the case mentioned the desmoplastic ameloblastoma progressed to Squamous cell carcinoma. This further supports their concept that desmoplastic ameloblastoma is possibly a distinct entity.

CONCLUSION:

The case series reported highlights the distinct histology of the DA that radiographically could mimic a fibro-osseous lesion. The true biologic nature of this tumour is not completely understood. Stromal desmoplasia occurs due to the inductive stimuli of the tumour cells on the

host cells. The role of stromal desmoplasia as towhether it acts as a host defense mechanism or accelerates the spread of the tumour is questionable. Its higher rate of recurrence ascompared to the other histological variants of ameloblastoma necessitates DA to be treated aggressively Malignant transformation of DA is possible. Thus in the event of a presentation of an intraosseous swelling with mixed radiopaque radiolucent appearance, a clinician must remain cognizant of this odontogenic tumour for correct diagnosis and treatment planning and should follow-up the patient adequately. Further research on its aggressive nature, recurrence and the malignant transformation could add more insight into the clinical and molecular biology of this unique tumour.

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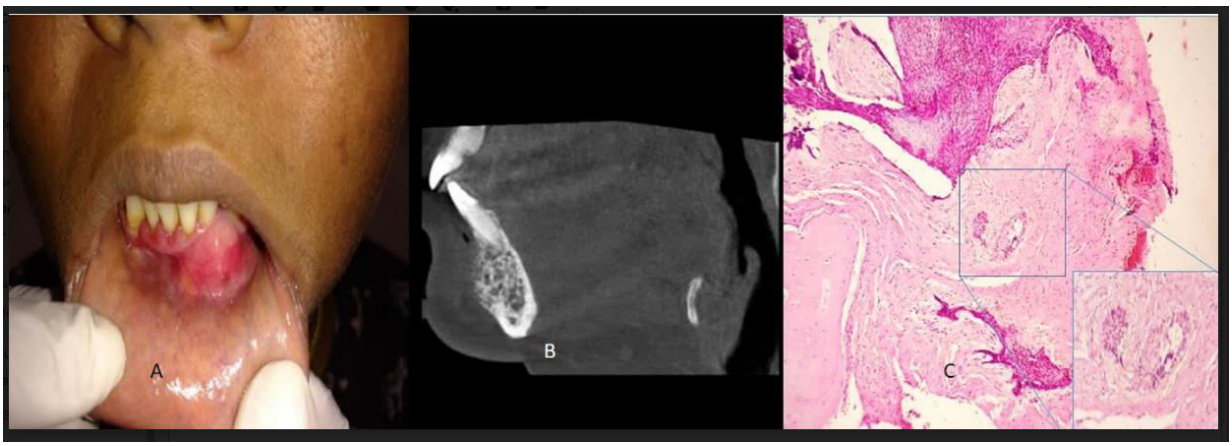
FIGURE LEGENDS

Figure 1 (Case 1):



A- Single hard, non-tender swelling, relation to 31-34
B- CBCT image - Sagittal section showing loss of labial and lingual cortical plate continuity with mixed radiopaque and radiolucent areas
C- Ameloblastomatous follicle exhibiting Vickers and Gorlin criteria, in a desmoplastic stroma

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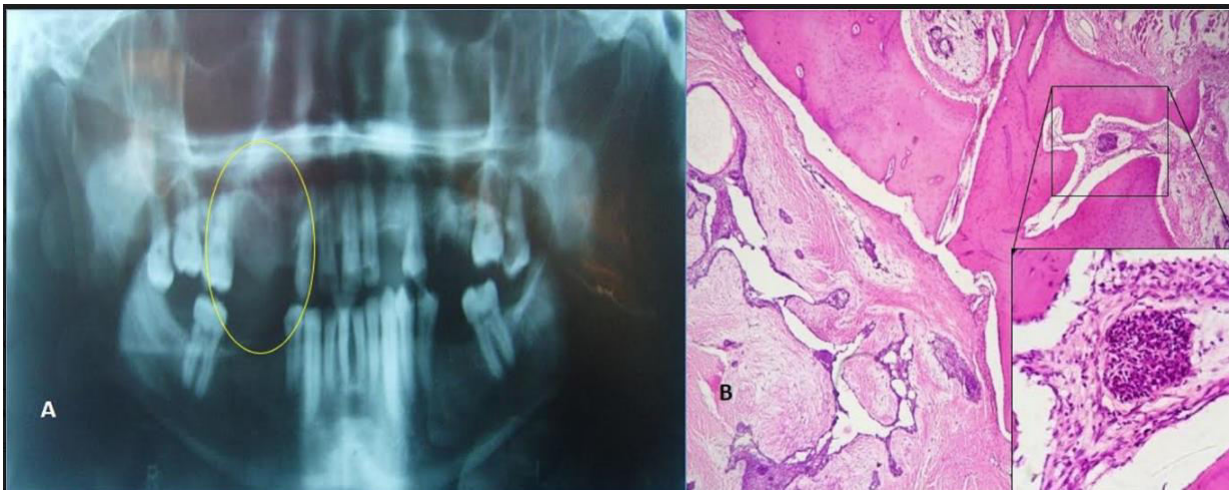
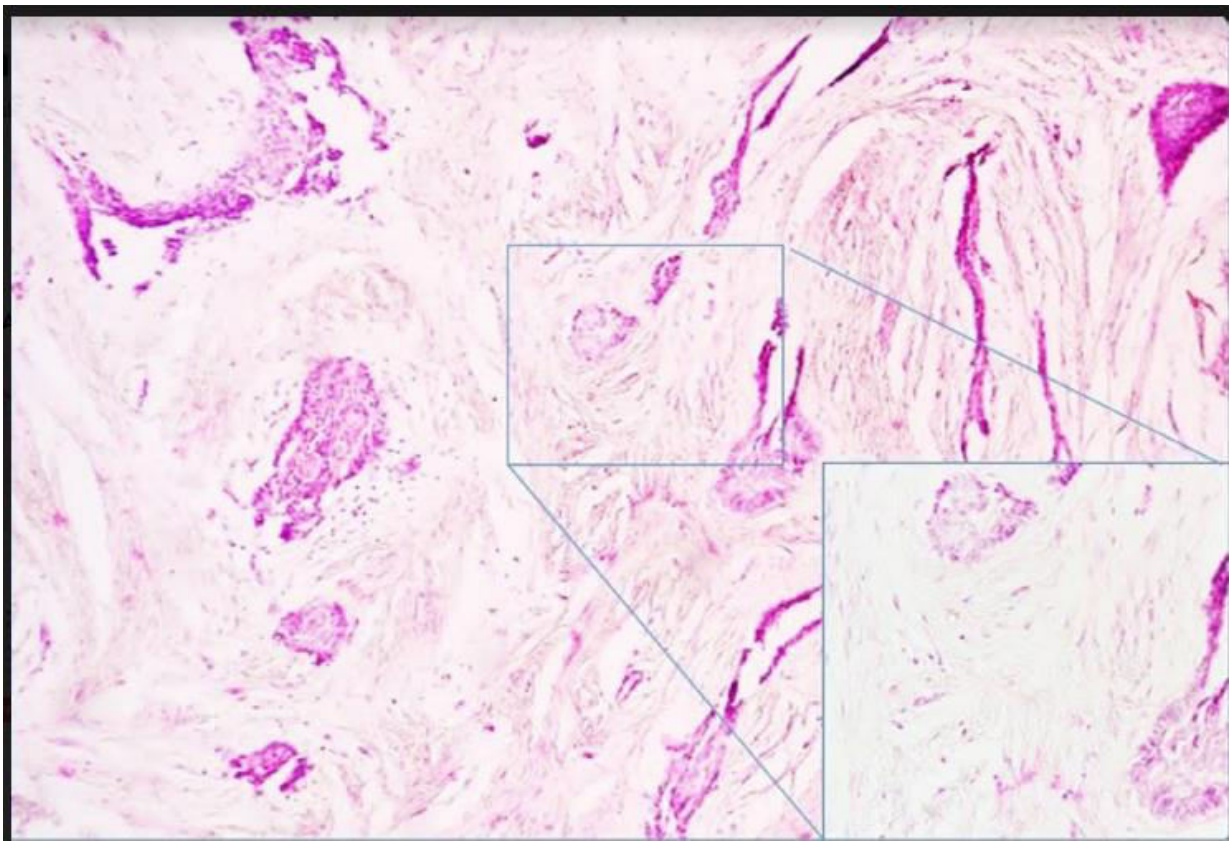
Figure 2 (case 2):



A- Mixed radiopaque- radiolucent lesion in relation to 13,14 and 15
B- Follicles invading the trabeculae of woven bone

Figure 3 (case 3):



Odontogenic follicles in dense collagenous stroma with evidence of Vickers and Gorlin criteria