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Case Report

Dentigerous cyst transmuted into Adenomatoid Odontogenic Tumor – A rare occurrence: case report and review of literature

[1]Shital Patel, [2]Zenish Bhatti, [3]Shyam Chauhan, [4]Rajan Savani, [5]Yasashvi Chavda, [6]Yashesh Patel

[1,3,4,5,6]Department of Oral and Maxillofacial Surgery, AMC Dental College and Hospital, Opp. Anupam Cinema, Bhalakiya mill compound, Khokhara, Ahmedabad, Gujarat, India;
[2]Department of Dentistry, All India Institute of Medical Sciences, Saket Nagar, Bhopal, Madhya Pradesh, India

ABSTRACT:
Background: Cysts and tumorsof odontogenic origin are common occurrences in the jawbones, but their coexistence is rare.Development of odontogenic tumors like ameloblastoma and adenomatoid odontogenic tumor as well as neoplastic conditions like squamous cell carcinoma and mucoepidermoid carcinoma from the epithelial lining of an odontogenic cyst has been reported. However, the likelihood of such occurrences is extremely rare. **Methods:** An attempt has been made to present one such unusual case of adenomatoid odontogenic tumor in a 14-year-old female that was arising from the wall of dentigerous cyst lining on the crown of an unerupted mandibular lateral incisor. Patient wasmanaged by surgical excisionand was followed up for long term (5 years) to check for signs of recurrence of lesion and was later rehabilitated. The PubMed, ScienceDirect, and manual/hand data base was searched within past 20 years (2004-2023).Including the current case, we found 16 matching reports representing 17 cases. **Conclusion:** The peculiarity of this case resides in lesion's unusual location in the anterior mandible and rarity of mandibular lateral incisor impaction. Also, it represents the neoplastic changes in the odontogenic cyst. A thorough histopathological examination is crucial to identify the potential coexistence of these two entities, despite their benign nature.
Keywords: Dentigerous cyst, Impacted Lateral incisor, Adenomatoid Odontogenic Tumor (AOT), Enucleation

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Corresponding author: Zenish Bhatti, Department of Dentistry, All India Institute of Medical Sciences, Saket Nagar, Bhopal, Madhya Pradesh, India

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INTRODUCTION

Steensland, in 1905 described Adenomatoid Odontogenic Tumor (AOT) as a benign, rare, and slow but progressively growing tumor. It is composed of odontogenic epithelium and originates from the complex system of dental lamina or its remnants, exhibiting a variety of histological patterns.[1] Its occurrence is less common and accounts only for 2.2-7.1% of all odontogenic tumors. It is also known as "tumor of two-thirds" because, 2/3rd of casesfound in females, in maxilla, in 2nd decade of life and associated with unerupted teeth, mainly maxillary canine.[2,3]It shows male: female ratio of 1:1.9 and maxilla: mandible ratio of 13:7. Clinically, majority of lesions are asymptomatic or having swelling due to expansion of surrounding bone typically measuring 1.5-3cm in its greatest diameterwith resultant facial asymmetry. Missing tooth, displacement of adjacent tooth, mobility of involved or adjacent teeth rather than root resorption are other common findings.[4]

Two distinct clinico-pathological variants are well recognized: Central (intra-osseous) and Peripheral (extra-osseous). Among them, follicular (associated with impacted teeth) and extra-follicular (not associated with impacted teeth) are types of central variant. Central variant accounts for 96% of all AOTs, of which follicular typeaccounts for 71% whereas peripheral variant accounts for 4.4%. [5, 6]

Histologically, AOT shows multiple spindle shaped cell arrangements, including ductlike structures, double-layered spheres, and rosettes in a scanty fibrous stroma. Its lumen may be seen empty or might contain an eosinophilic material. Variable amount of calcification foci may also be found scattered

throughout the lesion.[4]AOT may show a hamartomatous intraluminal proliferation of epithelial cells derived from the Hertwig's epithelial root sheath. Due to uncertainty in its histogenesis, it may appear partly cystic or in some cases presence of tumorous tissue masses in the walls of the cystic lining may be seen. [2, 7]

Therefore, the purpose of this case report is to present a relatively rare occurrence of AOT originating from the wall of dentigerous cyst in anterior mandible along with an impacted lateral incisor. Additionally, thisemphasizes how histological findings are cardinal for deciding its accurate diagnosis and best possible management strategies.

CASE REPORT

A 13-year-old female patient reported to Department of Oral and Maxillofacial Surgery at AMC Dental College & Hospital with a chief complaint of gradually increasing painless swelling on chin region since past 10 days. Patient's medical history was unremarkable and no previous history of extraction, extraoral trauma or episode of odontogenic infection were reported.

An extraoral examination revealed a diffuse, firm, non-tender, non-fluctuant, non-compressible oval shaped swelling of 3.5 x 3.5 cm in diameteron the lower left parasymphysis region with normal overlying skin. Presence of facial asymmetry and obliteration of mento-labial sulcus causing mild inversion of left corner of lower lip were appreciated.

Upon intraoral examination, a well-defineddome shaped swelling of approximately 3.5 x 2.5 cm in size with normal overlying mucosa was seen obliterating the lower left labial vestibule between inter-canine region with marked buccal cortical plate expansion. No signs of paraesthesia of lower lip, infection, sinus, or fistula formation were evident. The right central incisor and left canine showed marked mesial tilting whereas left central incisor showed distal tilting. All three teeth were non-vital and Grade I mobile. Clinically, lower left lateral incisor was missing and occlusion was normal. Aspiration of lesion drew dirty yellow straw-coloured fluid. (Figure 1)

Panoramic and CBCT radiographs showed a well circumscribed, unilocular radiolucency surrounding impacted lower left lateral incisor. The lesion was extending from right lateral incisor to left second premolar with mesial tilting of right central incisor and cross-arch displacement of left lateral incisor at inferior border of mandible. Displacement of roots of left and right lower central incisors, lateral incisor and left canine as well as apical root resorption of deciduous lateral incisor and canine were noted. Total nine teeth either involved or affected by the lesion were left and right premolars, canines, central and lateral incisors, and deciduous lateral incisor and canine of left side. No pathologic involvement or displacement of inferior alveolar nerve observed. (Figure 2)

Differential diagnosis of dentigerous cyst, unicystic ameloblastoma, and AOT were made. Enucleation of lesion via intraoral approach under general anaesthesia with extraction of involved teeth (33, 73, 72, 31, 32 and 41)was carried out and surgical specimen was sent for histopathological examination.

Detailed Microscopic analysis revealed presence of proliferation of spindle and cuboidal shaped epithelial cells forming sheets, strands, and whorled masses in scanty stroma of connective tissue. Duct like structures, foci of calcification and eosinophilic material was also noted. Periphery of cut-section showed dentigerous cyst like lining surrounded by fibrous capsule. (Figure 3)

This evaluation led to the final diagnosis of AOT arising from the dentigerous cyst. No signs of recurrence were observed till 5 years of follow up.An interim removable partial denture was delivered to address the functional and aesthetic concern which also served as space maintainer. Patient was explained and planned for the permanent rehabilitation thereafter. (Figure 4)

Due to retrospective nature and complete exclusion of patients' personal information, exemption from further review was granted by institutional review board. Prior to the study, patient was informed of its purpose and a written informed consent for the usage of her records, including photographs, medical reports, treatment records, etc., for publication was obtained.

Tabel 1 Clinical and radiographic details of previously reported cases in the English literature

Author	Year	Thnicity	Age /gender[a]	Impacted teeth in lesion[b]	Number of teeth involved in lesion	Radiograph	Aspiration/biopsy	Provisional diagnosis	Final diagnosis	Management		Follow-up period
										Surgery	Extraction[b]	
Litonjua LA et. al. [14] 2004		Philippine	20/F	37	1	OPG	Thin straw-coloured fluid	Dentigerous Cyst	AOT	Decompression: Marsupialization under LA and cavity was packed with iodoform gauze at weekly interval, irrigation and change of dressing done till 8 weeks. Enucleation under GA after 11 months.	46, Impacted 47	2 years
Handschel JG et. al. [13]	2005	German	23/M	43	5	OPG	NM	NM	AOT	Enucleation under GA + pelvic spongiosa (Bone Grafting)	NM	6 months
Khot K et. al. [7]	2011	Indian	17/F	43	11	OPG, CT scan	NM	Dentigerous Cyst or Unilocular Ameloblastoma	Mural AOT in a pre-existing cyst	Surgical Curettage under GA	43	NM
Moosvi Z et. al. [9]	2011	Indian	13/F	32	5	PNS	Incisional Biopsy	Dentigerous Cyst	AOT arising from the	Enucleation under GA	41,42 43, 31,32, 33	NM

									lining of a denti gerou s cyst			
Manjun atha BS et. al.[1]	2012	Ind ian	19/ M	34	4	OPG	Straw coloured fluid of about 1 ml and the protein analysis of the same was 5.2 mg/dl	NM	AOT in a pre-existi ng denti gerou s cyst	Curettage under LA	34	once in 3 month s
Kurra S et. al. [3]	2013	Ind ian	19/ M	37	2	OPG	NM	Denti gerou s cyst with an impac ted 38	AOC	NM	NM	NM
Latti BR et. al. [16]	2013	Ind ian	15/F	33	8	OPG	Incisiona l biopsy	Denti gerou s cyst	Denti gerou s Cyst with Aden omat oid Odon togen ic tumo r	Excisional Biopsy	NM	upto 3 month
Saluja H et. al. [17]	2013	Ind ian	18/F	33	7	OPG, CT	Straw-co loured fluid	Denti gerou s cyst associ ated with impac ted 33	AOT in the capsu le of denti gerou s cyst	Enucleatio n under GA	RCT of all involv ed teeth and impact ed 33 remov ed along with in toto lesion.	1 year
Munde AD et. al. [18]	2014	Ind ian	20/F	33	7	OPG, CT`	Clear yellow fluid of approx. 2.5 ml without any	Denti gerou s cyst	Denti gerou s cyst with AOT	Enucleatio n along with impacted 33 under GA + Alloplast grafting	Extrac tion: 33, RCT in 31, 41, 73,34, 35	1 year

							crystals					
Rathod V et. al. [19]	2014	India	13/M	34	4	OPG, Occlusal View	Blood mixed fluid	Dentigerous cyst	Dentigerous cyst converting to AOT and CEOT	Enucleation +Gel foam	74, 34	3 months
Jindal C et. al. 20	2014	Indian	15/F	43	7	OPG	NM	NM	AOT	Enucleation under GA	NM	NM
Kumar R et. al. [11]	2015	Indian	15/F	44	3	OPG	NM	NM	AOC (Adenomatoid odontogenic cyst)	Surgical Excision under GA	43,44, 45	NM
Uppada UK et. al. [12]	2015	Indian	16/F	43	3	OPG	Brick red-coloured fluid	Dentigerous cyst	AOC	Enucleation	43	NM
Belgaumi UI et. al. [22]	2015	Indian	21/M	44	2	OPG	NM	NM	AOT (HPE)	Surgical excision under GA	44	1 year
Gupta S et. al. [21]	2016	Indian	12/M	33	6	OPG, Occlusal View	Clear yellow-coloured fluid	Central giant cell granuloma, Dentigerous Cyst	AOT with dentigerous cystic lining	Incisional Biopsy, Enucleation under LA	NM	1year
S Neha et. al. [15]	2018											
Case 1		Indian	14/F	Absent	5	OPG, CBCT	NM	OKC	NM	Enucleation	NM	NM
Case 2		Indian	16/F	33	7	OPG, CT	NM	Dentigerous cyst	NM	Incisional Biopsy, Enucleation	NM	NM

NM Not Mentioned, *OPG* Orthopantomogram, *PNS* Paranasal Sinus View, *CT* Computed Tomography, *CBCT* Cone Beam Computed Tomography

AOC Adenomatoid Odontogenic Cyst, *AOT* Adenomatoid Odontogenic Tumour, *LA* Local Anaesthesia, *GA* General Anaesthesia

[a] Age in years, *M* is male, *F* is female

[b] Tooth numbering in FDI system

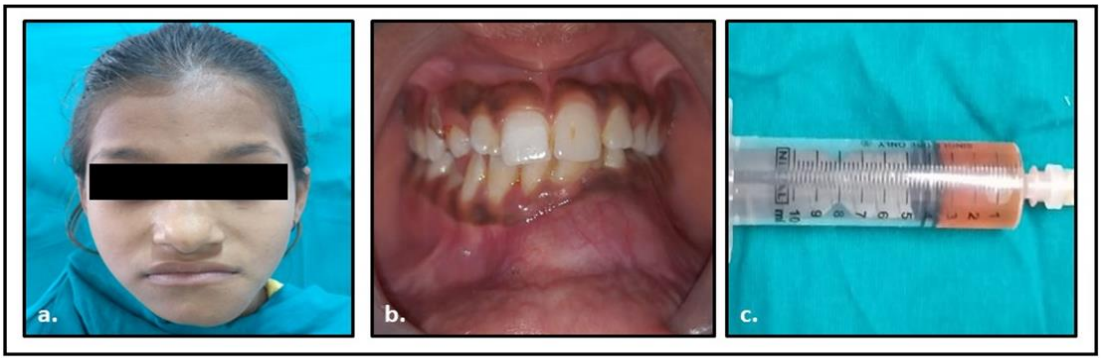

Fig 1 a. Preoperative front profile. b. Intraoral photograph showing dome shaped swelling in the left lower labial vestibule. c. Aspiration from the lesion

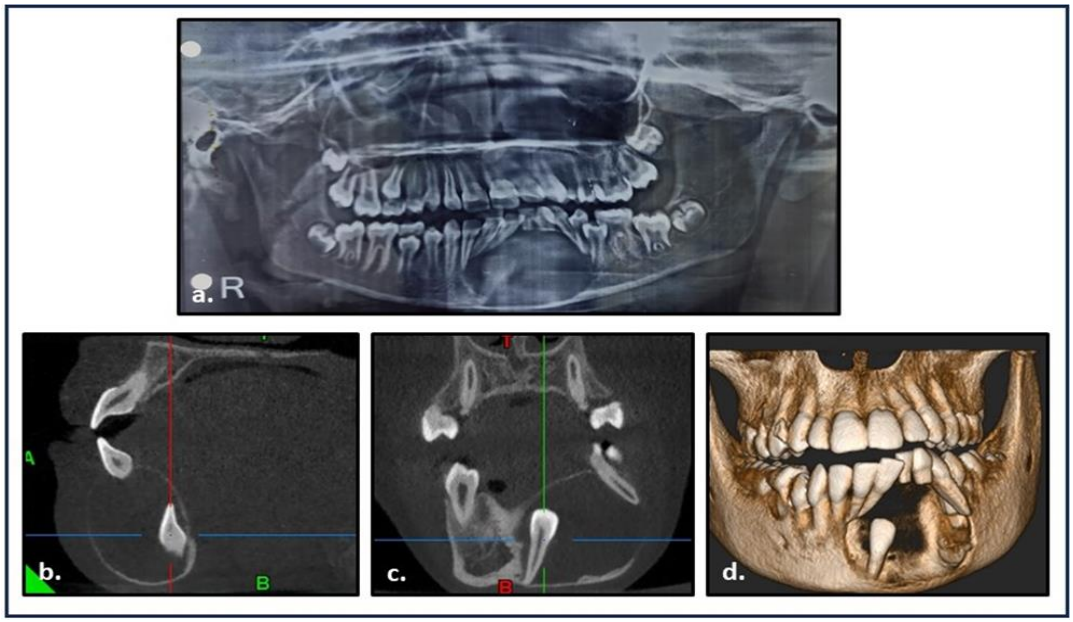

Fig 2 a. OPG showing well-defined unilocular corticated radiolucency in the anterior mandible with associated impacted left lateral incisor and its root reaching up to the inferior border of the mandible. b and c. CBCT showing sagittal view and coronal view. d. 3D view showing the tumor and impacted tooth.

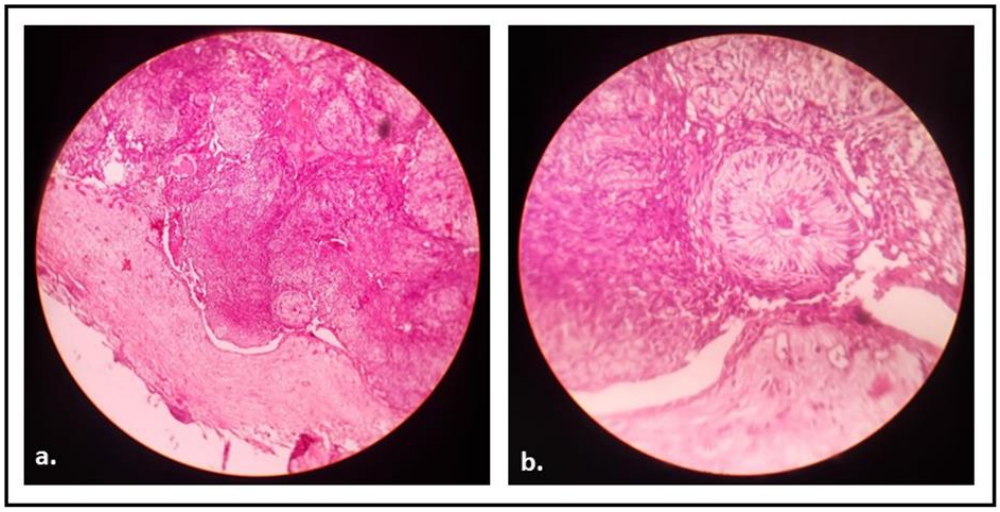

Fig 3 a. Low power view showing tumor arising from 2 to 3 cell layered dentigerous cystic lining (H & E x10). b. Photomicrograph showing islands of spindle shaped odontogenic epithelial cells arranged in a rosette pattern confirming adenomatoid odontogenic tumour arising from the lining of the dentigerous cyst (H & E x100).

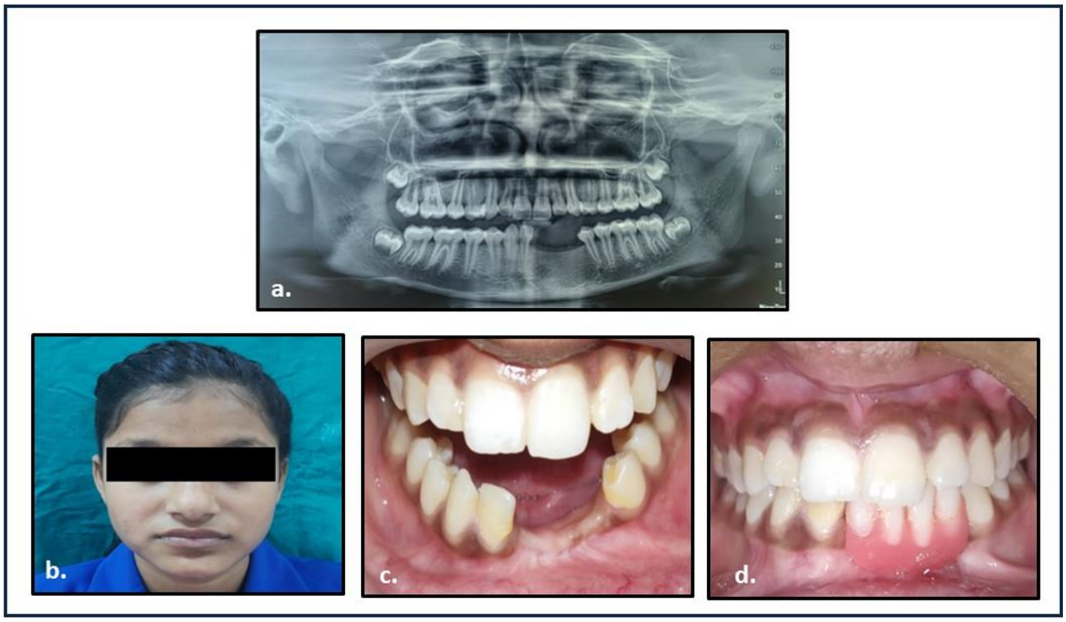

Fig 4 a. Post operative OPG showing bone formation no signs of recurrence. b. Post operative photograph showing front profile. c. Post operative healing intraoral healing. d. Rehabilitation with removable partial denture.

DISCUSSION

Steensland (1905) in his first ever report described AOT as “epithelioma adamantinum”. Later, the term "adeno-ameloblastoma" was used quite often for many years for its description because it was considered as a variant of "ameloblastoma". [5] In 1915, Harbitz described first incontrovertible case of AOT as “cystic adamantoma”. AOT was referred by a plethora of names, including adenoameloblastoma, ameloblastic adenomatoid tumour, adamantinoma, epithelial odontoma and teratomatous odontoma. Unal et al. highlighted a range of terminologies used between 1905 - 1969 to describe it in one of their case reports of AOT in a 4-year-old girl.[2] In 1969, Philipsen and Brin proposed the term “Adenomatoid Odontogenic Tumour”.Later, this term wasaccepted by WHO in their “Histological Typing of Odontogenic Tumours, Jaw Cysts and Allied Lesions” and it became a widely accepted nomenclature. WHO defined it as “a tumour of odontogenic epithelium with duct-like structures and having varying degrees of inductive change in the connective tissues. [3]

There was a long-term debate whether to consider AOT as an anomalous developmental hamartomatous growth or true benign neoplasm.Pointing to its limited size, minimal growth potential and lack of recurrence, many investigators believe it to be a hamartoma.[6] Because of its exclusive occurrence within the tooth-bearing areas of the jaws and its cytologic resemblance to the dental lamina and its components, it is considered to be of odontogenic origin. Philipsen et al.[2] postulated that most central AOTs (follicular type) surround the tooth as it develops from the nests of the cells within dental lamina. This hypothesis is further corroborated by both morphological and immunocytochemical analysis.[8]

Neoplastic and hamartomatous lesions can developduring any stage of odontogenesis. Odontogenic tumours featuring both epithelial and mesenchymal components may emerge within an odontogenic cyst [6]and sometimes odontogenic cysts may develop inassociation with odontogenic neoplasms.[1]Neoplastic potential of epithelium of dentigerous cyst to ameloblastoma, AOT and mucoepidermoid carcinoma has been reported. [9]

When occurrence of most central AOTs in a pericoronal relationship with an associated tooth is observed, it remained unclear whether the associated cyst’s lining represents a true dentigerous cyst, a secondary cystic change within the AOT, or as adistinct entity itself. Also, uncertainty exists regarding its potential to be more aggressive.[1, 6]

Radiographically, AOT typically displays radiolucency around both coronal and radicular parts of involved tooth.[2, 6]But, radiographs can be inconclusive when AOT develops from a wall of dentigerous cyst. However, the development of AOT may be indicated by the irregularity in the wall of cyst in some cases.[10]

Kumar et al.[11] referred to Marx and Stern who contemplated AOT as a cyst and not tumour, and even introduced a new term “Adenomatoid Odontogenic Cyst” (AOC). Similar to Marx & Stern observation, the present case also displayed mainly a cystic lesion having areas of AOT like proliferations into the lumen. Uppada UK et al.[12] in their case report replaced the term AOT with AOC and stated that “the time has come to bury the use of the term AOT.” In contrast, Rick GM[6] disapproved the change in term as the lesion is always not a fluid filled pathologic cavity but it often has a predominant solid component. He also pointed that AOT has been reported to develop

with many different types of cysts and tumours, such as calcifying odontogenic cysts, dentigerous cyst, ameloblastoma, odontoma, etc.

To our knowledge, only fewcases of AOT emerging from or in combination with dentigerous cyst in the mandible have been published till date. Using the keywords "AOT with dentigerous cyst, dentigerous cyst converting to AOT, and cystic variant of AOT in mandible" in PubMed, ScienceDirect, and using manual/hand search, a review of English-language medical literature for previous 20 years (2004-2023) found 16 matching reports representing 17 cases. (**Table. 1)**

When analysing the ethnic diversity, majority of patients 15 (87.5%) were of Indian descent, while only 1 (6.2%) was German[13]and 1 (6.2%) was Philippine[14]**.** Male: female ratio was 1:3. Almost all cases occurred during second decade of life with age range of 12 - 23 years and mean age of 16.82 years.

Considering from mandibular midline to canine as anterior region and from premolar to molars as posterior, 11 (64.70 %) cases were noted in anterior and 6 (35.29 %) in the posterior region. Irrespective of origin of lesion, 8 (47.06%) showed central compartment involvement as the lesion was extending beyond mandibular midline.

Considering involvement of associated impacted tooth as origin for initiation of lesion, 7 (41.17 %) cases were found on right side, while 9 (52.94 %) were on left side. Among these, canine involvement was the most prevalent (9, 52.94%), followed by first premolar (4, 23.53 %), second molar (2, 11.76 %), and lateral incisor (1, 5.88%). S Nehaet al.[15]reported a case without any associated impacted tooth within the lesion.

Differences were noted how authors documented size of the lesion, encompassing clinical parameters (intraoral/extraoral), radiographic assessment or histopathological specimens. The largest recorded lesion size was of 7 x15cm (intraorally)[7] while smallest was of 0.5 x 1cm (gross histopathological specimen)[12]

The most prevailing chief complaint was presence of swelling which was often but not always accompanied by pain, followed by incidental diagnosis during orthodontic consultation[15], tooth mobility and discomfort during mastication1, over-retained deciduous teeth with clinical absence of permanent counterparts.[13]

The range of teeth involved varied from 1-11 where Khot K et al. [7]documented the highest number of 11 teeth involvement. Involved teeth were reported either mobile (5,29.41%), immobile (1, 5.88%), and not specified by 11 (64.71%) cases. Associated teeth remained either vital(4, 23.53%), showing delayed or noresponse(1, 5.88%), or vitality was not mentioned (12, 70.59%). Munde AD et al.[18]reported delayed response with mandibular central incisors and no response to other teeth involved within the lesion.

In AOT, displacement of neighbouring teeth due to expansion of tumour is more common than root resorption.[2]Root resorption of involved teeth was observed in cases of AOT associated with dentigerous cyst. [3, 7, 9, 18] Present case too noticed root resorption in teeth 72 and 73. Rick GM[6]further emphasized that incidence of root divergence and teeth displacement is more common than root resorption. Gupta S et al. [21] noted that root resorption was not a usual finding of AOT and believed that this might suggest aggressive nature of the tumor associated with dentigerous cyst. Whereas Manjunath BS et al.[1] has reported unclarity regarding aggressive potential of AOT arising from dentigerous cyst.

On radiographs, displacement of teeth, [1, 3, 9, 11-13, 15-23] displacement of mandibular canal,[14]external root resorption,[3, 7, 9, 13, 16-21] thinning of inferior border of mandible,[7, 14, 15, 18-21] and displacement of tooth towards inferior border of the mandible was reported.[1, 11, 21, 22]Khot K et al.[7] reported absence of tooth displacement. OPG remained radiograph of choice in all the cases but one of the authors preferred PNS view for the diagnosis purpose. [9]

Depending on clinical and radiographic observation provisional diagnosis of dentigerous cyst was found to be most prevalent,[3, 7, 9, 12, 14-19,21] followed by central giant call granuloma (CGCG),[21] and unilocular ameloblastoma.[7] Aspiration of fluid from the lesion was performed in 7 cases. Among these, 3 cases[1, 14, 17] reported it as straw-coloured fluid devoid of any crystals, and 2 cases [9, 21]as clear yellow fluid. Uppada UK et al.[12] aspirated brick-red colour fluid while Rathod Vet al.[19] reported blood-mixed fluid. Incisional biopsy as diagnostic approach too was performed.[9, 15, 16]

Enucleation was favoured as primary treatment of choice, conducted under local or general anaesthesia. Surgical excision or curettage[1, 7, 22], excisional biopsy[16], and initially decompression of the lesion followed by enucleation[14] too was undertaken. Extraction [1, 7, 9, 12, 14, 19, 22] or root canal treatment [17, 18]of involved teeth along with removal of associated impacted teethwas performed.

Histologically, lining of cystic AOT may appear as a thin non-keratinized stratified squamous epithelium with nodular proliferation of spindle and cuboidal shaped epithelial cells forming sheets, strands, and whorled masses in the connective tissue stroma with sub epithelial hyalinization.[4]In accordance with observations by few of the previous researchers, [1,7,9,16]presences of AOT in the nodules of the cystic lining was evident in this case which validates the histological proof that AOT has transformed from the cyst. Rathod V et al. [19], reported that histologically the lesion was typical dentigerous cyst that was spreading toward the luminal side to form AOT-like structures, displaying the lesion's vivid histoarchitectural patterns.

Orthodontic and prosthodontic rehabilitation was recommended by Latti BR et al.[16] To address the

functional and aesthetic concerns, a removable partial denture was fabricated for our patient. Also, patient was encouraged to undergo definitive rehabilitation in the future.(Figure 4d)

Post-operative paraesthesia in the area innervated by right mental nerve was reported by Belgaumi UI et al.[22] which persisted for duration of 4 weeks before completely resolving within 1 year. In the present case, paraesthesia in the chin region was present postoperatively for 10 weeks and resolved within 15 weeks. Postoperative healing was described as normal or uneventful in most cases. There was no recurrence observed during follow-up period. [13, 14, 15, 18 - 21]

The interest and relevance of the present case is its location in anterior mandible and impacted lateral incisor which is unusual for both the dentigerous cyst and AOT as well as for order of frequency of impacted tooth. We believe that our case is the second such reported case after Moosvi Z et al. [9]This underscores the need for careful consideration of anatomical variation, precise specimen sectioning, and thorough histopathological examination, which can aid in diagnosing similar cases reported here. Given the limited number of cases reported thus far, it is challenging to speculate whether this represents a fourth type, a "hybrid variant" distinct from otherthree types of AOT.[8]However, in line with Jain MK et al.[23] we acknowledge that AOT is a 'master of disguise' and 'perfect imitator of dentigerous cyst.'

CONCLUSION

The potential for neoplastic transformation of odontogenic cyst to tumour is unpredictable. Considering the uncertainties about lesion's potential for increased aggression, we strongly recommended long-term follow-up in such cases.Timely rehabilitation is also proved to be utmost beneficial as most of these patients belong to younger age group. Rarity in report of such cases itself demand a detailed insight in its histopathologic examination to search coexistence of these two entities even though it's benign in nature.

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