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Case Report

AOT Arising from DC: Report of 5 Rare Cases with IHC and Review of Literature

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Abstract

Adenomatoid Odontogenic Tumour (AOT) is a rare benign tumour that only occurs in the maxillofacial region, accounting for 3% of all odontogenic tumours. It primarily affects females in their second decade, with a preference for the anterior maxillary region. It is divided into three types: follicular, extrafollicular, and peripheral. Follicular variations involving all four canines account for 60% and 40% of all canine variants, respectively. Dentigerous cyst is an odontogenic cyst that typically develops from impacted mandibular third teeth. The epithelial lining of a Dentigerous cyst may develop into an odontogenic tumour such as ameloblastoma. Adenomatoid odontogenic tumour (AOT) forming as a complication in a dentigerous cyst has been described as a hybrid variety of AOT. We show five such unusual examples including maxillary right premolar, lateral, canine, maxillary left canine, premolar and left deciduous lateral, canine, permanent central, premolars, and first molars in the second, third, fourth, and second decades, respectively. Thus, in this IHC, a Dentigerous cyst (DC) and AOT emerging from DC were compared using a panel of immunohistochemical markers, including cytokeratin (CK) 18 and 19, to explain the differences between the two. We also go over the clinical, radiological, histopathologic, and therapeutic aspects of these instances.

Keywords: ***Adenomatoid Odontogenic Tumor, Dentigerous Cyst, Hybrid variant***

Introduction

The odontogenic cyst's epithelial lining may develop into an odontogenic neoplasm-like ameloblastoma, or AOT. There have been just a few reports of odontogenic tumours originating from or related with odontogenic cysts. The goal of this study is to describe an unusual example of AOT that began in the wall of a Dentigerous cyst. AOT is an unusual benign odontogenic epithelial lesion. Steensland and Dreibaldt described it as pseudo adenoameloblastoma in 1905 and 1907, respectively [1]. The lesion is benign (hamartomatous) and non-invasive, growing slowly but steadily. It is less common and accounts for 2-7% of all odontogenic tumours. The odontogenic cyst's epithelial lining may develop into an odontogenic neoplasm-like ameloblastoma, or AOT. There have been just a few cases of odontogenic tumours originating from or related with odontogenic cysts. Such unique lesions must be properly diagnosed by an oral pathologist in order to meet the patient's treatment demands as best as possible. This paper will discuss a rare example of AOT that began in the wall of a dentigerous cyst. AOT is classified as 'odontogenic epithelium with mature, fibrous stroma but no odontogenic ectomesenchyme' in the WHO classification of 2005 [2]. Progenitor cells are most likely represented by dental lamina remnants. Philpsen et al. classified this syndrome into three types: follicular, extrafollicular, and peripheral [1]. The uncommon peripheral form is nearly always seen in the front maxillary gingiva. Intraosseous AOT can be observed in conjunction with unerupted permanent teeth (follicular type), particularly the four canines, which account for 60% of the total, with the maxillary canines accounting for 40%. Aside from the three categories already defined in the literature, we provide here uncommon occurrences of

a large follicular AOT or what could be a hypothetical "hybrid" form [2]. Clinical, radiographic, and histological examinations are used to diagnose odontogenic cysts. Histomorphology provides useful information, but these cysts might create overlapping characteristics, making a diagnosis difficult. In such circumstances, immunohistochemistry expression of cytokeratins can help with cyst diagnosis.

Cytokeratins (CK) or intermediate filaments are thought to be the primary indicators of epithelial cell development. Changes in their expression are not just regional, but can also be influenced by pathologic processes during histogenesis and tissue development. Cytokeratin 18 (CK 18) is a low molecular weight acidic cytokeratin that is expressed in histogenetic structures such as dental lamina and enamel epithelium, as well as respiratory and oesophageal squamous epithelium [25]. Cytokeratin 19 (CK 19) is the smallest known acidic cytokeratin that can be found in simple epithelia and basal cells of non-keratinized stratified squamous epithelia. It is also seen in practically all normal and pathological odontogenic epithelia, including Malassez cell rests, Serre cell rests, and junctional epithelia [26]. Cytokeratin (CK) expression studies have been conducted to assess diagnostic accuracy, aetiology, behaviour, and function in therapy procedures. However, discrepancies in the expression of CK patterns in these AOT and DC have been noted, which could be related to a lack of standardisation of laboratory procedures. The current work attempted to shed light on the expression of CK 18 and 19 in AOT and DC, as well as provide a brief overview of prior studies on these CK.

Case Description 1

A 16-year-old female presented with the major symptom of right cheek swelling and soreness that had been present for three months. The ache was dull in severity and came and went. Swelling was firm and extended from the distal side of the upper right central incisor to the mesial side of the same side's second premolar, which was non-tender, with a missing right first premolar and palpable right submandibular lymphnodes. Along with the impacted premolar, the mass was entirely enucleated.

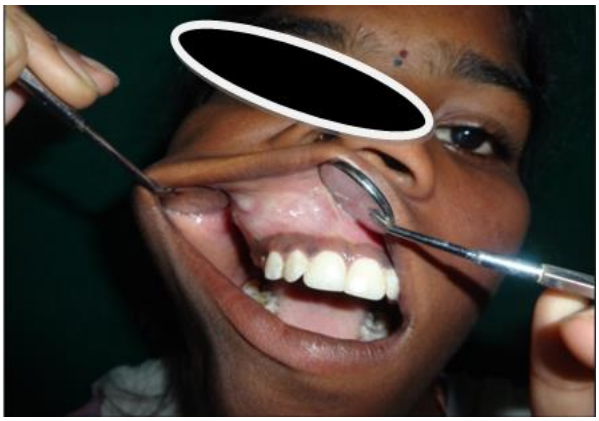


Image 1 Legend: Case 1: preoperative photograph showing the lesion

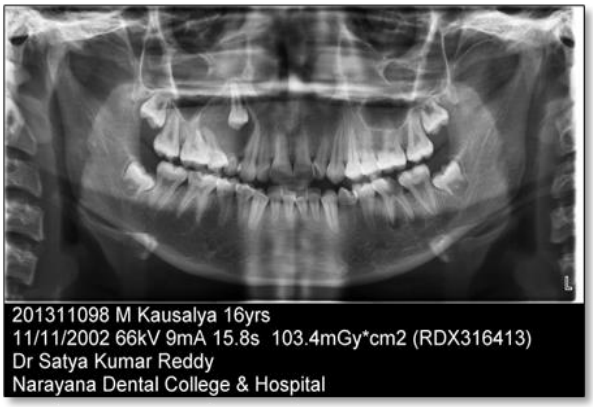


Image 2 Legend: Oral orthopantomogram showing unilocular radiolucency with well defined, margins, irt. apical regions of 13-15 with 14 impacted.

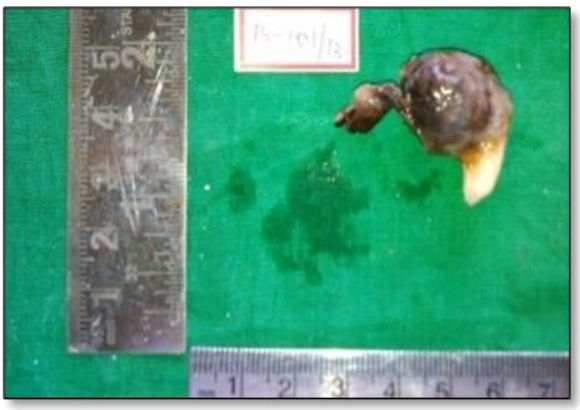
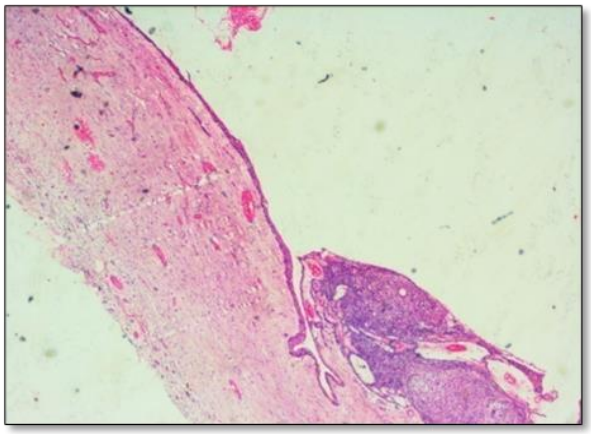


Image 3 Legend: Gross examination shows cystic lesion surrounding completely crown of a single rooted tooth.

Image 4 Legend: Cut section shows outer brownish, inner creamish with tiny nodular growths



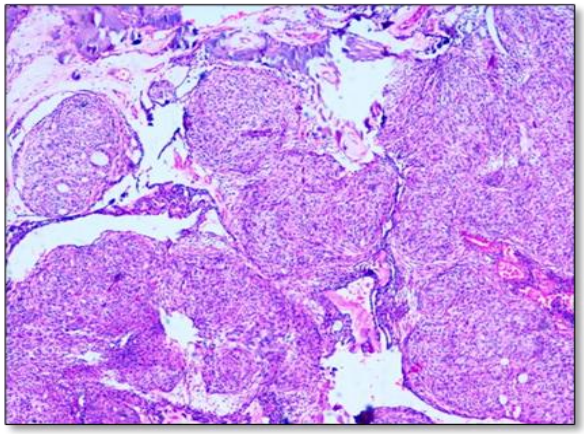


Image 5 & 6 Legend: Histopathological image shows H & E stain, x 100 for 10 x magnification, and x200 for 20 x magnification. Cystic lining of 2-4 layers thickness. A large area of luminal proliferation which is detached shows, many spindle, ovoid / cuboidal odontogenic epithelial cells arranged in the form of whorls/ sheets/ strands with scattered eosinophilic hyaline droplets and hyaline stroma.

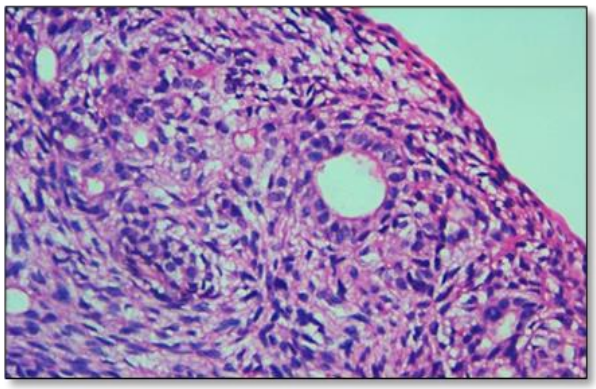


Image 7 Legend: Histopathological image shows H & E stain, x400 for 40 x magnification. Ducts lined by columnar cells and containing eosinophilic material seen.

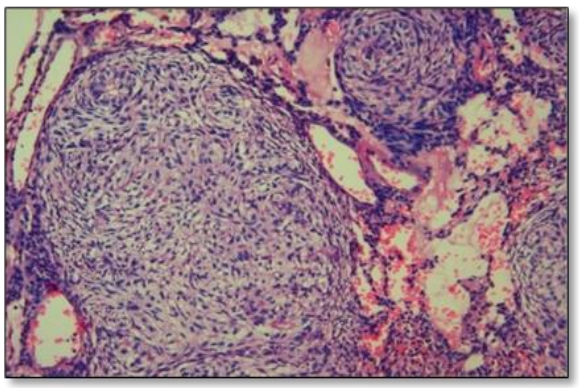


Image 8 Legend: Histopathological image shows H & E stain, x200 for 20 x magnification. Capsule is fibrocellular, spindle-shaped cells forming rosette-like.

Case Description 2

A 41-year-old female presented with the chief complaint of a swelling of the right cheek associated with pain for 3 months. The swelling was firm and well-defined, extending from the distal side of the upper right central incisor to the mesial side of the first molar anteriolaterally of the same side, obliterating the right buccal vestibule and palpating the right submandibular region.

Image 9 Legend: CASE 2: Shows swelling extends from upper right central to molar, obliterating he vestibular sulcus.

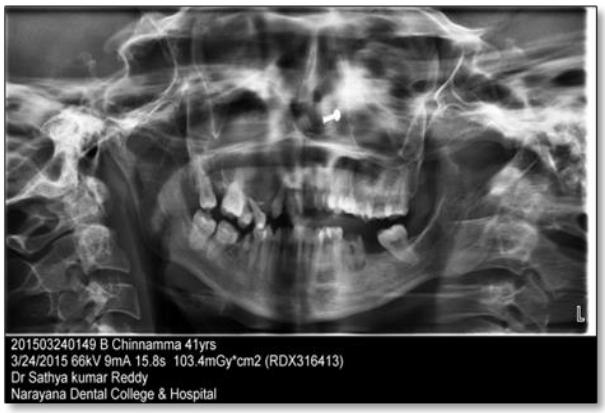


Image 10 Legend: OPG shows a large radiolucency extends from apical regions from central to first molar & displacement of anteriors

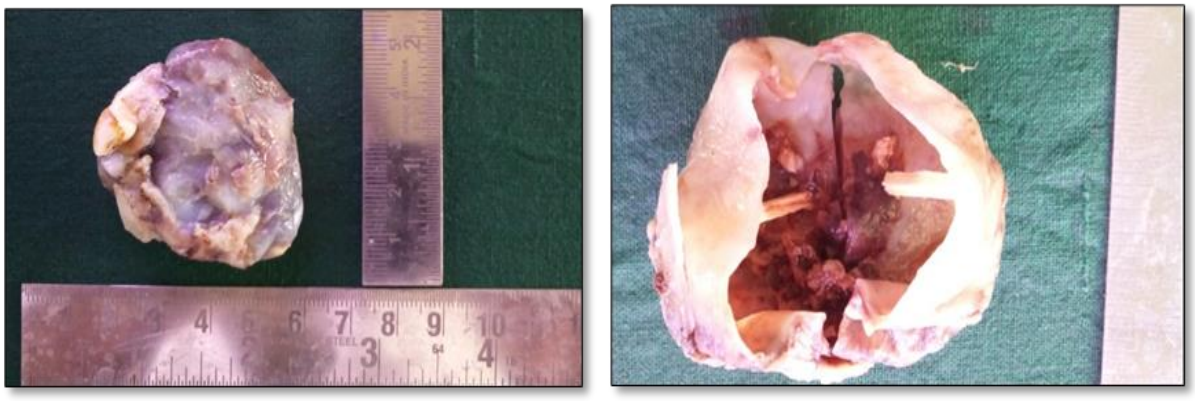


Image 11 & 12 Legend: Gross examination shows grayish brown in color with attached 13, oval in shape. Cut section shows smooth surface soft consistency which appeared cystic.

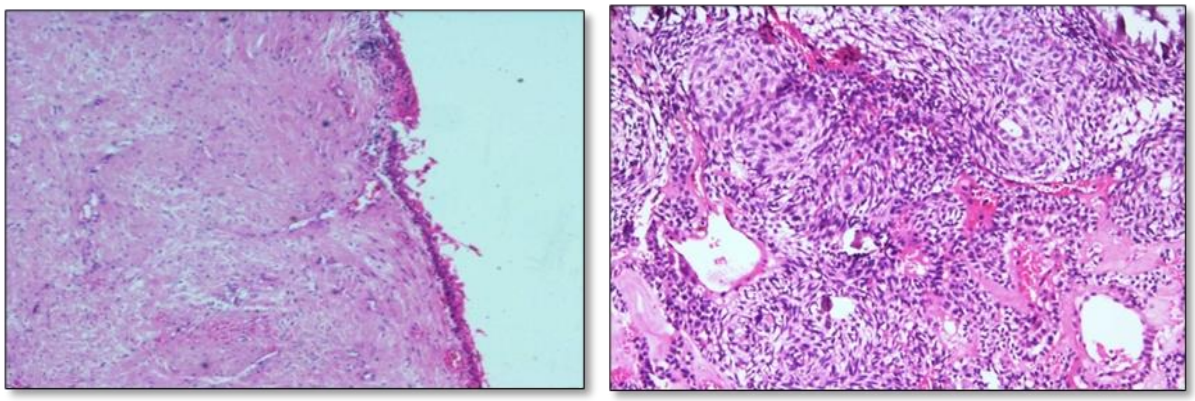


IMAGE 13 & 14 LEGEND: Histopathological image shows H & E stain, x 100 for 10 x magnification, and x200 for 20 x magnification. A cystic lining of 2-4 layers along with luminal proliferations. Ducts lined with columnar cells and containing eosinophilic material are seen scattered. Spindle cells forming rosette like structures.

Case Description 3

A 39-year-old man reported swelling of the right cheek with pain for 1 month. The swelling was firm and well-defined, reaching from the distal side of the upper right central incisor to the mesial side of the canine on the same side, with a palpable right submandibular region.

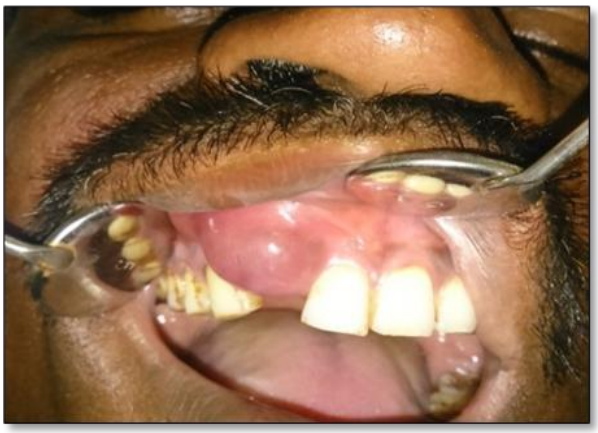


Image 15 Legend: Case 3: Shows swelling extends from distal of upper central to mesial of canine

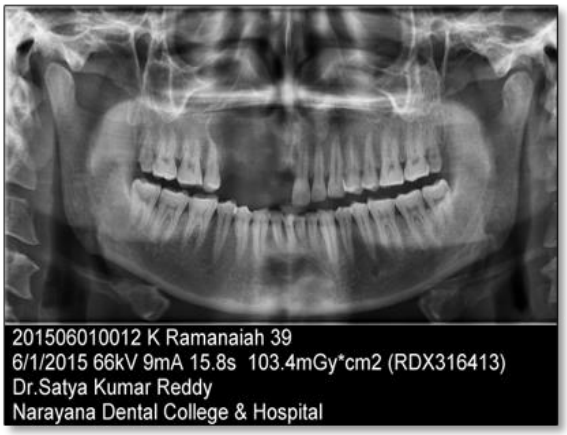
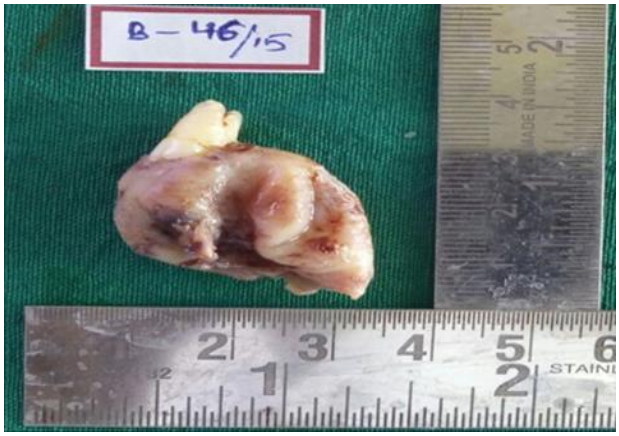


Image 16 Legend: OPG shows unilocular radiolucency with well, defined margins from apical 11-13 with 12 impacted.



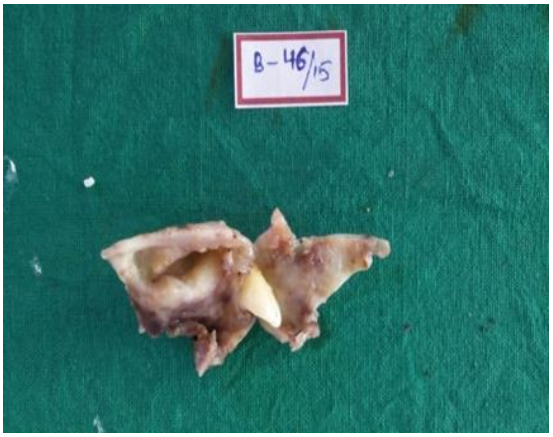


Image 17 & 18 Legend: On gross examination shows 3 x3.5 cm along with 12, thickness of 2 mm, birfurcated root of the upper right lateral incisor. Cut surface shows cyst was attached to neck of 12.

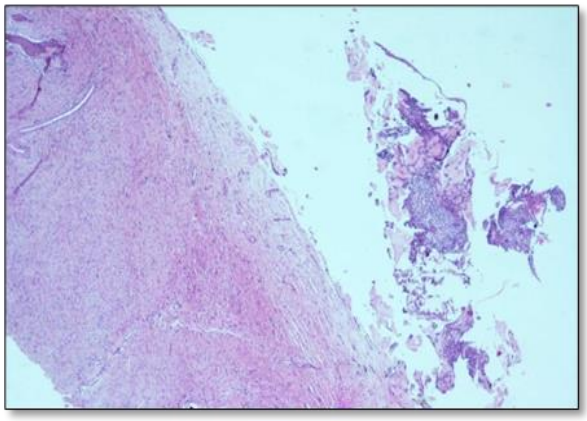


Image 19 Legend: Histopathological image shows H & E stain, x 100 for 10 x magnification, shows a discontinuous odontogenic epithelial cyst lining of variable thickness from 3-8 cell layers which is proliferating in areas. A large area of luminal proliferation which is adjacent to this.

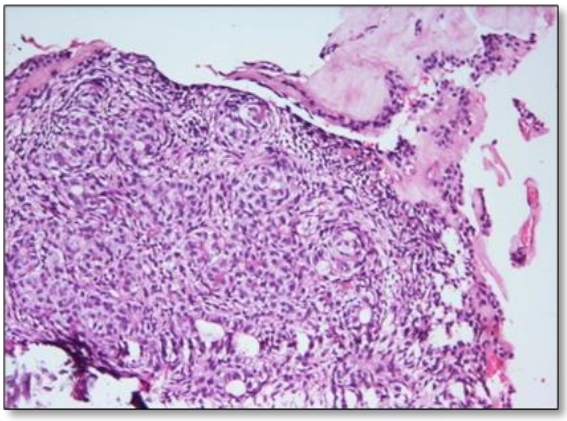


IMAGE 20 LEGEND: Histopathological image shows H & E stain, x 200 for 20 x magnification. A large area of luminal proliferation which is detached shows many spindle, ovoid / cuboidal odontogenic epithelial cells arranged in the form of whorls/ sheets/ strands with scattered eosinophilic hyaline droplets and a hyaline stroma.

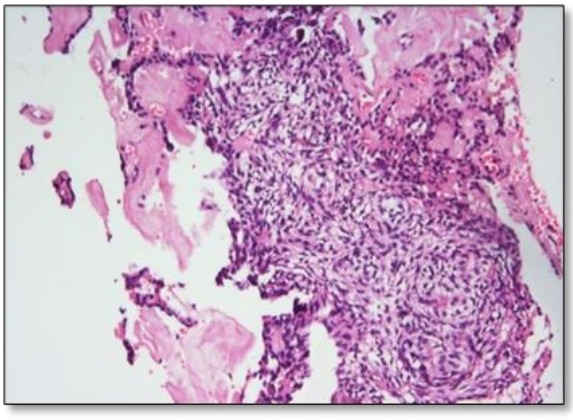


Image 21 Legend: Histopathological image shows H & E stain, x 100 for 10 x magnification. Ducts lined with columnar cells and containing eosinophilic material are also seen scattered.

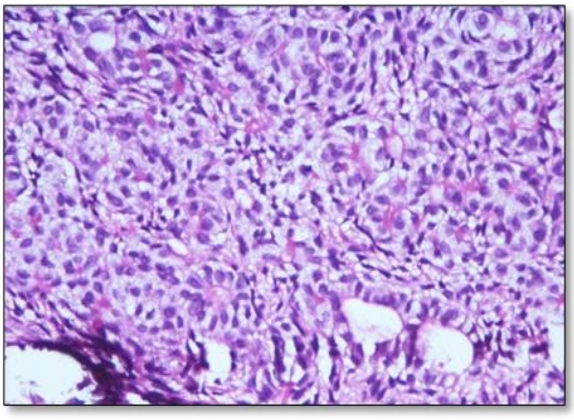


IMAGE 22 LEGEND: Histopathological image shows H & E stain, x 400 for 40 x magnification The capsule is fibrocellular with many spindle / plump fibroblasts and parallel aligned collagen bundles. Few calcification, are seen close to lining. Immature bony trabaculae are seen at the periphery of the capsule forming a discontinuous rim.

Case Description 4

A 14-year-old male presented with the major complaint of a swelling in his left side of the face that had been present for 2 years. The swelling was firm and well-defined, measuring 3x2 cm, oval, and extending from the distal side of the upper left central incisor to the mesial side of the first molar on the same side. Sessile, not attached to the underlying structure. On palpation, there is egg crackling and obliteration of the vestibular sulcus. The overlaying mucosa was non-tender and normal in colour, with obliteration of the left side of the nasolabial fold and deciduous canine movement.

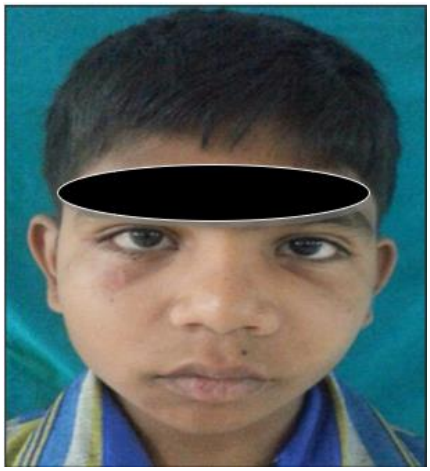


Image 23 Legend: Case 4: Swelling extends from anteroposteriorly from ala of nose to 4 cms posteriorly. Superior inferiorly 0. 5 cms below the infraorbital margin to 1 cm above the

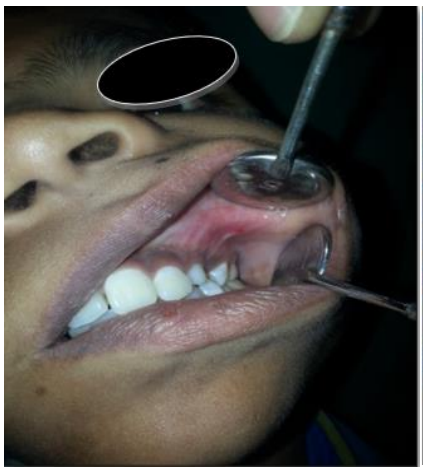


Image 24 Legend: Intraorally: obliteration of the vestibular sulcus.

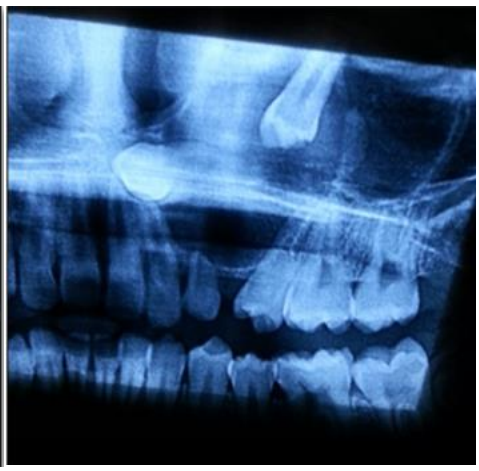


Image 25 Legend: OPG shows unilocular radiolucency extending from distal side of 21 to mesial of 25, with impacted 24.

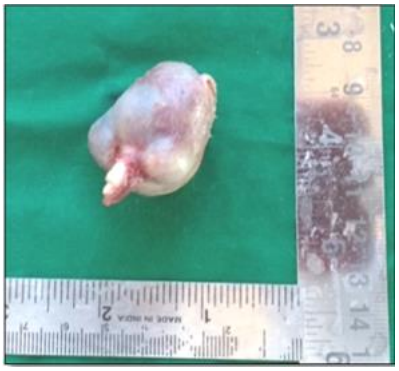


Image 26 Legend: Gross examination shows a cystic soft tissue specimen attatched 24 was received. It is about 3 x 2 cm, oval, bluish to brown, soft in consistency with smooth surface.

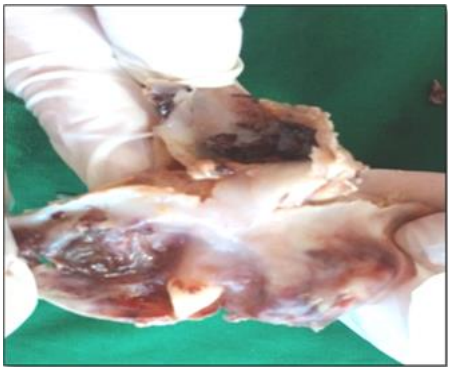


Image 27 Legend: It was cut open into 2 halves and the cystic lining is 2mm in thickness which is attatched to the neck of 24. A small nodule was seen inside the lumen which is attatched to cyst lining.

Image 28 Legend: Three bits were made and taken for processing

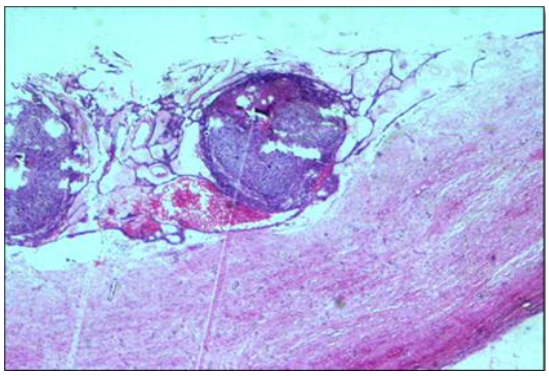


Image 29 Legend: Histopathological image shows H & E stain, x 100 for 10 x magnification They show nodules and discontinuous thick lining of adenomatoid odontogenic tumor tissue. It is composed of ovoid/ spindle vesicular cells arranged in large whorls / spherule.

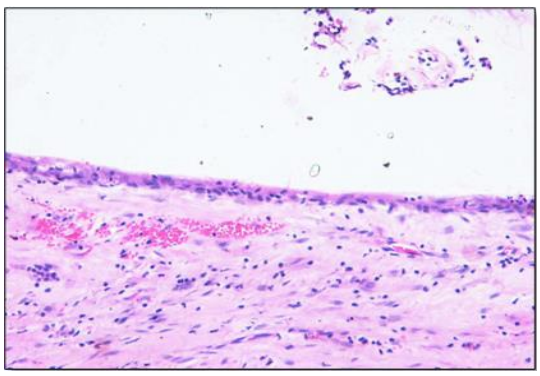


Image 30 Legend: Histopathological image shows H & E stain, x 100 for 10 x magnification. In other areas a thin odontogenic cyst lining is also seen

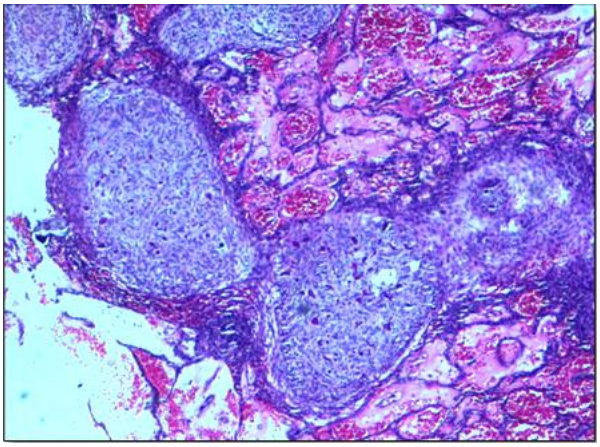


Image 31 Legend: Histopathological image shows H & E stain, x 200 for 20 x magnification. composed of ovoid/ spindle vesicular cells arranged in large whorls / spherules with scattered eosinophilic droplets, in the form of cords enclosing loose connective tissue with extravasated RBC's and many engarged capillaries.

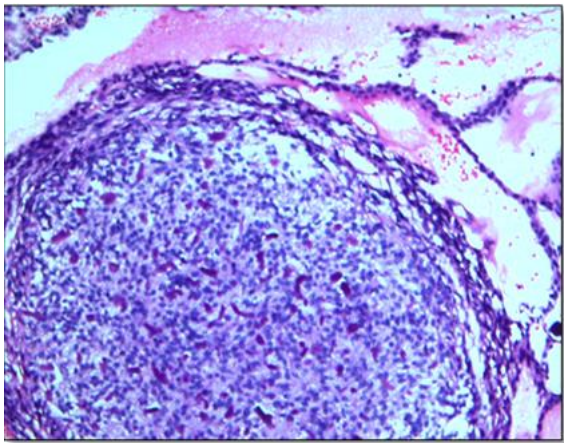


Image 32 Legend: Histopathological image shows H & E stain, x 400 for 40 x magnification. Few ductal forms with a lining of cuboidal to columnar cells enclosing eosinophilic. Spindle cells arranged in rosette pattern.

Case Description 5

A 14-year-old girl presented with the major complaint of a swelling in his left side of the face that had been present for 6 months and was solid and well-defined, measuring 3x2 cm, oval, and extending from the distal side of his upper left central incisor to the mesial side of his first molar on the same side. Sessile, not attached to supporting structures, with vestibular sulcus obliteration. The overlaying mucosa was non-tender and normal in colour, with the left side of the nasolabial fold obliterated. A tentative diagnosis of Dentigerous cyst was made based on the clinical and radiographic features in all three instances. AOT is one of the possible diagnoses. IHC was performed on all of the preceding cases, as well as 5 cases of dentigerous cyst reported in our department, using the markers CK 18 and CK 19.

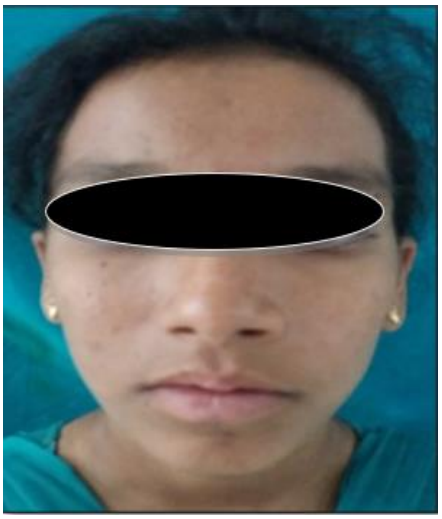


Image 33 Legend: Case 5: swelling extends anterioposteriorly from ala of the nose to 3 cms posteriorly. Superior inferiorly 1 cms below the infraorbital margin to 1.5 cm above the lower border of the mandible

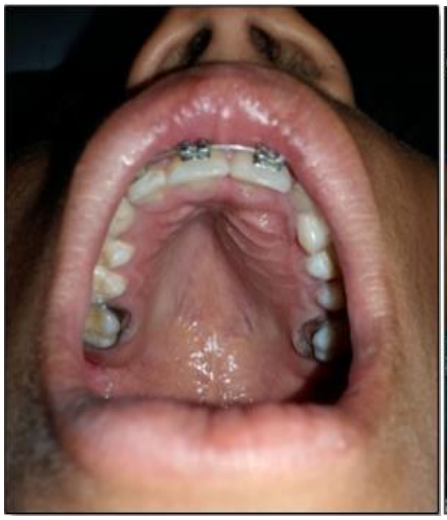


Image 34 Legend: Intraorally: obliteration of the vestibular sulcus.

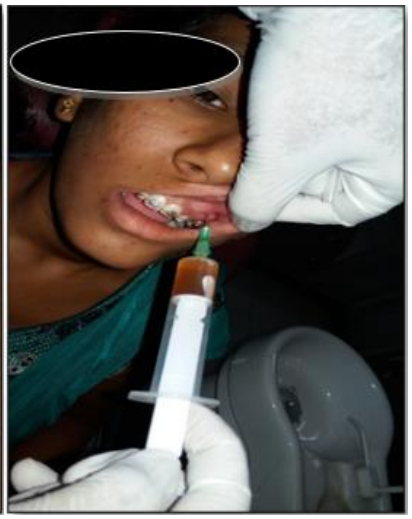


Image 35 Legend: Cystic fluid aspiration shows a brown thick fluid.

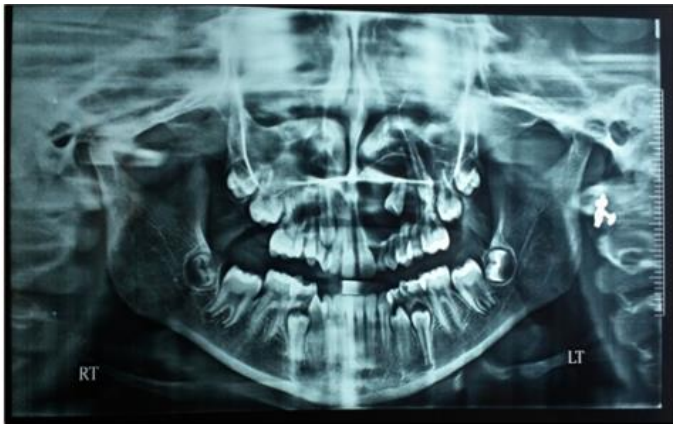


Image 36 Legend: OPG shows OPG shows unilocular radiolucency extending from 21-25 region with impacted 23.

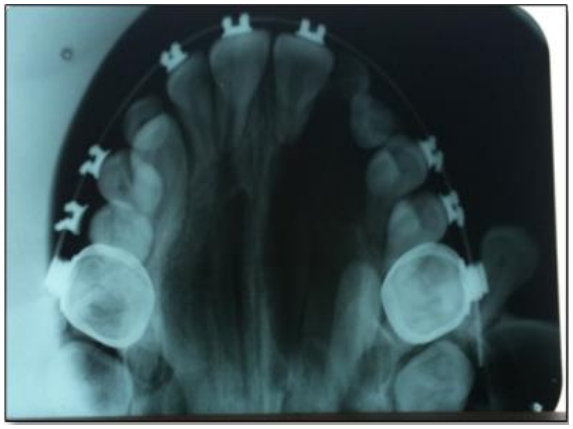


Image 37 Legend: Occlusal radiographs shows impacted 23 with radiolucency from 21-25.

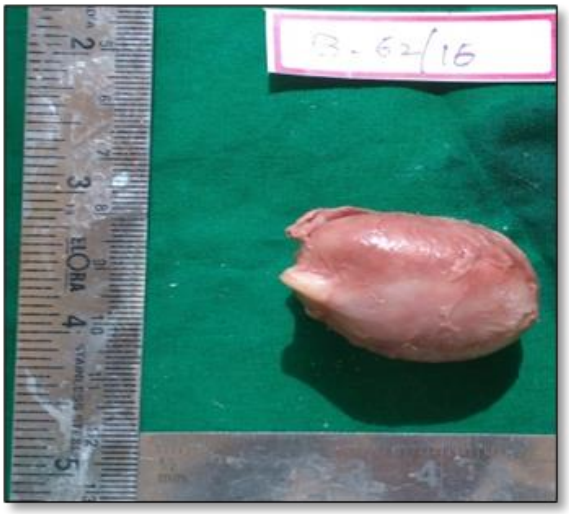


Image 38 Legend: Gross examination shows a cystic soft tissue specimen with attached tooth (23) was received. 3 x 5cms appears reddish brown, soft oval, with smooth surface. It was cut open into two halves. Cyst lining was attached to neck of the tooth and the lining thickness was about 2mm. lumen was filled with chocolate brown cheesy material. Two bits from one halve were taken for processing.

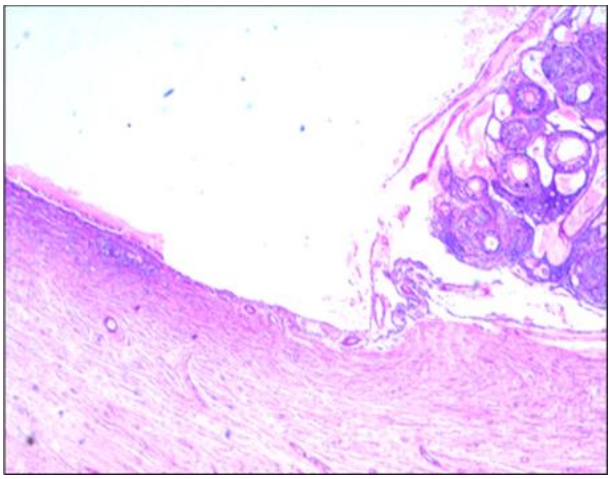


Image 39 Legend: Histopathological image, shows H & E stain, x 100 for 10 x magnification. Lesional tissue bordering the luminal surface of a cyst capsule.

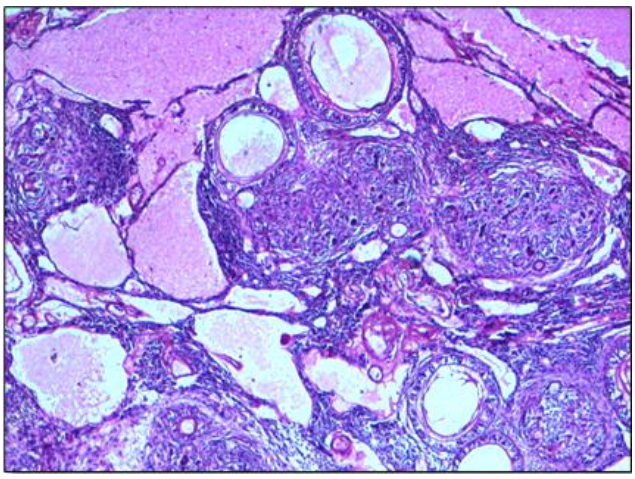


Image 40 Legend: Histopathological image, shows H & E stain, x 200 for 20 x magnification. Composed of spindle /ovoid, hyperchromatic/vesicular odontogenic epithelial cells arranged in islands, sheets, interconnecting strands and ductal forms containing with eosinophilic/ basophilic fibrillary material in the lumen.

Nomenclature of AOT

Steensland first reported AOT, a rather uncommon unique odontogenic tumour, in 1905. Dreibaldt labelled it 'pseudo adenoameloblastinoma' in 1907. Harbitz classified it as cystic adamantoma in 1915, and Ghosh described it as a maxillary adamantinoma in 1934. Staphne was the first to recognise AOT as a unique pathological entity in 1948. Bernier and Tiecke were the first to publish a case with the name 'adenoameloblastoma'. Gorlin et al. coined the term 'ameloblastic adenomatoid tumour' in 1961. Shafer et al. presented further evidence for this. Abrams et colleagues. proposed the name 'odontogenic adenomatoid tumour' in 1968. This publication was still in press when Philipsen and Brin proposed the nomenclature 'adenomatoid odontogenic tumour' in 1969. Shortly after, the latter word was used in the first version of the World Health Organization's (WHO) 'Histological typing of odontogenic tumours, jaw cysts, and allied diseases' in 1971, and it was kept in the second edition in 1992.

Unal et al. compiled a list of all AOT nomenclatures described in the literature in 1995, including adenoameloblastoma, ameloblastic adenomatoid tumour, adamantinoma, epithelioma adamantinum, and teratomatous odontoma. In 1999, Philipsen and Reichart provided a review based on papers published up to 1997 that revealed some intriguing epidemiological figures for this tumour. Leon et al. recently published a multicenter analysis of the clinicopathological and immunohistochemical characteristics of 39 AOT cases. Following that, adenomatoid odontogenic tumour became the widely accepted terminology, which appears to have assisted successful management of individuals with this lesion ever since [5].

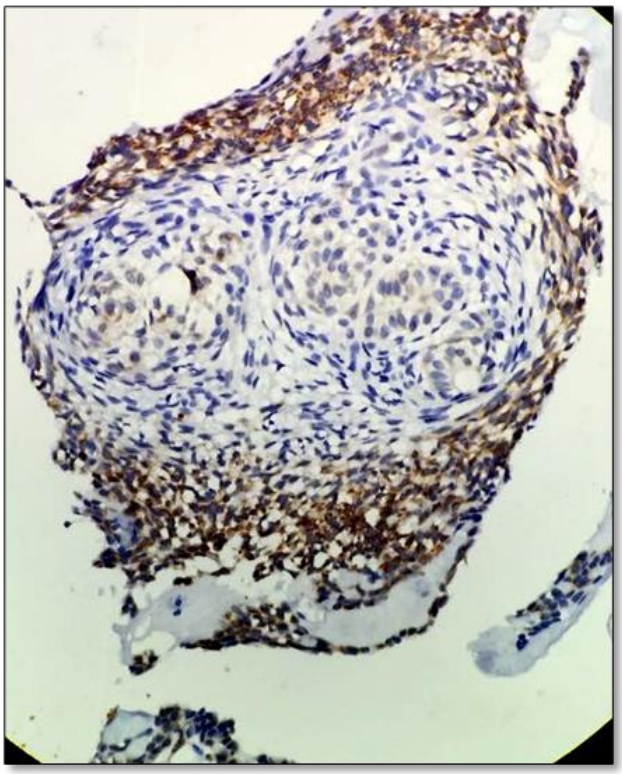


Figure 1: Photomicrograph of AOT showing cytokeratin 19 expression with intense (+++) intensity and "FOCAL" distribution arranged in whorls (40X magnification)

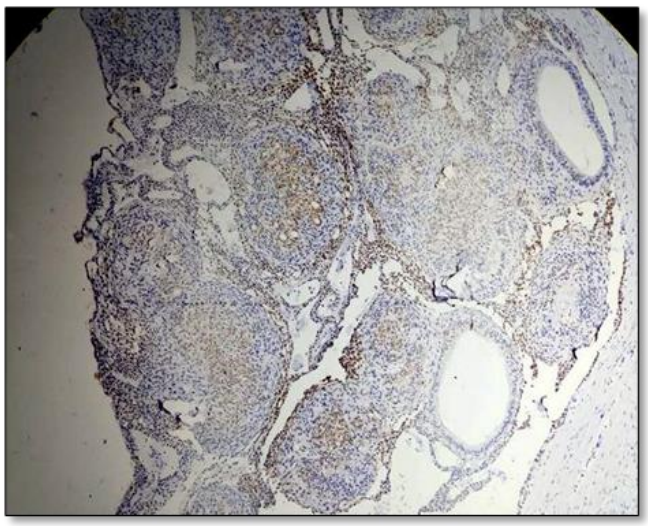


Figure 2: Photomicrograph of AOT showing cytokeratin 18 expression with mild (+) intensity and "FOCAL" distribution arranged in whorls (10X magnification)

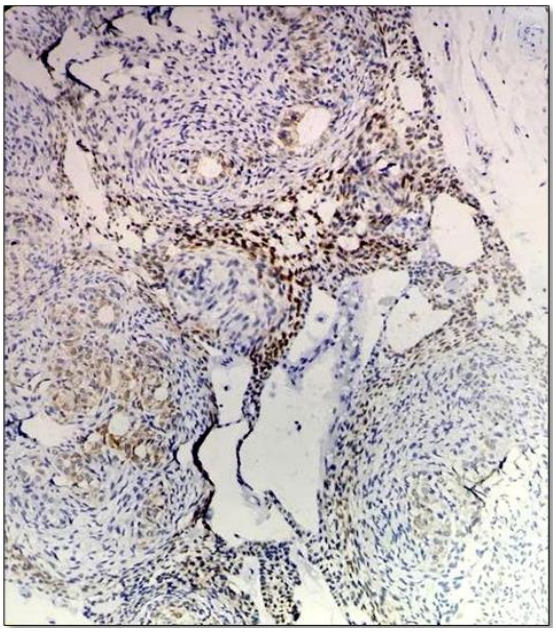


Figure 3: Photomicrograph of Spindle Cells Showing cytokeratin 19 expression with Mild [+] And Intense [+++] Intensity and "FOCAL" distribution Which Are Arranged in Ducts (10X)

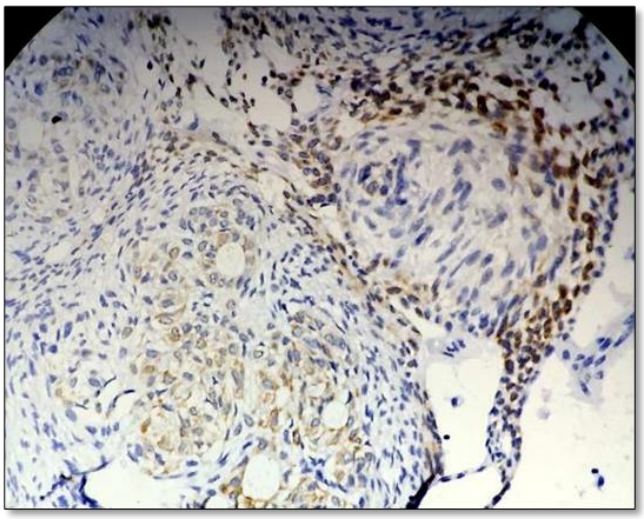


Figure 4: Photomicrograph of Spindle Cells Showing cytokeratin 19 expression with Mild [+] And Intense [+++] Intensity and "FOCAL" distribution Which Are Arranged in Ducts (40X)

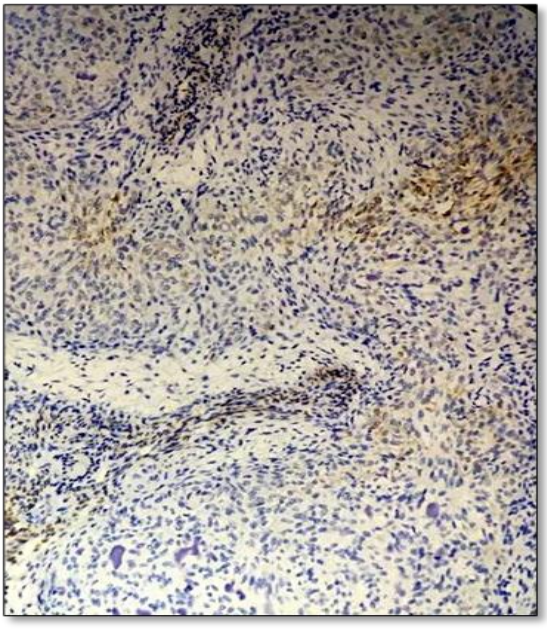


Figure 5: Photomicrograph of Spindle Cells Showing cytokeratin 19 expression with. Mild [+] And Intense [+++] Intensity and "FOCAL" distribution Which Are Arranged in Strands(10X)

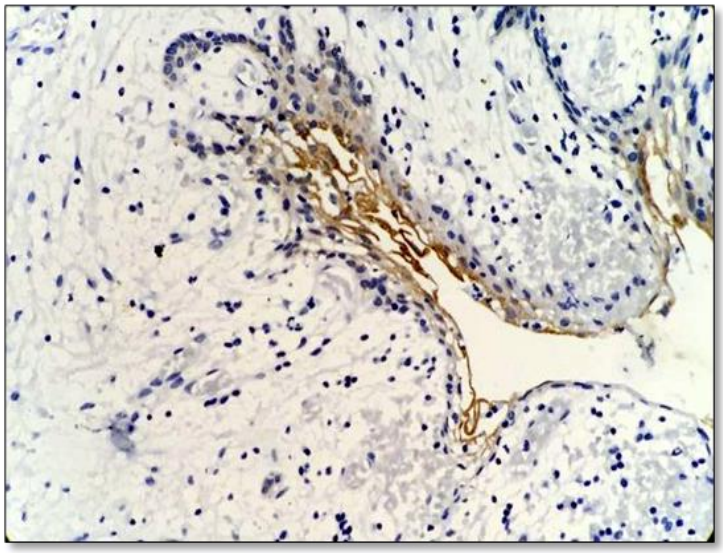


Figure 6: Photomicrograph of Spindle Cells Showing cytokeratin 19 expression with Intense [+++] Intensity and "FOCAL" distribution Which Are Arranged in Strands(40X)

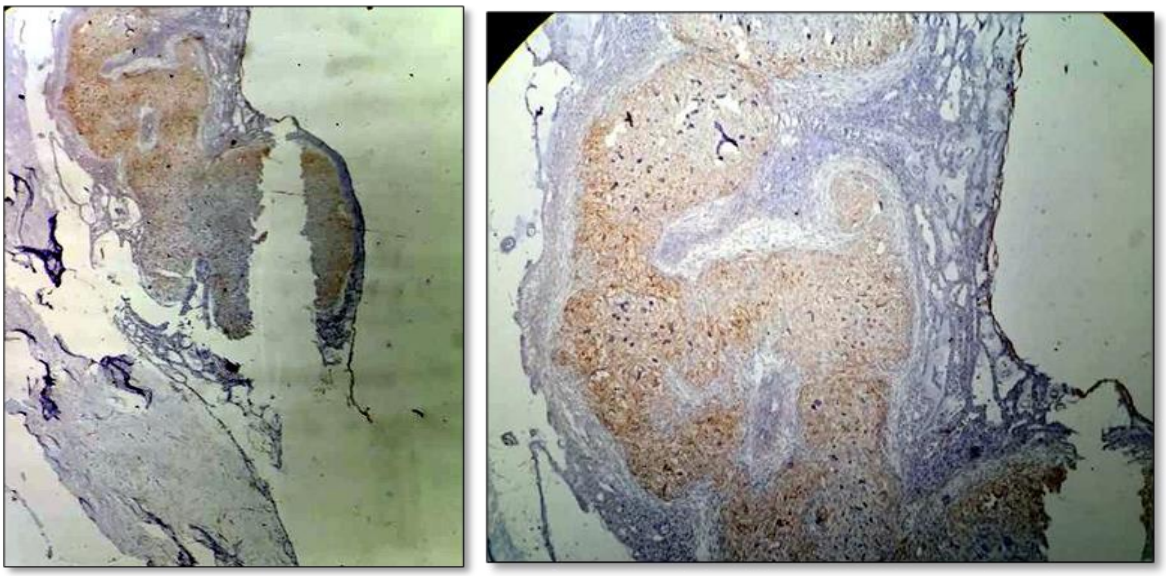


Figure 7 & 8: Photomicrograph of Spindle Cells Showing cytokeratin 18 expression with Mild [+] Intensity and "ALL" distribution (10X)

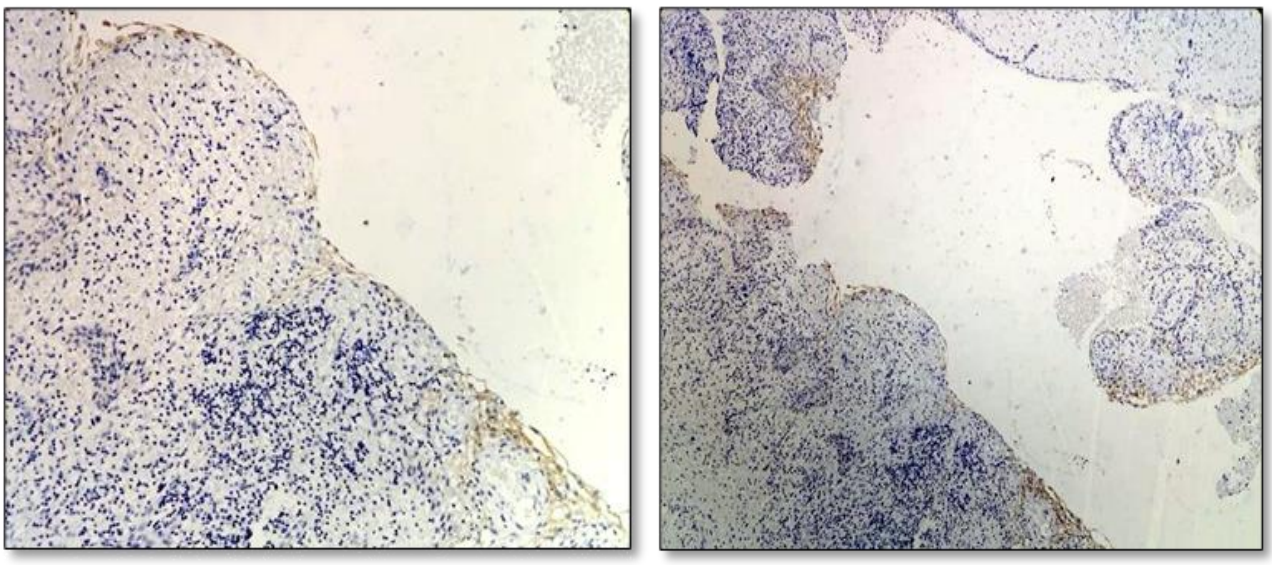


Figure 9 & 10: Photomicrograph of Reduced Enamel Epithelial Lining Showing cytokeratin 18 expression with Mild [+] Intensity and "ALL" distribution (10X)

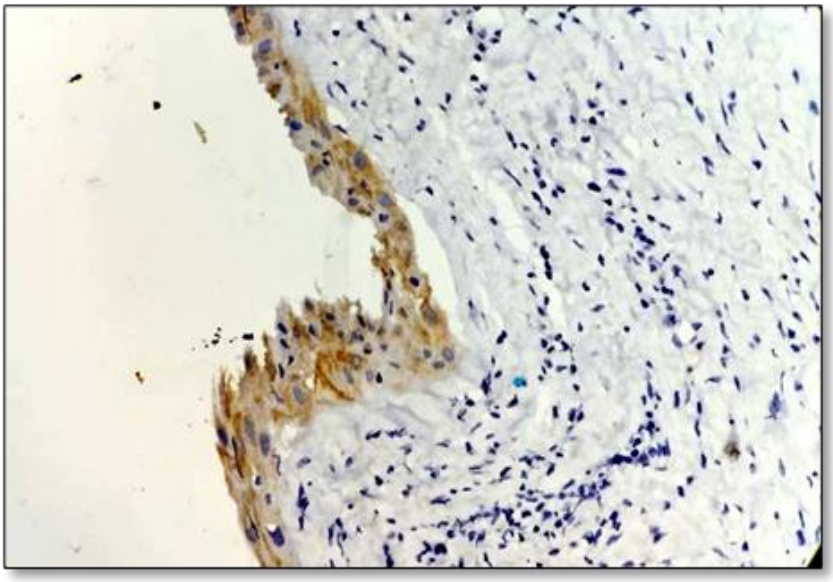


Figure 11: Photomicrograph of Reduced Enamel Epithelial Lining Showing cytokeratin 18 expression with Moderate [++] Intensity and "ALL" distribution (40X)

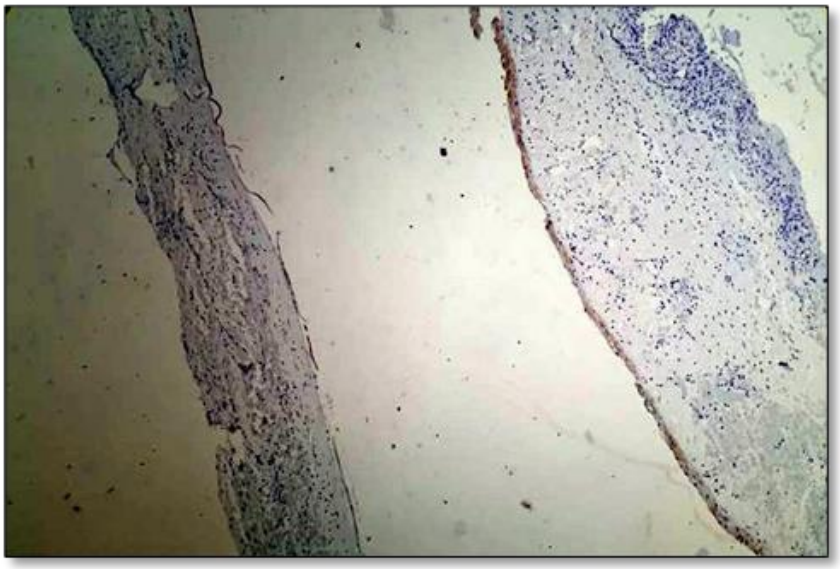


Figure 12: Photomicrograph of Reduced Enamel Epithelial Lining Showing cytokeratin 18 expression with Moderate [++] Intensity and "ALL" distribution (10X)

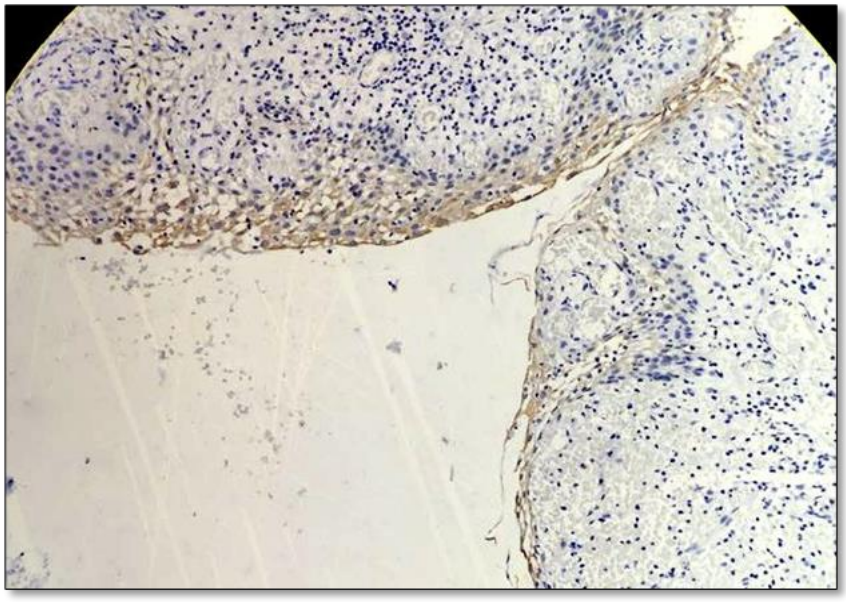


Figure 13: Photomicrograph of Reduced Enamel Epithelial Lining Showing cytokeratin 19 expression with Mild [+] Intensity and "ALL" distribution (40X)

Table: Reported cases of AOT arising from DC

S. No	References	Age/Sex	Race	Year	Site	Features
1	Valderrama	16/F	Philippino	1988	Maxilla	Unilocular radiolucency, surrounding tooth 14 crown
2	Warter et al.,	8/M	Nigerian	1990	Maxilla Sinus	Unilocular radiolucency, surrounding tooth 13 crown
3	Tajima et al.,	15/M	Japanese	1992	Maxilla	Well defined radiopaque mass and crown of unerupted 28
4	Garica-Pola et al.,	12/M	Spanish	1998	Maxilla	Unilocular radiolucency, surrounding tooth 23
5	Bravo et al.,	14/F	Not stated	2005	Maxilla	Unilocular radiolucency, surrounding tooth 23 crown
6	Nonaka et al.,	13/F	Brazil	2007	Maxilla	Unilocular radiolucency with few radiopaque areas 23 and 24
7	Chen et al.,	15/F	Chineese	2007	Maxilla	Impacted 23
8	Sandhu et al.,	25/F	Indian	2010	Maxilla	Impacted 13
9	J Baby John, Reena Rachel john	38/F	Indian	2010	Maxilla	Impacted 27
10	Khot and Vibhakar	17/F	Indian	2011	Maxilla	Impacted 33
11	Zama Moosvi	13/F	Indian	2011	Mandible	Impacted 32
12	Anita Dnyanoba Munde et al	20/F	Indian	2013	Mandible	Impacted 33
13	Vikramjeet Singh et al.,	15/F	Indian	2012	Maxilla	Impacted 13
14	Anisha Agarwal et al.,	15/F	Indian	2012	Maxilla	Impacted 23
15	Sushruth Nayak et al.,	32/M	Indian	2012	Mandible	Impacted43
16	Latti BR, Kalburge JV	15/F	Indian	2013	Mandible	Impacted 33
17	Harish Saluja et al.,	18/F	Indian	2013	Mandible	Impacted 43
18	Shivesh Acharya	14/F	Indian	2014	Maxilla	Impacted 13
19	Ludmila De Faro Valverde et al	17/F	unknown	2014	Maxilla	Impacted 23
20	Sumit Majumdar et al.,	14/F	Indian	2014	Maxilla	Impacted 23

Features

AOT is an odontogenic epithelial tumour with a variable number of ductlike structures and lumina of varied widths (often lined by hyaline rings), as well as varying degrees of stromal inductive change. It is a rare, benign, asymptomatic, slow-growing tumour that tends to originate in the anterior part of the maxilla. It accounts for 3% of all odontogenic tumours. It is more common in young people, with two-thirds of all occurrences occurring between the ages of 10 and 19 years. Females are about twice as likely as males to be affected [10]. When geographic/ethnic factors are considered for gender distribution, differences between Asian and non-Asian races were identified. Asian AOT cases (reported from Japan, India, China, Thailand, Taiwan, Sri Lanka, and Malaysia) indicate a female: male ratio of 2.3:1. When examples from Sri Lanka and Japan are independently considered, the ratios are 3.2:1 and 3.0:1, respectively [5].

The histology of all AOT variants is very similar. The WHO histopathological classification of AOT classified it as "a tumour of odontogenic epithelium with ductlike structures and varying degrees of inductive change in the connective tissue." The tumour is adequately encapsulated and behaves similarly benignly [10]." The tumour may be partially cystic, and the solid lesion may be evident only as lumps in the wall of a big cyst in rare situations. AOT is defined as "odontogenic epithelium with mature, fibrous stroma but no odontogenic ectomesenchyme [5]."

Some odontogenic cysts have been linked to odontogenic tumours, or the cyst's epithelial lining has been linked to odontogenic neoplasms such as ameloblastoma or AOT. Because neoplastic and hamartomatous lesions can develop at any stage of odontogenesis, odontogenic tumours with epithelial and mesenchymal components may form within the odontogenic cyst. Garica-pola et al. described an adenomatoid odontogenic cyst proliferating in the epithelial border of a dentigerous cyst [1].

The tumour appears as an intra-extraoral swelling in the maxilla and is sometimes referred to as a "two-thirds tumour" because it occurs in the maxilla in about two-thirds of cases, young females in two-thirds of cases, an unerupted tooth in two-thirds of cases, and canines in two-thirds of cases [3].

In 96% of instances, this tumour appears as an intraosseous lesion (central type). Lesions that are extraosseous or peripheral account for less than 4% of all lesions. Intraosseous AOT is classified radiographically as follicular (pericoronal) or extrafollicular (extracoronal).

AOT appears in three clinic-topographic variants, according to Philipsen and Reichart: the follicular type (73% of cases), which has a central lesion associated with an embedded tooth; the extrafollicular type (24% of cases), which has a central lesion but no connection with the tooth; and the peripheral variant (3% of cases). Because the histogenesis of AOT is unknown, there has been a long discussion over whether it represents abnormal hamartomatous development or a real benign tumour [3].

Difference Between AOT Arising from DC and DC

The cyst's form and placement around the crown of an unerupted tooth in this case were characteristic of a dentigerous cyst. Some think they come from the odontogenic epithelium of a dentigerous cyst. As a result, the idea that follicular AOT is caused by a reduction in the enamel epithelium that lines the follicles of unerupted teeth is fairly conclusive. This is backed further by morphological and immunocytochemical findings. According to the envelopmental idea, the lesions grow adjacent to or inside a nearby dental follicle [1].

If the tumour increases after cystic growth, it is certain that it originated from a dentigerous cyst. If it happens before cystic expansion, tumour tissue will cover the follicular area, and the AOT will appear as a solid tumour [1].

Some characteristics of AOT emerging from a Dentigerous cyst include being totally cystic with AOT-like growth, being attached at the CEJ, and having a greater volume of straw-colored fluid. The cystic lining is decreased enamel epithelium ie 2-4 layers / non keratinized stratified squamous epithelium or solid masses of AOT in walls of connective tissue wall or dentigerous cyst lining

may proliferate in the wall or AOT proliferation can be noticed in the lumen. It should be distinguished radiologically from a dentigerous cyst, which most commonly manifests as a pericoronal radioucency in the jaws. The dentigerous cyst encloses only the coronal region of the impacted tooth, but the AOT typically exhibits radiolucency enclosing both the coronal and radicular sides of the affected tooth. The irregularity in the cyst wall, on the other hand, may suggest the development of AOT. These lesions are generally radiolucent, but they contain fine specks of dystrophic calcifications or tooth material such as enamel, dentin, enamel and dentin, cementum, dentin and cementum, a trait that distinguishes AOT from dentigerous cyst [3].

The former is distinguished by a well-defined unilocular radiolucency encircling the crown and a portion of the root of an unerupted tooth. The latter is unrelated to an unerupted tooth, and the well-defined unilocular radiolucency is found between, above, or superimposed onto the roots of unerupted, permanent teeth. Both AOT and dentigerous cyst are benign, encapsulated lesions that are best treated with conservative surgical enucleation or curettage.

Materials and Methods

Immunohistochemistry: Formalin-fixed, paraffin-embedded tissues were sectioned at 4 microns, thickness from each block and immunohistochemically stained with the Polymer Horseradish Peroxidise (poly-HRP) detection method. This technology has numerous advantages, including'minimal background noise' and'minimal incubation time'. The 'heat induced antigen retrieval method' was used for antigen retrieval, in which tissue sections were placed in a pressure cooker with 10 mM aqueous citrate buffer (pH 6.0) and the pressure cooker was set to 120°C with full pressure. Tissue sections were then treated with antibodies to CK18 and CK19 overnight at 4°C after being incubated in 3% hydrogen peroxidase for 10 minutes to inhibit endogenous peroxidase. At room temperature, HRP-labeled rabbit anti-mouse antibody was applied to the tissue slices for 1 hour. The reaction product was created by combining tissue sections with 3, 3' Diaminobenzidine Tetrahydrochloride (DAB). After that, tissue sections were counterstained with Haematoxylin and Eosin stain and examined under a light microscope. The presence of brown end products at the region of the target antigen showed positive immunoreactivity, while the absence of staining indicated negative immunoreactivity. CK expressions were classified as negative, mild, moderate, or extreme. All stained sections were evaluated visually by three independent observers and graded as follows:

CK 18 and CK 19 intensity grading.

'+'	Negative	No staining
'+'	Mild	Staining restricted to single epithelial layer.
'++'	Moderate	More than one layer of epithelium stained but not its entire thickness.
'+++'	Intense	Staining in the entire thickness of epithelium.

The expression patterns were further assessed as "ALL" or "FOCAL" as per specified below: "ALL" Expression pattern - staining confined in entire layer of the epithelium. (Either basal, middle, upper or all the layers). "FOCAL" expression pattern - staining confined in scatter areas of the epithelium. (Either basal, middle, upper or all the layers).

Discussion

CK are components of a complex network that extends from the nucleus's surface to the peripheral cell sector, where they are inserted into various cell junctions such as desmosomes and hemidesmosomes. The presence of these CKs in tooth development lends credibility to the idea that they play an active part in the embryonic development of the dental organ, and hence their expression in odontogenic cysts and tumours has been studied by many authors. Keratin expression patterns can be used to study a cell's identity as an epithelial cell as well as its many stages of development. Numerous biomedical investigations have proved the value of CK 18 and 19 in identifying odontogenic epithelium, and thus in cases where an odontogenic origin of neoplasms or cysts is suspected, they have been proven to be a useful aid in diagnosis [27].

IHC For AOT:

CK 18 shows positivity of all spindle cells in rosettes and some shows focal areas of mild positivity.
CK 19 focal areas of spindle cells in rosette and in whorled masses shows mild positivity.

IHC for DC:

CK 18 shows mild positivity in focal areas of reduced enamel epithelial lining and the lining epithelium continuously.
CK 19 shows mild positivity in focal areas of reduced enamel epithelial lining.

Conclusion

The current instances looked to be typical Dentigerous cysts, however detailed microscopic investigation revealed that they were the Hybrid variety of AOT. As a result, rigorous histological study is required for all enucleated cysts, which could aid in accurate diagnosis and therapy. In these circumstances, regular follow-up is essential to evaluate their behavioural pattern.

Clinical Significance

To summarise, whereas histopathological characteristics are generally regarded as the gold standard for diagnosing most lesions. Furthermore, investigations into the feasibility of a fourth type of "hybrid" type of AOT, in addition to the already defined three forms of AOT, are required. It is critical to document such occurrences in order to identify the incidence and understand the pathogenesis of this specific variety. In total, 43 cases have been recorded in the systemic search, including our five examples.

Declarations

Ethical Approval and Consent to participate

Not applicable

Funding

None

Conflicts of interest

None

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