Type – A Case report.

Hybrid Tumors: A Diagnostic Dilemma - A Rare Case Report.

Running Title: Hybrid Tumors: A Silent Transformation.

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Abstract:

Odontogenic tumors are lesions arising from odontogenic apparatus, their remnants or their derivatives that present as a combination of established lesions which have been referred by researchers as “hybrid” or “combined” lesions. The components of hybrid odontogenic tumors are often histologically identical to other odontogenic tumors such as odontogenic keratocyst (OKC), glandular odontogenic cyst (GOC), ameloblastoma and adenomatoid odontogenic tumour (AOT). Their clinical presentation ranges from non-invasive cysts or hamartomas to benign and malignant neoplasms that vary greatly in their tendency for expansion and aggression. Nevertheless, such tumours have been reported in the literature for academic and research interest. However, it is still obscure whether they behave as a new entity or they solely present separate histopathologic patterns. Here, we present a rare case report of true hybrid tumour of combined odontogenic keratocyst with ameloblastoma with intermixed histopathologic patterns of both the cyst and tumour.

Key words: Hybrid tumours, odontogenic keratocyst, ameloblastoma.

Introduction:

Hybrid odontogenic tumor is defined as "A lesion showing the combined histopathological characteristics of two or more previously recognized tumours or cysts of different categories." [1], [2] Due to emerging new variants a revised classification has been updated which include hybrid odontogenic tumours, which are clinically difficult to diagnose. The histopathological variations of OKC and ameloblastoma are diagnosed as odontogenic lesions of the oral cavity. [3] There is evidence of the mutation or inactivation *PTCH* gene in aetiology of OKCs. This in turn, activates the sonic hedgehog signalling pathway resulting in aberrant cell proliferation of OKC epithelium producing hybridization. [4]

Patient Information

A 24 years male patient, reported to the department of Oral Medicine and Radiology, with a chief complaint of pain and swelling on lower left side of face since 3 months. On eliciting history, the swelling was spontaneous in onset and gradually increased to the present size with intermittent dull pain.

Clinical description:

Extra oral examination revealed a diffuse swelling on left side of face extending superior-inferiorly from ala tragus line to 2cm below the inferior border of mandible and medio-laterally from left corner of lip to angle of mandible approximately measuring 5 x 4 cm. On palpation, it was soft to firm in consistency, tender and expansile in nature. The overlying skin was normal, pinchable and febrile. Intraoral examination revealed, a solitary diffuse swelling on the left side extending antero-posteriorly from distal aspect of 36 to retromolar area and supero-inferiorly from free gingival margin to buccal vestibule. On palpation, it was soft to firm in consistency, tender with obliterating the buccal plate (Shown in figure 1a and 1b). A provisional diagnosis of benign cyst /tumor in relation to37 to retromolar area was given and dentigerous cyst / odontogenic keratocyst were considered as differential diagnosis.

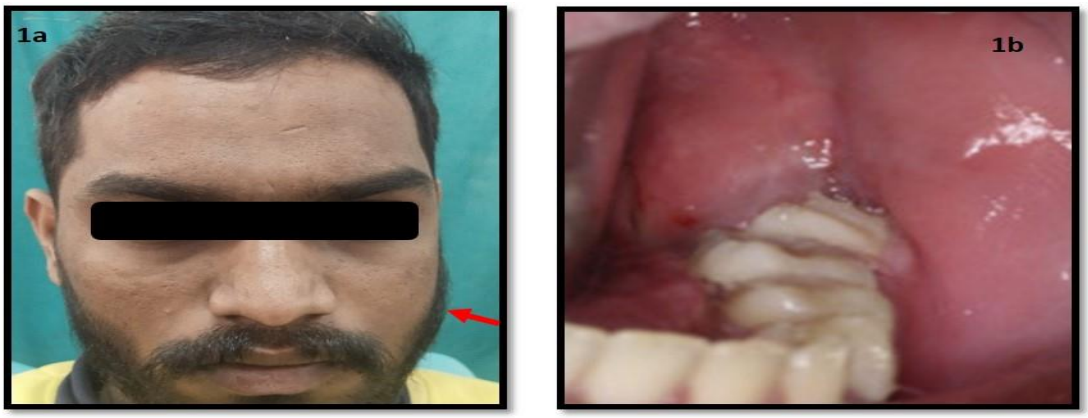

Figure 1a and 1b.Extra oral image showing diffuse swelling on left side of face and Intraoral image showing reduced mouth opening with partially erupted 38.

Diagnostic assessment

Patient was subjected for panoramic radiography, which showed a well-defined multilocular radiolucency in periapical area of 37 and 38 with scalloped and corticated borders, extending into the ramus approximately 4x3cm in dimensions. Internal structure was radiolucent with straight septa. The distal drifting of 38 was seen with resorption of distal root of 37. (Shown in figure 2a) A characteristic soap bubble appearance was appreciated near dilacerated mesial root of 38 (Shown in figure2b).On further investigations, CBCT of paraxial section showed thinning and perforation of lingual cortex along with displacement of mandibular canal towards the buccal cortex (Shown in figure 2c). Coronal section showed a well-defined oval hypodensity in the periapical area around 37 with scalloped corticated borders. (Shown in figure 2d). Radiographic differential diagnosis of Odontogenic Keratocyst, Ameloblastoma, and Odontogenic myxoma was made.

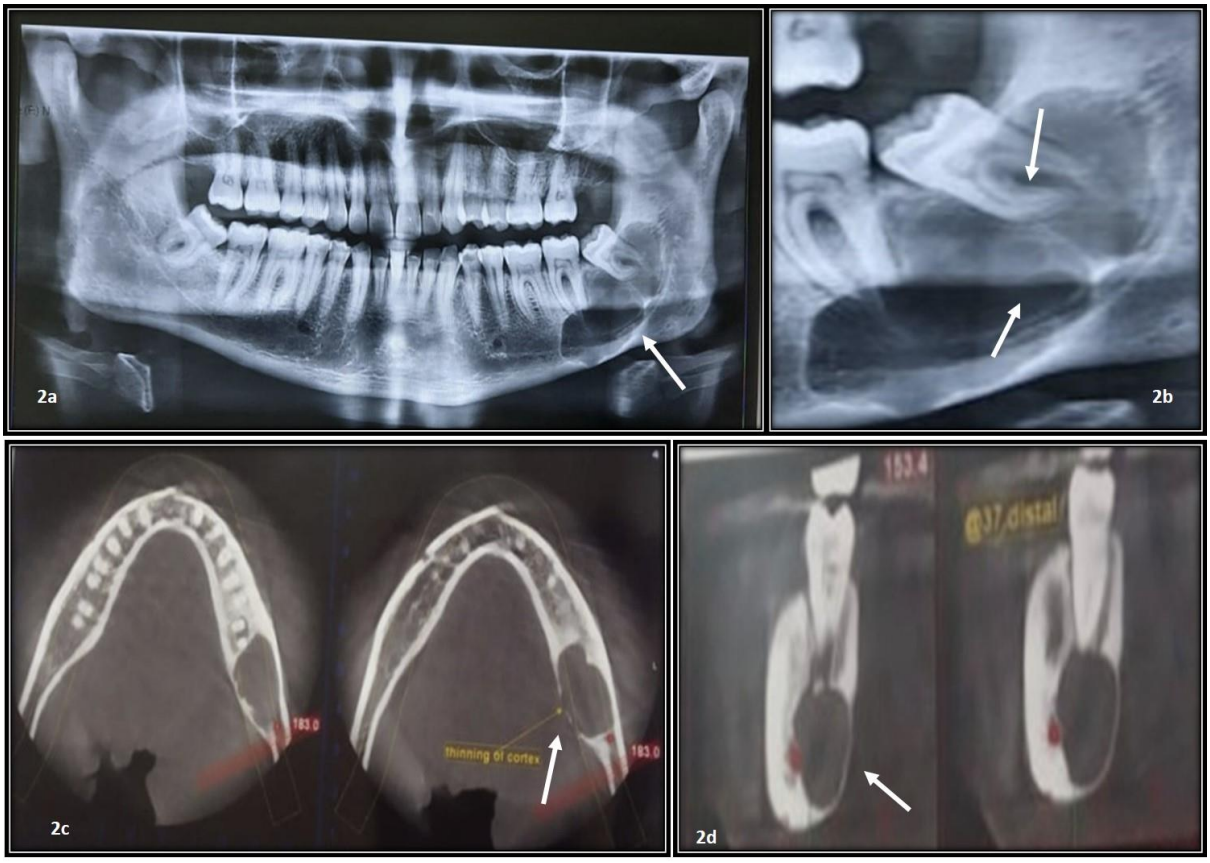

Figure 2.a. OPG shows a well-defined multilocular radiolucency with scalloped and corticated borders in periapical area of 37 and 38. **Figure 2.b.** OPG-cropped image showing soap bubble appearance withdilacerated mesial root of 38. **Figure 2.c.** CBCT in Para-axial section shows thinning and perforation of lingual cortex along with the displacement of mandibular canal towards the buccal cortex. **Figure 2.d.** CBCT in Axial image showing the well-defined hypodense area with scalloped corticated border in relation to 37.

Therapeutic intervention:

An incisional biopsy was done which showed a cystic lumen lined by parakeratinized stratified squamous epithelium with picket fence appearance, palisading, hyperchromatic

nuclei and reversal of polarity. The capsule showed loosely arranged collagen fibres, cholesterol clefts and chronic inflammatory cell infiltrate. A histo-pathological diagnosis of infected odontogenic keratocyst was given (Shown in figure 3a1,a2). After complete blood investigations, a surgical enucleation of cyst was done which showed similar features as seen in incisional biopsy along with stellate epithelium like cells resembling amelobatomatous epithelium and satellite cysts in connective tissue which is characteristic feature of Odontogenic Keratocyst. Based on the histopathological findings, a final diagnosis of Odontogenic Keratocyst with Ameloblastic Transformation with respect to 37 and 38 was made (Shown in figure 3b1,b2, b3, b4). Patient was prescribed Capsule Amoxicillin 500 mg twice a day for 5 days and Tablet Ibuprofen twice a day for 5 days.

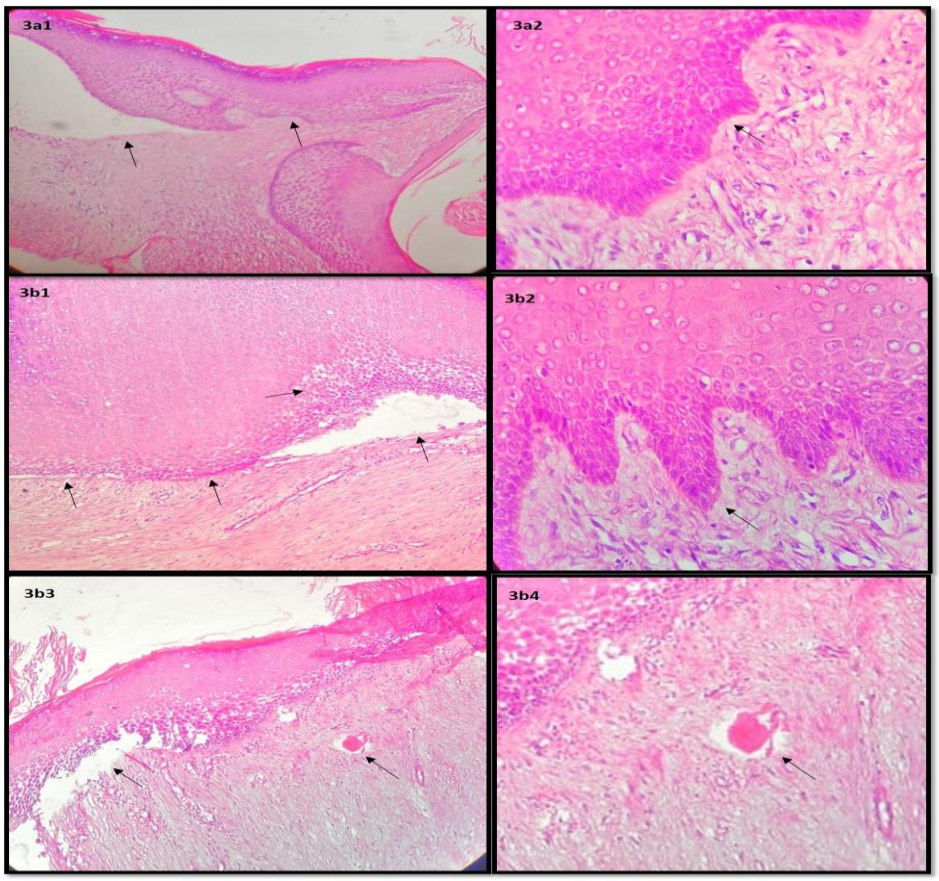

Figure 3.a1, a2: H and E section of Incisional biopsy specimen shows basal cell layer with picket fence appearance, reversal of polaritywithabundant cholesterol cleftsin connective tissue. **Figure 3.b1, b2, b3, b4:** H and E section of excisional biopsy specimen shows mixed features of tombstone appearance and with stellate epithelium like cells resembling amelobatomatous epithelium and satellite cysts in connective tissue which is characteristic feature of Odontogenic Keratocyst.

Follow up and outcome

Patientwas kept under observation with periodic recall after one month and follow up for 1 year with no signs of recurrence and had good prognosis. The time line from the history till treatment plan and follow up is given in Table 1.

1.	History given by patient	Pain and swelling on lower left side of face since 3 months.
2.	Clinical description	Extra oral - diffuse swelling on left side of face. Intraoral - reduced mouth opening with partially erupted 38.
3.	Provisional diagnosis	Benign cyst /tumor in relation to 37 to retromolar area (based on clinical findings)
4.	Diagnostic assessment	Hematological Investigations. Radiographic Investigations-OPG and CBCT Incisional biopsy-H and E staining
5.	Radiographic differential diagnosis	Odontogenic Keratocyst, Ameloblastoma, and Odontogenic myxoma.
6.	Histopathological diagnosis after incisional biopsy	Infected odontogenic keratocyst
7.	Surgical intervention	Surgical enucleation of cyst.
8.	Final diagnosis after excisional biopsy	Odontogenic Keratocyst with Ameloblastic Transformation with respect to 37 and 38.
9.	Therapeutic intervention	Pre-surgical medication: Capsule- Amoxicillin 500 mg b.i.d. for 3 days. Post- surgical medication: Capsule Amoxicillin 500 mg b.i.d. for 5 days and Tab Ibuprofen b.i.d. for 5 days.
10.	Follow-up and outcome	Periodic recall after one month and follow up for 1 year. No recurrence. Asymptomatic till date. Good prognosis

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Table 1 - Time Line of Events

Discussions

Hybrid tumours of jaws are complex are misdiagnosed clinically hence histopathological examination plays a vital role incorrect diagnosis and prognosis. The simultaneous occurrence of ameloblastoma and OKC was first described by Siar and Ng under the name kerato-ameloblastoma (KA). KA is exceptionally rare and only 9 cases have been identified as per literature. [5, 6, 7, 8] The average age range is from 26-57 years with male predilection involving the posterior mandible, which is consistent with present case. Pain,swelling, paraesthesia and bony expansion with egg shell crackling are present but in present case, patient had pain, swelling with bony expansion. Radiographic features include – uni/multilocular radiolucency with corticated and scalloped borders,bony expansion,drifting of adjacent teeth and root resorption with characteristic "Soap bubble/honey comb" appearance which is found in present case. CBCT is a noteworthy imaging modality which demonstrates 3D view and gives an insightto the extensions in adjacent structures aiding in surgical approach hence was done.CBCT sections shows a well-defined hypodensity with scalloped and corticated borders along with thinning and perforation of cortical plates involving the mandibular canal, all findings are similar except involvement of mandibular canal. Histopathology shows columnar to cuboidal cells with reverse polarity, picket fence appearance, stellate reticulum,few dysplastic features and daughter/satellite cyst in stroma. The present case is analogous with the literature. The two types of KA exist, ameloblastoma-like KA nearly similar to papilliferous KA and OKC-like KA. The present case showed characteristics of OKC with ameloblastic changes in some portions in epithelial lining giving diagnosis of OKC like KA.Various treatment modalities include curettage, enucleation, segmental resection and hemi-mandibulectomy. In present case surgical enucleation of the cyst was donewith no recurrence till date.[8, 9, 10]Due to the high recurrence rates the need for careful management plan and prevention with post-surgical follow-up is required. This case highlights the importance of identifying accurate diagnoses for such lesions which may prompt clinical implications.

Conclusion:

Odontogenic tumors and cysts occur at any stage of odontogenesis, as they support the same embryonic derivatives and have close interrelation with each other. It's very difficult to diagnose these tumors clinically, hence challenging for the clinicians. The histopathology remains gold standard in diagnosing such rare transformations.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his/her images and other clinical information to be reported in the journal.

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