Case Report

Papilliferous keratoameloblastoma – A rare entity: A case report with a review of literature

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Abstract

Ameloblastoma is the most common odontogenic tumor which presents with a variety of histopathological patterns. Among all, papilliferous keratoameloblastoma (PKA) is a very rare type which is characterized by multiple epithelial cysts of varying size, which are lined by non-keratinized papilliferous epithelium which is filled with necrotic desquamated epithelial cells. In this study, we reported PKA with characteristic ameloblastic features in a 65-year-old male patient who presented with a swelling in the right mandibular body region. This is the seventh case of PKA to be reported in the English literature till date. Present case showed multicystic areas in incision biopsy which lead to misdiagnosis as calcifying odontogenic cyst with adenomatoid odontogenic tumor, but in excision biopsy which turned out to be papilliferous keratoameloblastoma, further in this paper we had discussed all the areas which lead to misdiagnosis of calcifying odontogenic cyst with adenomatoid odontogenic tumor. In outlook, more cases will put an insight to the behavioral aspects of this rare histological type of ameloblastoma.

Keywords: Adenomatoid odontogenic tumor, ameloblastoma, calcifying odontogenic cyst, papilliferous keratoameloblastoma

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INTRODUCTION

Ameloblastomas are common slow growing true neoplasm of jaws, which can be of solid/multicystic and unicystic type, developing from odontogenic epithelium showing variety of histological patterns.[1,2]

Recognition of various histomorphic patterns is of diagnostic significance for histopathologists because various types exhibit various rates of recurrences, although all are locally aggressive and destructive.[3,4] Among all types, papilliferous keratoameloblastoma (PKA) is a rare distinct histological variety.[1,5]

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Pindborg reported the first case of keratoameloblastoma, but later reviewing the various histomorphic types in the 1970s, he coined the term papilliferous keratoameloblastoma.[5,6] Subsequently, five additional cases of ameloblastoma with a papilliferous component were reported in 1991,[3] 1994,[7] 2002,[8] 2013,[4] and 2016.[9] We reported a case of PKA, which is probably the 6th case to document in the English literature.

CASE REPORT

A 65-year-old male patient reported to the dental hospital with a chief complaint of swelling and pain in the right

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side of the lower jaw present for 4 months. Past dental history revealed that the patient had undergone extraction of the mandibular right premolar 7 months ago due to deep caries and following that swelling had appeared in the same region.

On extraoral examination, the swelling was present from the lower jaw midline to the right side body of the mandible, measuring approximately 3 cm × 2 cm in size. The swelling extends from the midline to 1 cm anterior to the angle of the mandible on the right side anterio–posteriorly. The swelling extends from the angle of the mouth to the line joining the tragus of the ear to the lower border of the mandible superio–inferiorly [Figure 1]. The skin over the swelling appeared normal with no secondary changes. On palpation, the lesion was nontender, was firm in consistency and was noncompressible, and there was no local rise in temperature.

Intra-orally, a diffuse swelling was present on the edentulous alveolar ridge extending from the distal aspect of 31 to the mesial aspect of 47 measuring approximately 3.5 cm × 2.5 cm. The swelling extended from the lingual vestibule to the labial vestibule anterio–posteriorly. The mucosa over the swelling appeared partly erythematous and partly bluish hue, and the surrounding mucosa appeared normal [Figure 2].

Panoramic examination revealed a multilocular radiolucency extending from 33 to 46 region, with intact lower border of the mandible with root resortion of 31 and 32 [Figure 3a]. Occlusal radiograph showed buccal cortical expansion with internal multilocular radiolucency [Figure 3b]. Based on clinical and radiographic features, a differential diagnosis of odontogenic keratocyst (OKC), ameloblastoma and congenital gingival granular cell tumor was made, with a provisional diagnosis of ameloblastoma.

Incisional biopsy was taken from the right buccal vestibular region in relation to 43.

Microscopically, the lesion shows cystic lining, with basal columnar cells showing nuclear reverse polarity and cytoplasmic vacuolization, and basilar hyperplasia with hyperchromatic nuclei are seen in few areas. The overlying layer of the epithelium resembles stellate reticulum, with the surface epithelial cells demonstrating ghost cells. Focal epithelial lining shows luminal proliferation consisting of nodule of odontogenic epithelium showing rosette formation and pseudo glandular structures. Subepithelial hyalinization areas with multinucleate giant cells are evident with mature connective tissue. Based on these features, calcifying odontogenic cyst (COC) with adenomatoid odontogenic tumor (AOT) was suspected [Figure 4a and b].

After that, the patient was referred to the oral surgery department for complete excision of the lesion. Excisional biopsy was sent to the department, where the representative tissue was grossed, processed, sectioned and stained with H&E.

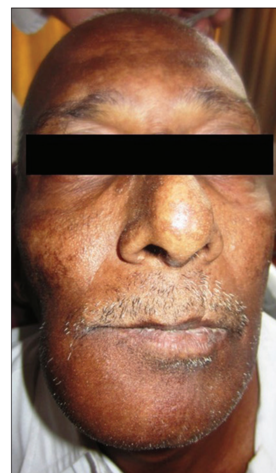

Figure 1: Clinical photograph showing diffuse swelling from midline to the right side of the mandible causing facial asymmetry

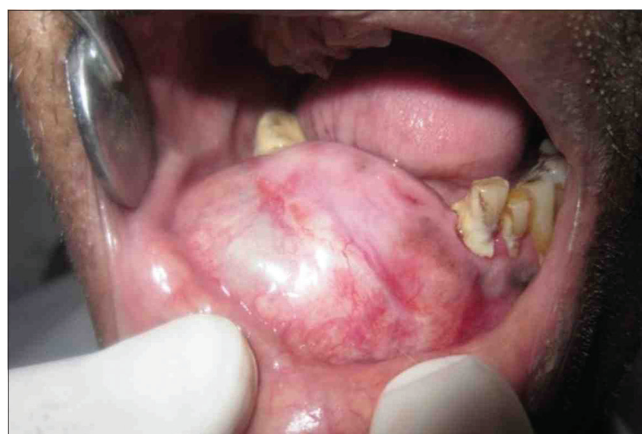

Figure 2: Clinical photograph showing diffuse swelling on the edentulous alveolar ridge extending from the distal aspect of 31 to the mesial aspect of 47

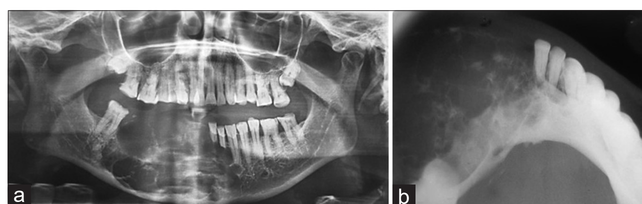

Figure 3: (a) Orthopantomograph showing multilocular radiolucency extending from 33 to 46 region, with intact lower border of mandible with root resorption of 31 and 32. (b) Occlusal radiograph showing buccal cortical expansion with internal multilocular radiolucency

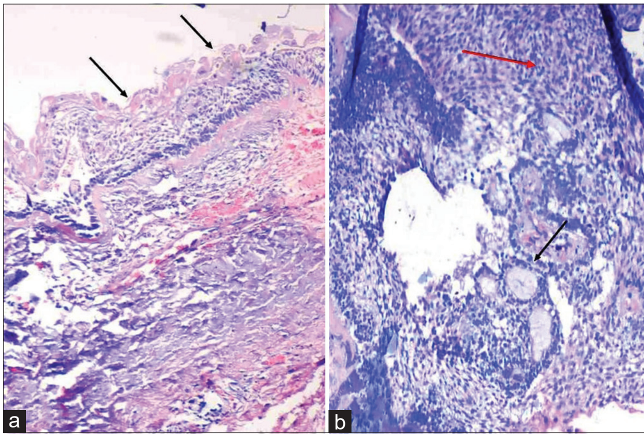

Figure 4: (a) Photomicrograph showing cystic lining with ghost cells (black arrows) (H&E, ×10). (b) Photomicrograph of the same section showing duct like structures (black arrow) with focal rosette like pattern (red arrow) (H&E, ×10)

Microscopically, the lesion was un-encapsulated consisting of solid tumor islands and multiple cystic spaces of variable size lined by a thin stratified epithelium separated by narrow bands of fibrous connective tissue. Under ×40, the cystic spaces were lined by a keratinized stratified squamous epithelium which is made up of 4–5 cells in thickness, consisting of polygonal cells with distinct cell outline and abundant eosinophilic cytoplasm with focal papillary projection into the lumen. Surface cells of the cystic lining showed loss of intercellular adherence, resulting in desquamation, and individual cell keratinization with faint nuclear outline [Figure 5a-c]. Papillary projections extending into the lumen and connective tissue were made up of 2–3 layers of cells made up of low columnar cells with sparse central cells [Figure 5d-e]. These papillary projections arising from the cystic lining are interconnected, giving a plexiform appearance [Figure 6]. Odontogenic islands are lined peripherally by tall columnar cells with hyperchromatic nucleus, showing reverse polarity, and subnuclear vacuolization and center angular cells resembling stellate reticulum are seen. Many islands showed squamous metaplasia with keratin pearl formation [Figure 7], and even focal areas showed plexiform variant [Figure 8]. Correlating histopathological features, a definitive diagnosis of PKA was made.

DISCUSSION

Ameloblastomas are highly polymorphic, benign odontogenic tumors, giving rise to many histologic variants such as acanthomatous, granular cell, desmoplastic, basal cell, keratoameloblastoma and clear cell ameloblastoma.[10,11] The cause or stimulus for these varied presentation is

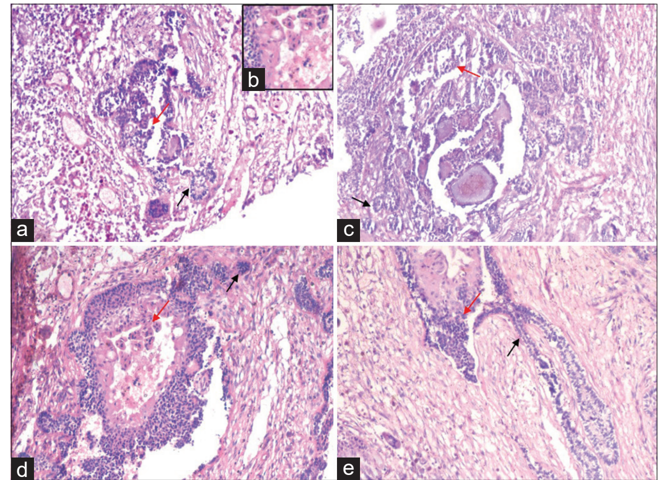

Figure 5: (a) Photomicrograph showing cystic space lined by a keratinized stratified squamous epithelium which is made up of 4–5 cells in thickness with papillary projections into the cystic lumen (red arrow) and into connective tissue (black arrow) (H&E, ×10). (b) Photomicrography showing abundant desquamated keratin bodies showing faint nuclear outline (H&E, ×40). (c-e) Photomicrography showing follicle with papillary projections into the lumen (red arrow) and into the connective tissue (black arrow) (H&E, ×20)

unknown; however, it is due to chronic irritation or attributed to the multipotential nature of odontogenic epithelium.[11]

Keratoameloblastoma is an extremely rare variant of ameloblastoma, with only 17 cases reported till 2015.[12] According to few authors, PKA is a histological subtype of keratoameloblastoma, as Whitt *et al*.[1] have classified keratoameloblastoma into four histological groups, namely, (1) papilliferous histology, (2) simple histology, (3) simple histology with OKC-like feature and (4) complex histology.

According to previous five case reports [Table 1], PKA has been reported in various age groups ranging from 26 to 76 years, with peak incidence between sixth and seventh decades, with almost equal gender distribution (male:female, 3:3). All the cases have been reported in the mandibular jaw, with molar–ramus area being the most common site. Although a clear review of the clinical symptoms is not available for most of the cases, few reported with nontender swelling and others were associated with pain. Radiographically, majority of the lesions revealed multilocular radiolucency with cortical plate expansion. The clinical history of the present case is in accordance with that of the previous literature as mentioned above.

Histologically, the tumor presented with multiple cystic spaces of varying size which is separated by fibrous

Table 1: Clinical details of present and previously reported cases of papilliferous keratoameloblastoma

Author	Age (years)/ gender	Clinical site	Radiographic	Ameloblastic features	Treatment	Follow up and recurrence
Present case	65/male	Right mandibular body	Multilocular radiolucency with labial cortical plate expansion	Yes	Wide excision of lesion	Followed up for 2 months with no recurrence
Pindborg *et al*.[1,6]	57/female	Right mandibular body and ramus	Multilocular radiolucency	No	Not reported	Unknown
Altini *et al*.[3]	76/male	Right mandibular body, angle and ramus	Multilocular radiolucency	No	Hemi-mandibulectomy	Followed up to 12 months with no recurrence
Norval *et al*.[7]	26/male	Right mandibular body, eroded buccal cortex	Lobulated radiolucency	No	Segmental resection	Unknown
Collini *et al*.[8]	62/male	Ramus and condyle of the right mandible	Irregular radiolucency with soft tissue extension and internal calcification	Yes	Hemi-mandibulectomy	Two local recurrences at 39 and 58 months
Mohanty *et al*.[4]	46/male	Right-sided angle of the mandible	Multilocular radiolucency	Yes	Unknown	Unknown
Konda *et al*.	44/male	Lower right tooth region	Well-defined unilocular radiolucent region	Yes	In toto excision of lesion	Followed up for 1 year with no recurrence

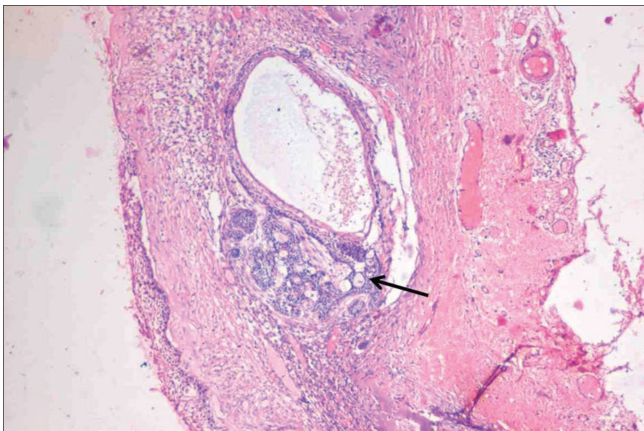

Figure 6: Photomicrography showing a plexiform appearance of papillary projection (black arrow) arising from the cystic lining extending into the connective tissue

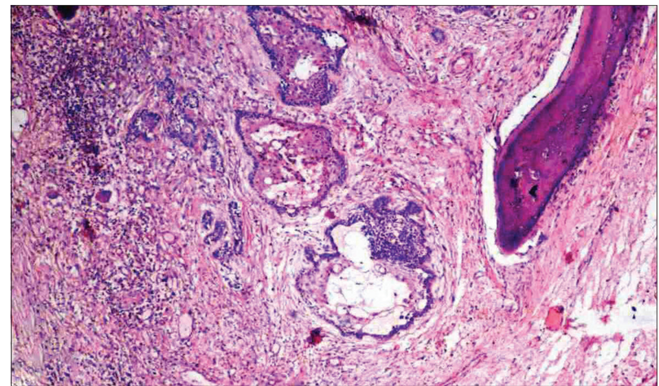

Figure 7: Photomicrograph showing tumor islands with squamous metaplasia (H&E, ×20)

connective tissue. Few cysts were lined by keratinized stratified squamous epithelium in papillary pattern, which is made up of 3–5 cells in thickness, consisting of polygonal cells with distinct cell outline and abundant eosinophilic cytoplasm; this feature is in accordance with Pindborg's case description.[6]

Out of six cases reported till now, only three cases showed convincing evidence of ameloblastoma; hence, still, there is chiasm that PKA should be represented as a separate entity. However, in our case, solid tumor islands showed histological features of ameloblastoma with predominant acanthomatous changes.

As PKA shows complex histological features, we misdiagnosed incisional biopsy as COC with AOT due to the following appearance:

- Incisioal biopsy showed single, large cystic space line by prominent basal layer of cubiodal to columnar cells which resembles ameloblast. Overlying layer is made of polygonal cells resembling stellate reticulum like cells and upper surface layer shows abundant keratin bodies with faint nuclear outline resembling ghost cells.
- The ductal structures in incisional biopsy may be due to the cross section of papillary projection, which were lined by a single layer of low columnar cells or may be due the cross section of papillary pattern. The desquamated, acantholytic cells arranged in the whorl pattern gave a rosette appearance, leading to misinterpretation of AOT-like areas of cells.

According to some authors, papilliferous nature of epithelium seems to have occurred due to loss of intercellular adherence and different rates of necrosis of individual cells in surface cells. The necrotic cells separate from the remainder epithelium, resulting in the formation of numerous pseudopapillary structures, which project into the lumen of cystic follicle.[4]

As PKA is a variant of keratoameloblastoma, we believe that the papilliferous nature of the epithelium is due to excessive and uneven proliferation of cystic epithelium because a

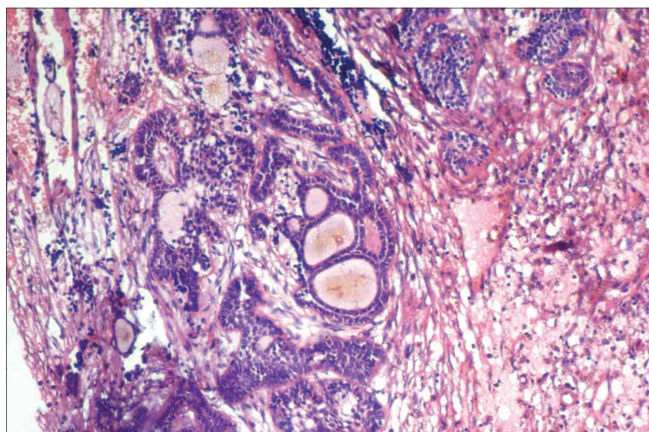

Figure 8: Photomicrograph showing tumor cells arranged in plexiform form pattern (H&E, ×20)

study done by Whitt *et al*. showed ki-67 proliferation index of 22.8%[1] in PKA, when compared with conventional ameloblastoma with ki-67 index of 16.6%[13] and 16.9%.[14]

Well-differentiated squamous cell carcinoma (WDSCC), ameloblastic carcinoma and primary intraosseous carcinoma should be accounted for histological differential diagnosis for PKA.

Absence of mitosis, varying degree of nuclear and cellular pleomorphism and other dysplastic feature and WDSCC and and primary intraosseous carcinoma.[2]

Features such as hypercellularity, hyperchromatism, loss of ameloblastic differentiation, spindling and more than two mitotic figures per high-power field, vascular invasion and neural invasion differentiate ameloblastic carcinoma from PKA.[6]

Due to a few number of cases and lack of follow up after treatment, it is difficult to evaluate whether biological behavior contrasts from other histological types of ameloblastomas. Among all the five cases reported till now, only one case recurred twice at 39 and at 58 months. The present case was followed up for 2 months with no signs of recurrence. Treatment may vary from enucleation to hemi-mandibulectomy and partial maxillectomy, but as the tumor is nonencapsulated with a locally infiltrative pattern, wide excision convoyed by close clinical follow-up is the appropriative treatment.

Further, these types of thought-provoking neoplasms should be reported to know their biological behavior with long-term follow-up.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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