Keratoameloblastoma, a Rare Separate Entity or Rare Histologic Variant? Case Presentation in a Nigerian

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ABSTRACT

Background: Keratoameloblastoma (KA) presents with histologic and pathologic features of ameloblastoma with extensive keratinization. Cases have been sparsely reported as only 17 cases have been documented in the scientific literature. As a result of its rarity, its precise clinicopathologic appearance as well as its biologic behaviour remains unclear.

Case Summary: We present a rare case of keratoameloblastoma in a 31 year old male subject with an 8-year painless firm anterior mandibular swelling that had been progressively increasing in size. Segmental mandibulectomy with reconstruction using 2.7 mm KLS Martins Recon plate was done.

Conclusion: As this tumour presents with identical clinic-pathological and radiographic features of the classic ameloblastoma, and so far the various histomorphologic types have not been proven to connote any clinical relevance to management, we see no purpose to label KA a separate entity.

Keywords: Keratinizing, ameloblastoma, rare, histologic type.

INTRODUCTION

Ameloblastoma is a daunting aggressive tumour of odontogenic epithelium that does not contain odontogenic ectomesenchyme (1, 2). While it usually occurs in the jaw bones, it also occurs, though rarely, in soft tissue areas like the buccal and sinonasal mucosae (3). Ameloblastoma has a local invasive nature and the potential for high recurrence especially if improperly managed. It is therefore regarded as 'formidable', though it is often asymptomatic and slow growing (4-8). The tumour may also metastasize and/or undergo malignant transformation (9-10). It also presents with diverse histologic patterns which may make diagnosis and management challenging.

The 2005 WHO classification (11) broadly grouped ameloblastoma into benign and malignant categories due to clinical presentation and management. The benign category comprise of solid multicystic, unicystic, peripheral and desmoplastic ameloblastoma, while the malignant category comprise of ameloblastic carcinoma and malignant ameloblastoma. Solid multicystic ameloblastoma presents with 2 main histologic types, namely follicular and plexiform types, the follicular pattern being reported as the most common type (12–14). The central stellate reticulum like cells in both types may go through numerous forms of metaplasia giving rise to different histologic sub-types such as acanthomatous, basal cell, clear cell, and granular cell (2).

Keratoameloblastoma (KA) is an odontogenic epithelial tumour that presents with histologic and pathologic features of ameloblastoma and in addition consists of areas of extensive keratinization (usually parakeratinization). The World Health Organization (WHO) classification in 1992 recognized KA as a distinct entity and categorized it as a rare histologic type of ameloblastoma (15). Although there is a general consensus on it being rare, there still remains a variance on the concept of the tumour being regarded as a distinct entity, as some authors simply regard KA as a variant of acanthomatous ameloblastoma (16, 17). Approximately 17 cases of the tumour have been reported in the scientific English literature (16–29; Table 1). As a result of its rarity, the precise clinicopathologic appearance, biologic nature and recurrence potential of KA remains unclear and is still being investigated. We therefore report the first case in our series to update cases already documented in the scientific literature and also concisely review literature on KA.

CASE REPORT

A 31-year old male subject presented in the Oral and Maxillofacial surgery clinic of the Lagos University Teaching Hospital with a painless firm anterior mandibular swelling that had been progressively increasing in size for about 8 years, although the patient claimed that the tumour was treated 2 years earlier in a general hospital where a diagnosis of solid multicystic ameloblastoma was made.

Table 1: Summary of Reported Cases of Keratoameloblastoma by Various Authors

No.	Author	Age/Gender	Site	Histopathology Features	Radiographic Features	Treatment	Follow-Up
1	Whitt *et al.*[16]	45 years/Male	Anterior maxilla	Complexhistology	Unilocular radioluscency with calcification	Curettage	No recurrence up to 10 months
2	Sangeta *et al.*[18]	65 years/Female	Anterior mandible	Complex histology with hard tissue formation	Unilocular radioluscency	Excision and resection of mandible	Recurrence 4 months after excision, unknown after resection
3	Siar *et al.*[19]	39 years/Female	Anterior mandible	Simple histology with KCOT-like features	Unilocular radioluscency	Enucleation	Unknown
4	Siar *et al.*[19]	35 years/Female	Right maxilla	Simple histology with KCOT-like features	Ground glass appearance with indistinct borders	Unknown	Unknown
5	Siar *et al.*[19]	30 years/Male	Anterior mandible	Simple histology with KCOT-like features	Multilocular radioluscency	Resection	Unknown
6	Siar *et al.*[19]	35 years/Female	Left mandible	Simple type with KCOT-like features	Unknown	Hemi-mandibulectomy	Unknown
7	Adeyemi *et al.*[20]	38 years/ Male	Right posterior mandible	Stromal parakeratin deposition, areas of myxoid change, focal cystic change in epithelial islands	Multilocular radioluscency	Resection	Unknown
8	Norval *et al.*[17]	26 years/Female	Right mandible	Complex histology	Lobulated radioluscency	Segmental Resection	Unknown
9	Mohanty *et al.*[21]	46 years/Male	Right posterior mandible	Papilliferous histology	Multilocular radioluscency	Unknown	Unknown
10	Said-al-Naief *et al.*[22]	26 years/Male	Right posterior maxilla	Simple histology with KCOT features	Well defined unilocular radioluscency	Curettage and partial maxillectomy	Recurrence 6 months after curettage, unknown after maxillectomy
11	Kaku *et al.*[23]	35 years/Male	Right body of mandible	Simple histology	Unilocular radioluscency between roots	Unknown	Unknown
12	Takeda *et al.*[24]	76 years/Male	Left body of mandible	Complex histology	Multilocular radioluscency	Resection	Unknown
13	Pindborg[25]	57 years/Female	Right mandibular body and ramus	Papilliferous histology	Multilocular radioluscency	Unknown	Unknown
14	Altini *et al.*[26]	76 years/ Male	Right mandible	Papilliferous histology	Multilocular radioluscency	Hemimandibu-lectomy follow-up	No recurrence at 12 months
15	Altini *et al.*[27]	28 years/ Male	Anterior maxilla	Simple histology	Multilocular radioluscency	Wide local excision	Unknown
16	Ketabi *et al.*[28]	21 years/Female	Right anterior mandible	Complex histology	Unilocular radioluscency	Enucleation	No recurrence at 12 months follow-up
17	Raj *et al.*[29]	22 years/Female	Right posterior mandible	Simple histology, stoma with myxoid areas and cystic degeneration	Unilocular radioluscency	Segmental resection	No recurrence at 24 months follow-up
18	Present case	31 years/Male	Anterior mandible	Simple histology	Multilocular radioluscency, locules well separated	Segmental resection	No recurrence at 5 months follow-up

Clinical examination revealed a firm intra oral mass. The over lining mucosa of the mass which was generally the same colour as the normal oral mucosa showed an area of mucosal scarring. The mass which was located within the mandible, extended from the region of lower right second premolar to the lower left first molar. There was also an obvious lingual expansion of the mandible (Figure 1). The tumour mass approximately measured 8 cm × 5 cm. No tooth was observed to be missing or mobile in the subject's mouth.

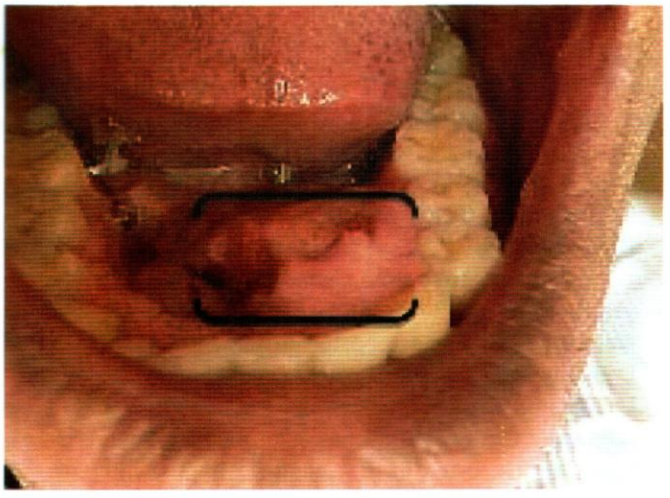

Fig. 1: Clinical Picture showing Area of Mucosal Scarring and Marked Lingual Extension of Tumour Mass (Demarcated Area).

Radiological examination with the aid of Orthopanthomogram (OPG) revealed a well-defined multilocular radiolucent lesion that extended from the lower left molar to lower right molar (Figure 2). A provisional diagnosis of ameloblastoma was made.

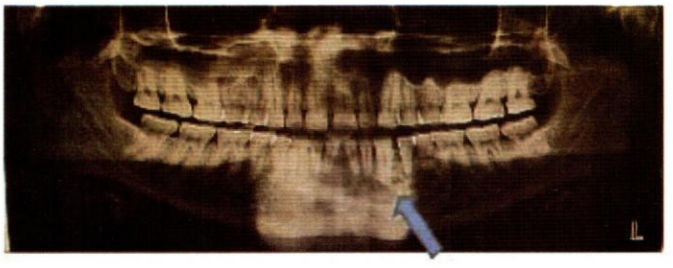

Fig. 2: Orthopanthomogram (OPG) of the Jaws showing the Lesion in the Mandible with mMultilocular Radiolucency. Locules are well separated from each other (blue arrow).

Following an incisional biopsy, histopathology report revealed a mature fibrocollagenous connective tissue which contained follicular islands and nests of odontogenic epithelial cells and interconnecting cords of odontogenic epithelium in other areas. The odontogenic epithelial cells in many areas presented with peripheral basal cells which showed reverse polarity and loose central stellate reticulum-like cells. Keratinization was present within the odontogenic epithelial cells (the stellate reticulum-like cell area) and the fibro collagenous connective tissue stroma. Keratinization within the odontogenic epithelial cells was extensive and prominent keratin lamellar formations were seen stuffed within numerous follicles (Figures 3a-e).

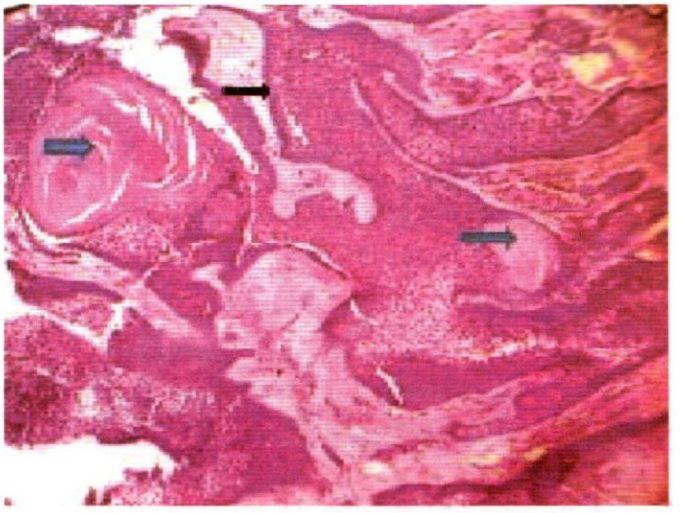

Fig. 3a: Photomicrograph H&E Stain (×40) showing Follicular Islands of Odontogenic Epithelium (black arrow) with Extensive Keratinization (blue arrow).

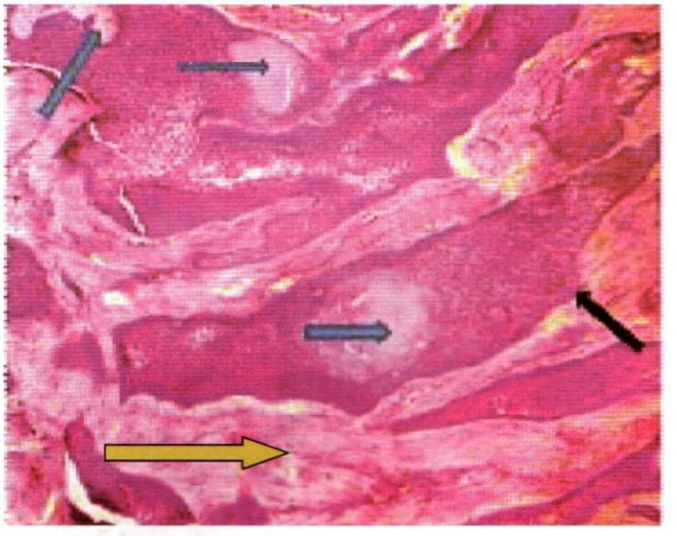

Fig. 3b: H&E Stain (×40) showing Keratin Pearls/Pacinian Mounds (blue arrow) Stuffed within Follicles of Odontogenic Epithelial Cells (black arrow) arranged in Mature Fibro Collagenous Connective Tissue Stroma (yellow arrow).

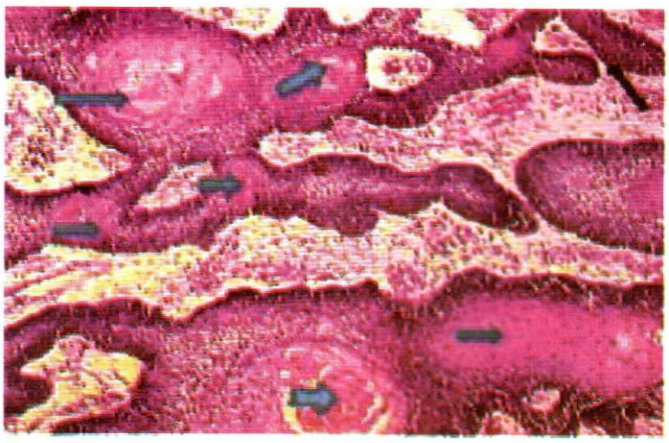

Fig. 3c: H&E Stain (×40) showing Keratin Pearls/ Pacinian Mounds (blue arrow) Stuffed within Follicles of Odontogenic Epithelial Cells. Notice the Plexiform Pattern of Arrangement of the Odontogenic Epithelium (black arrow).

Fig. 3d and 3e: H&E Stain (×40) showing Keratin Pearls/ Pacinian Mounds (blue arrow) Stuffed within Follicles of Odontogenic Epithelial Cells and Keratinization within Connective Tissue (green arrow).

A definitive diagnosis of KA was made. Segmental mandibulectomy with reconstruction using 2.7 mm KLS Martins Recon plate was done under general anaesthesia (Figures 4 and 5a/b). Post-operative histopathology examination also confirmed the diagnosis of KA.

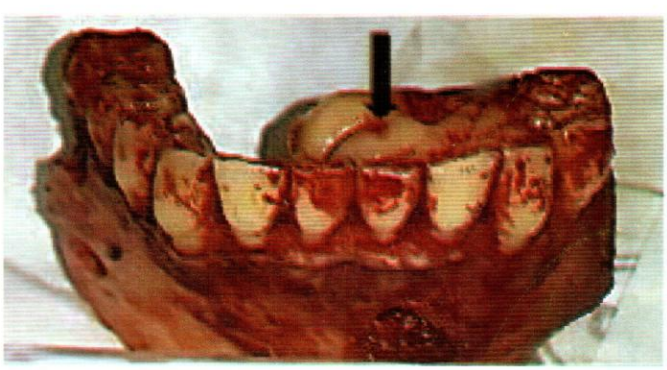

Fig. 4: Surgical Specimen of the Resected Mandible. Black arrow shows Tumour Extent.

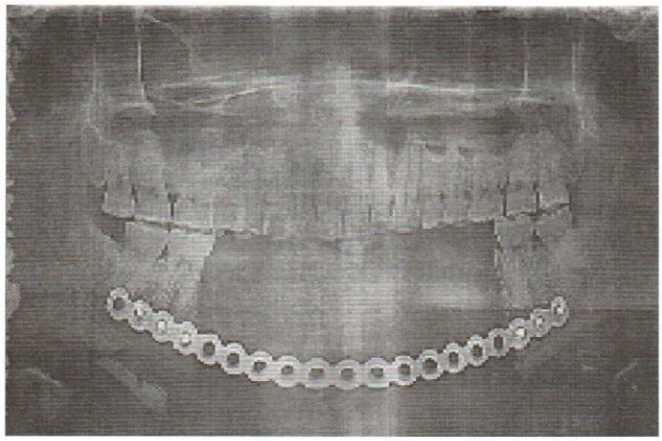

Fig. 5: OPG of the Jaws showing Reconstruction of Resected Mandible using 2.7 mm KLS Martins Recon Plate.

DISCUSSION

Keratoameloblastoma is indeed a rare tumour. Over a 44 year period (1972-2016), a total of 1318 cases of ameloblastoma were diagnosed and reported in the biopsy service of the Department of Oral and Maxillofacial Pathology/Biology, Lagos University Teaching Hospital. Less than 0.001% (1 case) accounted for KA. As far as we know, only 2 Nigerian cases have been reported in the scientific English literature; that reported by Adeyemi et al. (20) and the present case.

Clinical and radiologic presentations of KA do not differ from those of classic ameloblastoma. Keratoameloblastoma like classic ameloblastoma has been observed to occur among a wide age group of between the 3rd to 7th decades of life (mean age of 43.8 years, with a peak incidence in the 3rd and 4th decades of life) (21, 29). It presents with a strong mandibular site predilection (14 cases- 78.0%; Table 1) and has slight male gender preponderance. Reports from documented cases of KA (16, 19-24, 26, 27) show a male gender preponderance (Table 1). The present case was diagnosed in a male subject.

Keratinization majorly occurs among stellate reticulum-like cells within ameloblastomatous follicles. However, keratinization may also occur within the connective tissue stroma. It has been indicated that keratin stuffing of ameloblastoma follicles cause splits resulting in keratin extrusion into the connective tissue stroma (16). Histology of KA in this case, which is similar to the histology of KA from a previous Nigerian study (20), showed extensive keratinization of follicles and less keratinization of connective tissue stroma.

Arriving at a diagnosis of KA may be demanding especially for inexperienced pathologists as it presents with diverse histomorphological features which may make definitive identification rather confusing. Moreover, some cases have been observed to lack reverse polarity of the peripheral/basal cells of follicles that is needed for positive identification of an ameloblastoma (19, 26).

Keratoameloblastoma has been grouped into 4 types according to histologic presentations (16), including Papilliferrous type (consists of odontogenic epithelium that appears as papillary projections into the cystic space); Simple

type (consist of odontogenic epithelial follicles filled with parakeratin or orthokeratin and lined by ameloblast like cells with reversed polarity); Simple with odontogenic keratocyst-like (OKC-like) features type (shows similar features of simple type and also has features of odontogenic keratocyst); and Complex histologic type (consist of epithelial follicles packed with parakeratin or orthokeratin, extrusion of keratin masses into connective tissue stroma in the form of pacinian-like stacks with or without foreign body reaction; also there may be hard tissue formation resembling cementum and woven bone).

Norval *et al.* (17), Pindborg (25), Altini *et al.* (26), and Collini *et al.* (30) reported cases of KA with papilliferrous histology. Siar and Ng (19) reported KA with odontogenic keratocyst like component. Keratoameloblastoma has also been reported as comprising of keratinizing cysts lined by papilliferous epithelium or showing a combination of areas which contain keratinizing cysts and papilliferous tumour islands (29). Complex histologic type of KA described by Takeda et al. (24) consists of epithelial follicles packed with parakeratin / keratin structures and / or pacinian-like mounds (16, 20, 24, 29).

The present case showed few histologic variations. It presented with proliferation of odontogenic epithelium in follicles and interconnecting cords (mixed pattern) rather than the classic follicular pattern commonly observed with KA. The peripheral basal cells of some of the follicles in the tumor were also observed to be lacking of reverse polarity of nuclei. Nevertheless, the presence of extensive keratinization within areas of ameloblastomatous proliferation made diagnosis relatively simple and we categorize the present case a "simple histology type". Observation from the inspection of previous studies on KA shows a total of 2, 4, 5, and 6 cases for simple, papilliferous, simple + OKC-like features and complex histology types respectively. Connective tissue stroma observed was mature fibrocollagenous stroma typical for KA, although a case with myxomatous loose connective tissue stroma has previously been reported (29). Although the diverse histomorphic features of KA distinguish it from the classical ameloblastoma, there have been no reports to show that these types are of any clinical significance. Future large sample studies which compare the histologic types of KA by relating their clinicopathological appearance with recurrent potential and biologic nature in order to determine biologic aggressiveness should be done.

Classic ameloblastoma has histologic types (plexiform and follicular) and several variants (e.g. acanthomatous, basal cell, granular cell, spindle cell, and clear cell) (2, 12, 13). There are histologic similarities between acanthomatous ameloblastoma, solid variant of KCOT and KA. All 3 lesions exhibit production of keratin. It is important to differentiate these 3 lesions. KA and acanthomatous ameloblastoma exhibit squamous metaplasia and keratin pearl formation among the stellate reticulum cells. However, KA unlike acanthomatous ameloblastoma usually presents with large amounts of keratinization and keratin pearls among the stellate reticulum cells and also within the connective tissue stroma (16). These features however do not occur in the solid variant of KCOT (18).

Clinical and radiologic presentations of KA have not been observed to differ from those of classic ameloblastoma. Keratoameloblastoma has been regarded as a variant of acanthomatous ameloblastoma (16, 17). Although it is difficult to determine if KA has a different biologic behaviour from other histologic types of ameloblastoma due to scarce reports of cases in the scientific literature, it is worth noting that so far, the different types/variants of ameloblastoma have not been shown to have clinical significance to its aggressiveness or recurrence (16). Perhaps, future molecular studies on mutational status of these microscopic variants may shed more light on this.

There is variance among oral pathologists as regards the concept of histologic categorization of KA. Though there is a general consensus on it being rare, some pathologists believe it should be categorized as a distinct entity while others believe it should simply be regarded as a histologic variant of acanthomatous ameloblastoma (15-17). Wright et al. (3) however recommend that in order to label a tumour a pathological entity, ample radiological, clinical, histologic/molecular and biologic behavioural features of the tumour must be well integrated into odontogenic classifications.

The well-defined multilocular radiolucency with well separated locules presentation is similar to previous radiographic presentations from previous studies (Table 1), although radiographic variations ranging from multilocular to unilocular with central calcifications have been reported (16, 30). Siar *et al.* (19) reported a case of maxillary KA with ground glass radiographic appearance and distinct borders similar to desmoplastic ameloblastoma and fibroosseous lesion. The standard treatment for classic ameloblastoma is surgical resection with 1–2 cm margin from radiographic margin of the tumour which appears to be disease free and immediate autogenous bone graft reconstruction to assist with speech and swallowing, and improve quality of life (8, 31). High recurrence rate of 60-90% has been reported for conservative treatment methods such as enucleation (8). Although the patient has been followed up for an approximate period of 2 years, the incidence of recurrence cannot be determined as follow up of 2 years is inadequate to comment on recurrence of the lesion.

CONCLUSION

Keratoameloblastoma is indeed an extremely rare tumour among Nigerians. Whether or not KA is considered a distinct entity is disputable. As this tumour presents with identical clinico-pathological and radiographic features of the classic ameloblastoma, and so far the various histomorphologic types have not been proven to connote any clinical relevance to management, we see no purpose to label KA a separate entity. It should simply be considered a histologic variant of ameloblastoma. The precise clinical behaviour and biologic nature of KA is not yet well understood. Although 3 cases of recurrence have been reported, it is still unclear if the tumour has more potential for recurrence than conventional ameloblastoma, hence we recommend a lifetime follow up of all cases.

CONFLICT OF INTEREST

None declared.

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