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CYSTIC AMELOBLASTOMA: A CLINICO-PATHOLOGIC REVIEW

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ABSTRACT

Objective: **Cystic ameloblastoma represent 10-15% of all intra osseous ameloblastomas and appear to be less aggressive than the solid ameloblastomas. The aim of this study was to examine the clinico-pathologic characteristics of cystic ameloblastomas seen at a tertiary health care centre.**

Materials: **All cases diagnosed as cystic ameloblastoma in the Oral Pathology Department of University College Hospital, Ibadan over a 10 year period were investigated for age, gender, location of lesion, treatment, and follow-up. The cases were classified as luminal, intra-luminal or mural, based on Ackermann classification. The data was entered into the statistical package for the social sciences version 18 (SPSS 18) and results expressed as percentages.**

Results: **Fifteen cystic ameloblastomas, representing 14.3% of a total of 105 ameloblastoma cases were seen. The mean age was 28.9(±14.5) years with 73.4% occurring in the second and third decades. The male:female ratio was 2:3. Fourteen (93.3%) of the lesions were in the mandible while only one (6.7%) was in the maxilla. The mural variant was the most common histological variant with 6(40%) cases while the luminal and intra-luminal had 4(26.7%) and 5(33.3%) respectively. The multilocular radiologic appearance was more common than the unilocular in this study (ratio 8:4). Cystic ameloblastoma with multilocular appearance occurred in a higher age group (mean age 31yrs) when compared with the unilocular type which had a mean age of 16.3years.**

Conclusion: **This study shows similar findings with previous studies but shows a higher multilocular radiological appearance as compared to unilocular variant and no case of recurrence.**

Keywords: Cystic ameloblastoma, Clinico-pathologic review, Uni-locular, Multi-locular

INTRODUCTION

Ameloblastoma is the commonest odontogenic tumour in Africans and Asians and arguably the most clinically significant, odontogenic tumour.[1] Ameloblastoma is classified clinically into solid, cystic, peripheral, malignant and carcinomatous types.[2] The cystic ameloblastoma was first identified by Robinson and Martinez in 1977.[3] Unicystic ameloblastoma (UCA) is a more common term used to designate these pathological entities, however, this name became less desirable because they can occasionally present as multilocular radiolucencies. The term 'cystic ameloblastoma' is therefore more appropriate.[2]

Cystic ameloblastomas represent 10-15% of all intra osseous ameloblastomas[1] and appear to be less aggressive than the solid ameloblastomas therefore many authors have recommended a less aggressive treatment protocol for this variant of ameloblastoma.

Cystic ameloblastomas is classified into 3 histologic subsets. Group 1(luminal) consists of a cystic lesion lined by simple odontogenic epithelium. The epithelial lining of the lumen is uniform in thickness and has a slightly hyperchromatic layer of palisaded basal cells, most of which exhibit reversed polarization of the nucleus. Group 2 (intra-luminal) consists of a cystic lesion showing intra-luminal proliferation of the epithelial lining. Group 3 (mural) consists of a cystic lesion with epithelial invasion of the supporting connective tissue in either a follicular or plexiform pattern.[4]

Although diagnosis of cystic ameloblastoma may connote treatment and prognostic significance, few studies in Nigeria[5] have examined the clinico-pathologic features of cystic ameloblastomas. The aim of this study was to examine the clinico-pathologic

characteristics of cystic ameloblastomas seen at a tertiary health centre in Ibadan, Nigeria.

MATERIALS AND METHODS

All histologically diagnosed cases of ameloblastoma over a 10 year period (2001-2010) in the Oral Pathology Department of the University College Hospital Ibadan were reviewed. Out of these, all haematoxylin and eosin stained slides of cases diagnosed as cystic ameloblastoma were reviewed to confirm the initial diagnosis. Case notes were reviewed for age, gender, location of lesion, treatment, and follow-up. Radiographs were also assessed for the radiologic appearance of the lesion (unilocular or multilocular). A diagnosis of cystic ameloblastoma was made when a well-defined single cystic sac lined by odontogenic (ameloblastomatous) epithelium was seen. The histological patterns were then categorized as luminal, intra-luminal or mural based on Ackermann et al classification (1988). The data was entered into the statistical package for the social sciences version 18 (SPSS 18) and results expressed as percentages.

RESULTS

20 cases of cystic ameloblastoma were retrieved from the oral pathology files, of these 15 were confirmed histologically to be cystic ameloblastoma representing 14.3% of the total number of ameloblastoma cases seen over the 10 year period.

Table1 shows an overview of clinical, histological, radiology as well as follow up data of the fifteen cases. Cystic ameloblastoma occurred more in females (n=9, 60%) than males (n=6, 40%). The age of patients ranged between 15-67 years with a mean age of 28.9(±14.5) years. Majority (73.4%) of the cases were in the second and third decades. Only 3(20%) were seen in patients aged 40 years and above.

Fourteen (93.3%) of the lesions were in the mandible while only one (6.7%) was in the maxilla. Of the mandibular cases, 10 (66.7% of all cases) were in the posterior mandible while 4(26.7%) were in the anterior mandible. Four (26.7% of all cases) of the posterior mandibular lesions extended to the anterior mandible crossing the midline, while two (13.3%) of the anterior lesions, crossed the midline and extended to the contra-lateral side.

Radiographic reports were obtainable in 12 cases out of which 8(66.7%) were multilocular while 4(33.3%) were unilocular. Two cases (one multilocular and one unilocular) were associated with an impacted tooth. Lesions with unilocular presentation had age range 15-19 years and a mean age of 16.3years while multilocular presentations had age range of 18-48years and mean age of 31years. The mural variant was the most common histological variant with 6(40%) of cases while the luminal and intraluminal had 4(26.7%) and

Table 1: Shows clinical/histologic overview of cystic ameloblastoma cases

S/N	Sex	Age(yrs)	site	PBP (months)	Histologic Variant	Radiologic Variant	Treatment type	FUP (months)
1	M	67	Mn	72	mural	_	enucleation	36
2	M	20	Mn	60	mural	_	Seg. Resection	36
3	F	45	Mn	8	Intra-luminal	multilocular	Seg. Resection	24
4	M	29	Mn	36	Intra-luminal	multilocular	Seg. Resection	12
5	M	18	Mn	12	mural	multilocular	Seg. Resection	_
6	F	28	Mn	12	Intra-luminal	multilocular	Seg. Resection	12
7	F	23	Mn	6	luminal	multilocular	Seg. Resection	12
8	F	15	Mn	2	luminal	Unilocular +embedded tooth	enucleation	12
9	F	36	Mn	12	mural	Multilocular + embedded tooth	Seg. Resection	36
10	M	23	Mn	3	Intra-luminal	unilocular	Seg. Resection	72
11	M	48	Mn	72	Intra-luminal	multilocular	Seg. Resection	12
12	F	21	Mn	2	luminal	Multilocular	Seg. Resection	2
13	F	19	Mn	48	mural	unilocular	Seg. Resection	6
14	F	16	Mx	2	luminal	unilocular	Seg. Resection	12
15	F	26	Mn	14	mural	_	Seg. Resection	_

Mn – mandible, Mx – maxilla, M – male, F – female, Seg – segmental, FUP – follow-up period, PBP – period before presentation, S/N – serial number

Table 2: Shows comparison of clinical features of cystic ameloblastoma with previous studies.

Authors	No of cases	M:F	Site Mn	Site Mx	Mean age(yrs)	Recurrence N (%)	Radiologic presentation (U:M)
Lawal *et al*[*]	15	6:9	14	1	28.9	0(0.0)	4:8
Olaitan *et al*[6]	21	12:9	21	0	22.0	3(14.3)	_
Rosenstein *et al*[9]	21	10:11	21	0	35.0	9(43.0)	15:6
Tie-Jun Li *et al*[8]	33	21:12	30	3	25.3	6(18.1)	22:7
Nakamura *et al*[10]	24	15:9	24	0	27.0	9(37.5)	15:9

**Present study*

M= male, F=female, Mn=mandible, Mx=maxilla, U=unilocular, M=multilocular

5(33.3%) respectively. Most of the patients presented late with mean time of presentation of 28 months (2-84 months) after first noticing the swelling. Twelve of the patients had segmental resection while two had enucleation and there were no cases of recurrence after a mean follow up period of 23 months (range 2-72 months).

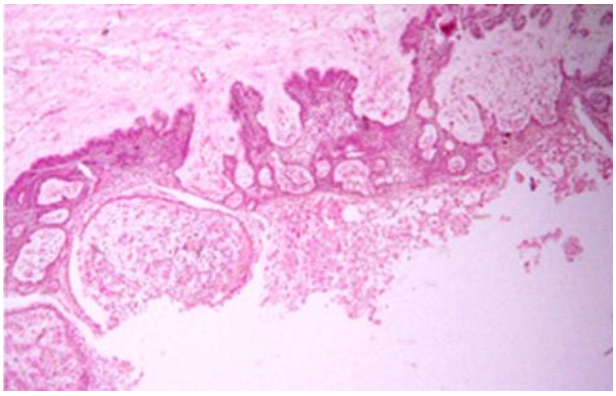

Fig. 1: (H&E X50) Luminal cystic ameloblastoma showing mural involvement

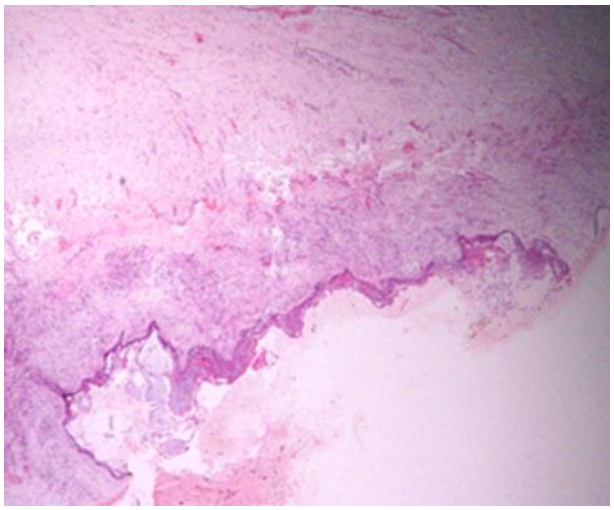

Fig. 2: (H&E X50) Luminal cystic ameloblastoma

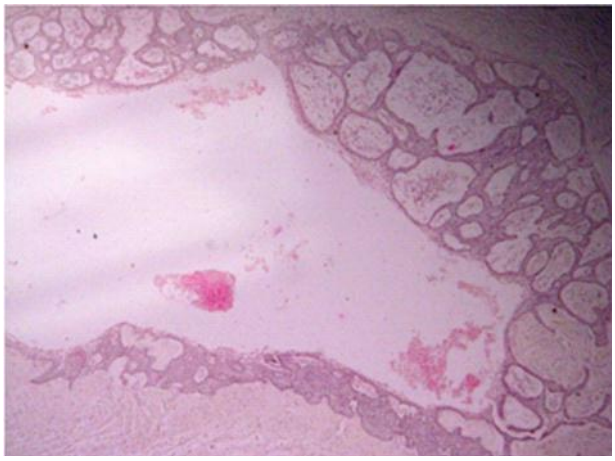

Fig. 3: (H&E X50) Intra-luminal cystic ameloblastoma

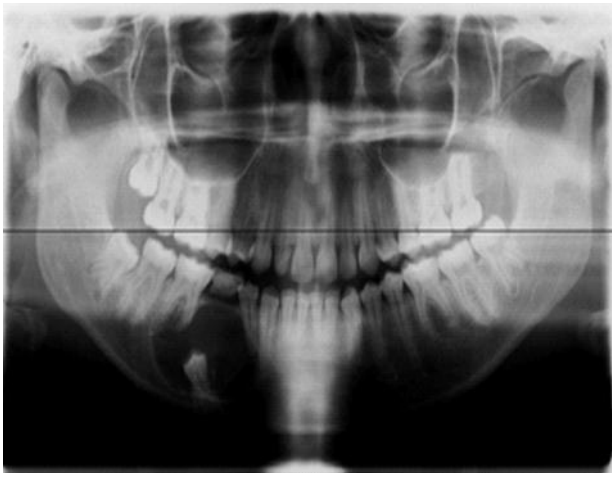

Fig. 4: Radiograph of Unilocular cystic ameloblastoma with impacted tooth

DISCUSSION

Fifteen cystic ameloblastomas were seen out of a total of 105 ameloblastoma cases representing 14.3% which was similar to 10-15% previously reported in the USA[6] but less than the 18.9% reported by Tie-Jun Li *et al*[8] in China.

Cystic ameloblastoma occurs more in a younger age group when compared to the solid variant, with most cases seen before the age of forty years.[1, 5, 6, 7] This was the trend in this study where the mean age was 28.9 years and only 20% occurred at age forty and above. Our finding is similar to that of Tie-Jun Li *et al*[7] in China who also reported a mean age of 25.3 years and 70% of their cases occurred in the second and third decades of life. However, Rosenstein *et al*[6] in California, reported a mean age of 35 years and suggested that the relative high mean age in their study may be due to the fact that most of their cases were not associated with impacted teeth. Eversole *et al*[8] in their study found that cystic ameloblastomas not associated with impacted teeth had a higher mean age of 35 years compared to those that were associated with impacted teeth which had a mean age of 16.5 years.

More cases were seen in females with a male: female ratio of 2:3. Previous studies have reported varying gender predilection. Rosenstein *et al*[6], reported a slight female predilection (M: F=10:11), while Tie-Jun Li *et al*[8] reported an obvious male preponderance (M: F=7:4). Also, Tie-Jun Li *et al*[7] reviewing 150 cases from the literature, found 55% of the cases were males while 45% were females. However, Philipsen[9] in a review of 193 cases reported a higher incidence of impaction associated cystic ameloblastoma in females (M: F=1:1.8).

Mandibular lesions were more prevalent in this series with just one case (6.7%) occurring in the maxilla. All available studies show a marked mandibular predilection[2, 7, 8] with some series[5, 6, 10] reporting an exclusive mandibular occurrence. The reason for this striking mandibular preference is not known but conventional solid ameloblastoma also has a predilection for the mandible and some authors have suggested a cystic degeneration of solid ameloblastomas as one of the possible aetio-pathogenesis of cystic ameloblastomas[2]. The reason for this striking mandibular involvement is a subject for further research.

The multilocular radiologic appearance was more common than the unilocular in this study (ratio 8:4); this is probably the first study to observe this trend as all previous studies[6, 7, 10] had observed unilocular appearance to be more common. Rosenstein *et al*[6] reported that only 29% of their cases were multilocular while Tie-Jun Li *et al*[7] reported 22:7 unilocular: multilocular ratio. However, Eversole *et al*[8] found a unilocular:multilocular ratio of 13:3 when the cases were associated with an impacted teeth but this changed to 8:7 for non-impaction cases. The large number of multilocular cases seen in this study may be due to the fact that most cases were not associated with impacted teeth and thus, were not the "dentigerous type" of cystic ameloblastoma[12].

Furthermore, cystic ameloblastoma with multilocular appearance occurred in a higher age group (mean age 31yrs) when compared with the unilocular type which had a mean age of 16.3years. Philipsen[9] had previously reported a mean age of 22years for cystic ameloblastoma with unilocular appearance while those with multilocular appearance had a mean age of 33years.

The mural variant of cystic ameloblastoma was the most common histological variant representing 40% of the cases seen, which compares favorably with Philipsens[9] findings who also found the mural variant to be most common, although, they found a higher prevalence for mural variant which accounted for over 60% of their cases.

In addition, cystic ameloblastoma series by Ackerman *et al*[4] and Wang *et al*[11] showed that up to half of cystic ameloblastomas had mural nodules[8]. It has been suggested that lesions with mural invasion had worse prognosis when compared with the luminal and intra-luminal types and should be treated more aggressively, [6] however, this could not be ascertained in this study as there were no cases of recurrence, possibly due to the more aggressive approach to treatment.

There were no cases of recurrence in this series after an average follow up period of 23 months (range 2-72months). Most authors have claimed that cystic ameloblastomas have a better prognosis than the solid type but the complete lack of recurrence in this series may be due to the more radical approach adopted in treatment. Twelve cases were treated by marginal resection and two by enucleation. The more aggressive approach to treatment in this series may be because most lesions were quite large. Rosenstein *et al*[6] observed that cystic ameloblastomas may be more aggressive than previously thought and recurrence rates in cases treated by enucleation (64%) was similar to the recurrence rates of solid ameloblastomas treated by enucleation or curettage while no recurrence were reported in the more aggressively treated cases[6].

The pathogenesis of cystic ameloblastomas is quite obscure. Some authors believe that they arise from preexisting odontogenic cysts; others argue that they develop de-novo. Robinson and Martinez proposed that, considering the fact that, the epithelium of odontogenic cyst and ameloblastoma has a common ancestry, the transition from a non-neoplastic cyst to a

neoplastic cyst is a possibility[9]. Cystic ameloblastoma may also arise as a result of ameloblastic transformation of reduced enamel epithelium of a developing tooth and subsequent cystic development. Leider *et al*[12] proposed that cystic ameloblastoma may be due to cystic degeneration of a solid amelo-blastoma; it has been suggested that this may be related to epithelial dys-adhesion due to defective desmosomes, or to the intrinsic production of proteinases (e.g. metalloproteinases, serine proteinases); enzymes that normally degrade the central zone of the enamel organ after tooth development. However, in spite of differing opinions by many authors[9, 11, 12,] convincing evidence for any of the proposed pathogenesis is still lacking.

Although, definitive inferences could not be drawn from this study because of the small sample size, this study showed many similarities to previous studies except that the multi-locular radiological appearance was more common than the unilocular appearance, a finding which was at variance with all other previous studies. Also, there were no cases of recurrence in this series, which may be due in part to the more radical approach of treatment in many of the cases. A larger series with longer follow-up period is recommended to better understand the relationship between clinicopathologic presentations and the prognosis of cystic ameloblastoma.

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