

EPIDEMIOLOGY OF AMELOBLASTOMA

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ABSTRACT

Objective: The objective of the review was to comprehensively review the epidemiology of ameloblastoma.

Methods: Available information on ameloblastoma were sourced from publications in goggle, goggle scholar, pubmed, African Journal Online Line (AJOL) and textbooks. Information were also obtained from textbooks and publications that were not online. The retrieved informed were synthesized and grouped.

Results: Age gender racial and site distributions, pathogenesis, biological behaviour, classification radiological pattern, histological presentation and treatment of ameloblastoma were found and discussed.

Conclusion: Ameloblastoma was documented to affect individuals of all ages, gender and race. Site distributions, pathogenesis, biological behaviour, radiological pattern, histological presentation and treatment of ameloblastoma were seen to be varied.

Keywords: Ameloblastoma, epidemiology, oral tumour

INTRODUCTION

Ameloblastoma, historically known as adamantinoma, is defined as a true neoplasm of odontogenic epithelium, especially of enamel organ-type tissue which does not undergo differentiation to the point of enamel formation (Woo et al., 1987). It is a benign but locally aggressive and infiltrative odontogenic tumour with a rare capacity to metastasize and strong tendency to recur (Kramer et al., 1992). Ameloblastoma is usually unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent, causing extensive tissue destruction and resulting in facial and jaw deformities, if left untreated (Gbom & Mhaske, 2009).

Ameloblastoma of the jaws has been cited as the most frequent odontogenic tumour in Africa, constituting about 1% of all jaw tumours

(Daramola et al., 1978; Odukoya, 1995; Akinosi & William, 1969; Arotiba et al., 1997; Becelli et al., 2002).

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An incidence rate of ameloblastoma documented by Simon et al. in Tanzania was 0.68 per million (Simon et al 2005). The reports from studies in Nigeria revealed ameloblastoma, as the most common odontogenic tumour in children and adults (Adebiyi et al., 2004; Adebayo et al., 2005). Adebayo et al. reported that ameloblastoma is a fairly common tumour constituting 73% of odontogenic tumors and 24% of all tumours and tumour-like lesions of the oral and perioral structures among Nigerians (Adebayo et al., 2005)

(Table 1). Adebisi et al. also reported ameloblastoma as the most prevalent benign ectodermal odontogenic tumour (Adebisi et al., 2004). This implies that biopsy for ameloblastoma constitutes a significant minor surgical procedure and diagnostic workload in Oral Surgery and Oral Pathology Departments in hospitals respectively. In Nigeria, the management of ameloblastoma, a dominant odontogenic tumour, appears to constitute the bulk of specialized oral and maxillofacial care (Adebayo et al., 2008).

Ameloblastoma has been reported to originate from sources like residual epithelium from tooth germ, epithelium of odontogenic cysts, stratified squamous epithelium, epithelium of the enamel organ and heterotopic epithelium in other parts of the body (Shafer et al., 1983). It occurs in all age groups but the lesion is most commonly diagnosed in the third and fourth decades of life (Olaitan et al., 1993). Adebayo et al. reported ameloblastoma as the predominant odontogenic tumour among Nigerian children though with prevalence lower than that in the adult population (Adebayo et al., 2002). Several studies reported no sex predilection but a few reported a higher male to female ratio (Mosadomi, 1975; Subbuswamy & Shamia 1981; Günhan et al., 1990; Olaitan et al., 1993; Kim & Jang, 2001; Di Cosola et al., 2007)

The vast majority of ameloblastoma arise in the mandible with the majority occurring in the angle and ramus region (Adebisi et al., 2004; Adebayo et al., 2005). There are conflicting reports whether it is more common at the anterior or posterior region of the mandible but some African studies documented its predilection for the anterior mandibular region (Akinosi & William, 1969).

In advance setting, the general dental practitioner is the first port of call for most dental patients, so it is important they are well educated in recognizing this tumour and making appropriate referral. The high index of suspicion about ameloblastoma among dentists will facilitate the early diagnosis with histology and ultimately a positive treatment outcome with minimal or no obvious disability (Simon et al., 2005). The early and adequate treatment also excludes the

possibility of malignant transformation and development in ameloblastoma (Becelli et al., 2002). The objective of the review was to comprehensively review the epidemiology of ameloblastoma.

EPIDEMIOLOGY

Ameloblastoma is a term derived from the early English word amel, meaning enamel and the Greek word blastos, meaning germ (Brazis et al., 1995). Ameloblastoma is a true neoplasm of enamel organ-type tissue which does not undergo differentiation to the point of enamel formation. Robinson, (1937) described it as a tumor that is usually "unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent". The annual incidence rates per million for ameloblastoma are 1.96, 1.20, 0.18 and 0.44 for black males, black females, white males and white females respectively (Shear & Singh, 1978). An incidence rate of 0.68 per million was documented by Simon et al. in Tanzania (Simon et al., 2005). Biopsy for ameloblastoma constitutes a significant minor surgical procedure and diagnostic workload in Oral Surgery and Oral Pathology Departments in hospitals respectively. In Nigeria, the management of ameloblastoma, appears to constitute the bulk of specialized oral and maxillofacial care (Adebayo et al., 2008). Surgery for ameloblastoma is one of most common oral and maxillofacial procedures done under general anaesthesia thereby accounting for significant manpower activity and theatre surgical time (Adebayo et al., 2008).

HISTORIC PERSPECTIVE

The report of neoplasm of this nature in the scientific literature was credited to Cusack and Broca in 1827 and 1868 respectively. This type of odontogenic neoplasm was designated as an adamantinoma in 1885 by the French physician, Louis-Charles Malassez. The tumour was finally given the modern name, ameloblastoma in 1930 by Ivey and Churchill. However, the first thorough description of ameloblastoma was that of Falkson, (1879).

Table 1: Prevalence of ameloblastoma in relation to odontogenic tumors of the jaws

Country	Author (s)	Series	Category	Amel (%)	Others Odont. tumour (%)
Brazil	Fernandes et al., 2005	340 cases (50 yrs period)	Nil	45.2	Odontomas (24.91) myxomas (9.1).
Chile	Ochsenius et al., 2002	362 cases (25 yrs period)	Nil	20.4	Odontomas (44.7) Myxomas (8.8)
Jamaica	Ogunsalu, (2003)	70 cases (15 yrs period)	benign (98.6) malignant (1.4)	82.9	AOT (4.3) Odont myxoma (4.3) Odont fibroma (2.9) Amel. fibroma (2.9) Amel. carcinoma (1.4)
India	Gupta & Ponniah (2010)	489 cases (38 yrs period) Age range 5-75 years Mean age: 32.64years	benign (96.9) malignant(3.1)	67.7	AOT (9) odontoma (7.77) CEOC (5.52)
Sri Lanka	Siriwardena et al., 2012	1677 cases Age range 1-80 years Mean age 30.6	benign (98) Malignant (2)	48.7	AOT 25.7 odontoma 10.1
China	Jing et al., 2007	1642 cases Age range: 3-84years Mean age: 32.1years	benign (97.0) malignant (3.0)	40.3	AOT (35.8) Odontoma (4.7) Odont. myxoma (4.6).
Egypt	Tawfik & Zyada, (2010)	82 cases (15-year period) Age range: 4-80 years Mean age: 29.57 years	benign (96.3) malignant (3.7)	41.5	AOT (19.5) Odontoma (13.4) Odont. myxoma (8.5)
Zimbabwe	Chidzonga et al. 1996	148 cases (10 year period)	benign (99.3) malignant (0.7)	79.1	amel fibro-sarcoma 0.7
Nigeria	Ladeinde et al., 2006	319 (23 years period) Age range:4-85 years Mean age: 29.9	benign (96.6) malignant (3.4)	63	AOT (7.5) myxoma (6.5) CEOC (5.3) Odont. fibroma (5.3)
Nigeria	Adebayo et al.2005	318 cases(20 years period). Age range 1-78 years	benign (99) malignant (1)	73	Odont myxoma (12) Amel. fibroma (3) AOT (2) CEOC (1)
Nigeria	Arotiba et al., 1997	128 (15 years period) 8 -75 years	Nil	16	AOT (13)

Key: Amel.-Ameloblastic, Ame-Ameloblastoma, AOT-adenomatoid odontogenic tumor, CEOC- calcifying epithelia odontogenic cyst, Odont.-Odontogenic, yrs-years,

AGE DISTRIBUTION

The reported cases of ameloblastoma occurred over a wide range of ages, 10 to 90 years has been reported and highest incidence was recorded in the 3rd to 4th decade of life (Shafer et al., 2006). Average age of diagnosis is 33 to 39 years, but most cases are reported between 20 to 60 years (Shafer et al., 2006). Olaitan et al. reported peak

presentation of ameloblastoma in the third and fourth decades of life (Olaitan et al., 1993) and the mean age of presentation for ameloblastoma reported as 31.67 years by Ladeinde et al (2005). Siar and Ng, (1993) found 72% of the ameloblastoma in their study among patients in their second, third and fourth decades of life. In three hundred and forty cases of ameloblastoma

reviewed by Siar et al., a wide age range of 7 to 85 years with mean onset age of 30.3 years and peak incidence in the second decade of life was reported (Siar et al., 2012). In a report in Kenya, the overall age range of patients in the 10 years audit was 10 to 80 years with mean age of 30.2 years. The mean ages for males and females were 29.9 years and 30.5 years respectively which means that females presented at a slightly older age than males (Adeline et al., 2008). Approximately 10% of cases are reported in children and less than a third of those occur in children less than 10 years (Davies & Davies, 1960). Arotiba et al.³⁰ reported that 21.9% and 2.5% of ameloblastoma among patients under 20 years and under 10 years of age respectively. Zhang et al. reported ameloblastoma among 4 to 20 years old patients with a mean age of 14.5 years in their 16 years review of ameloblastoma in children and adolescents (Zhang et al., 2010) while Huang et al. in a 13 year review revealed the mean age of 13.7 years among 9 to 17 year old among Taiwanese children (Huang et al., 2007). Report of ameloblastoma among patients as younger as 2 years and as old as 82 years also exists in the literature (Fregnani et al., 2010). It can be deciphered from the literature review that ameloblastoma is not a congenital disease but rather an acquired disease that may have possible link with ageing and environmental exposure as the peak incidence is in the third and fourth decades of life (Olaitan et al., 1993; Shafer et al., 2006). According to Reichart and Philipsen, (2004), the following are the mean ages recorded for ameloblastoma in various continents of the world: North America-39.0 years, South America-13.2 years, Europe-43.3 years, Africa-30.0 years, Asia-35.2 years and Australia-39.5 years.

GENDER DISTRIBUTION

Several studies revealed no significant gender predilection in the prevalence of ameloblastoma (Mosadomi, 1975; Günhan et al., 1990; Odukoya, 1995; Arotiba et al., 1997; Adeline et al., 2008; Darshani Gunawardhana et al., 2010). However, Olaitan et al. (1993) in Nigeria reported a male to female ratio 1.6:1 and Siar et al. in Malaysia reported a male to female ratio 1.4:1 (Siar et al., 2012). The other reports of male predilection of ameloblastoma exist in the literature (Subbuswamy & Shamia, 1981; Di Cosola et al.,

2007; Ladeinde et al 2005). Few studies reported female predominance in some series (Regezi et al., 1978; Fregnani et al., 2010). Fregnani et al. in their 50 years review of cases of ameloblastoma seen at the Sao Paulo Cancer Hospital, Brazil reported a slight female prevalence (Fregnani et al., 2010) It can be implied from the information available that ameloblastoma is non-X and non-Y sex gene related disease because of the varied gender reports.

RACIAL DISTRIBUTION

Ameloblastoma of the jaws is the most commonly encountered odontogenic tumour in Africa and Asia but the second most common odontogenic tumour in North and South America. There is conflicting reports on the incidence rate in different races (Wu et al., 1985; Chidzonga et al., 1996; Lu et al., 1998; Ladeinde et al., 2005). Some studies have suggested a greater frequency of ameloblastoma in individuals of African descent; however, other studies have demonstrated the absence of a racial predilection. Ameloblastoma with its different subtypes appears to be particularly frequent in African (Odukoya, 1995; Adebisi et al., 2004) and in some Asian populations (Chung et al., 1969; Reddy, 1974; Tay, 1999; Budhy et al., 2001; MacDonald –Jankowski et al., 2004). Asians have fewer tumors involving the ramus than whites or blacks (MacDonald – Jankowski et al., 2004) while blacks have increased frequency of ameloblastoma in the anterior mandible (MacDonald –Jankowski et al., 2004). Racial variation was noted in a study in Malaysia as 50.1% Malays, 34.7% Chinese, 8.2% Indians and 7.0% other races were found to have ameloblastoma (Siar & Ng, 1993). Racial variation in terms of histology of the tumour was noted in a report which revealed more western children have unicystic ameloblastoma and also more African children develop tumours in the mandibular symphysis (Ord et al., 2002). A study which categorically stated that ameloblastoma is not rare in a Chinese population noted geographic differences in the relative incidence of ameloblastoma among the Chinese/African, North American and Turkish/German groups which is an evidence for racial variation (Lu et al., 1998). The racial variation may link ameloblastoma to environmental exposures in different geographical areas and genetic variation of different races.

SITE DISTRIBUTION

Ameloblastoma can affect any of the jaw bone. However, the vast majority of ameloblastoma arise in the mandible. Darshani et al. in a study of 286 cases of ameloblastoma in Sri Lanka found 87.8% of them occurred in the mandible while 10.8% occurred in the maxilla, giving a ratio of 8:1 (Darshani et al., 2010) and Reichart et al. reported the ratio of ameloblastoma of the mandible to maxilla as 5:1 (Reichart et al., 1995).

Ameloblastoma can occur at any location in the mandible or maxilla, but the regions of the posterior molars and mandibular ramus are the most prevalent anatomical locations (80%) (Becelli et al., 2002; Nakamura et al., 2002; Reichart et al., 1995; Martins et al., 1999). In Blacks, ameloblastoma occurs more frequently in the anterior region of the jaws (Reichart et al., 1995). However, ameloblastoma with a predilection for the posterior mandibular region was reported to be relatively common in Nigeria (Ladeinde et al., 2005). Larger tumors may rupture the bone cortex and infiltrate adjacent soft tissues on the lingual surface of the mandible and if it occurs in the ascending ramus area of the mandible will result in extensive and grotesque deformity of the mandible (Pizer et al., 2002).

In the maxilla, it occurs in the third molar area followed by the maxillary sinus and floor of the nose. The evolution and invasion of the tumour in posterior region of the maxilla may compromise the maxillary sinus, orbit and nasopharynx (Zwahlen et al., 2003). Maxillary ameloblastoma is more dangerous than mandibular type due to the tendency to spread more extensively in the more porous maxillary bone and possibility of involving the cranial base.

AETIOLOGY OF AMELOBLASTOMA

Aetiology of ameloblastoma is not clearly understood but several aetiological factors have been proposed in the literature (McMillan & Smillie, 1981; Eversole et al., 1984; Leider et al., 1985) and they are as follows:

1. **Irritation:** Ameloblastoma is common in the mandibular angle region. Here there is constant pooling of saliva containing various irritating factors and microorganisms. This irritation is thought to cause ameloblastoma. Nonspecific irritating factors such as

extraction, caries, trauma, infection, inflammation, or tooth eruption have also been postulated.

2. **Oral sepsis:** In blacks, oral hygiene was found to be poor and so it was thought to be a factor.
3. **Trauma:** Few patients gave history of either trauma or extraction prior to the development ameloblastoma. So trauma can be a causative factor.
4. **Dietary deficiency:** Dietary deficiency has been considered to be a possible factor. For example, pronounced defect in development of tooth germ, as seen in rickets, may lead to irregularity in the ameloblastic layers.
5. **Virus:** Few ultrastructure studies of ameloblastoma showed presence of viral particles which were thought to be polyoma viruses. Recently, various studies indicate that *Human papilloma virus* (HPV) also plays a role in the development of ameloblastoma. HPV types 16 or 18 and type 6 have been detected. Few studies have shown that even *Epstein-Barr virus* genes are present in few cases of ameloblastoma.
6. **Chemical carcinogens:** Injection of chemical substances like nitrosoureas have been shown to produce ameloblastoma-like lesion in animals.

PATHOGENESIS OF AMELOBLASTOMA

Most authorities consider ameloblastoma to arise from varied origin (Shafer et al., 2006), although the stimulus initiating the process is unknown. However, it is thought that it is likely that the result of alterations or mutations in the genetic material of cells that are embryologically programmed for tooth development may play some role. Fukumoto et al. concluded that, although the mechanism of ameloblastoma formation remains unclear, deregulation of ameloblast differentiation due to lack of ameloblastin is likely to be the primary cause of the tumour, because no calcification is found in ameloblastoma (Fukumoto et al., 2004).

Environmental factors and individual patient variability such as patient's general health status, nutritional status also may play a role in modulating the incidence of the disease. Also, Kessler, (2002) found that the average age of occurrence in industrialized nations is 10 to 15 years greater than in developing countries.

The tumor may be derived from the cell rests of the enamel organ, (e.g. rests of Malassez or gland of Serres), the lining epithelium of odontogenic cysts (e.g. dentigerous cyst), or the basal cells of the surface epithelium of the jaws (Eversole et al., 1971; Stoelting & Bronkharst, 1988; Gold, 1991; EL-Sissy & Rashad, 1999; Slootweg, 2004). It may also arise secondary to disturbances of the developing enamel organ or from heterotopic epithelium in other parts of the body e.g. the pituitary gland (Shafer et al., 2006).

Histologically, the epithelium of the ameloblastoma resembles that of the enamel organ of the developing tooth. The peripheral cells of the epithelial follicles resemble the stellate reticulum of the tooth germ (Heikinheimo, 1993; Kumamoto et al., 2001; Reichart & Philipsen, 2004). Furthermore, some cases of ameloblastoma share features with basal or squamous cell carcinomas, squamous odontogenic tumors, adamantinomas of the long bones or craniopharyngiomas of the central nervous system (Shafer et al., 2006; Rosai, 1977; Paulus et al., 1997; Gallagher & Shaklar, 2000).

The resemblance of the tumour epithelium to the normal enamel organ indicates that ameloblastoma arises from dental epithelium. The possibilities are as follows:

1. Enamel organ

Due to histological similarities such as in origin, it has been thought the tumour growth starts at an early age, i.e. in a period which is long after regression of the enamel organ. However, the occasional occurrence of the tumour as unilocular cystic lesions surrounding the crown of an unerupted tooth also suggests that in some cases, the enamel organ may give rise to it. During the bell stage of tooth formation, the dental lamina begins to disintegrate and form small islands of epithelial cell residues (gland of Serres). This lengthy recapitulation of the activity of the embryonic oral epithelium, before initiation of the intricate inductive process of morphodifferentiation in tooth formation, is suggested to emphasize the importance of this tissue as a source of ameloblastoma.

2. Cell rests

Cell rests of enamel organ, either remnants of dental lamina (Rest cells of Serres) or remnants of

Hertwig's root sheath (epithelial cell rests of Malassez) have potential of transforming into ameloblastoma. Rests of Malassez which are the remnants of the Hertwig's sheath persist in the periodontal ligament and the alveolar bone as epithelial strands and rests throughout adult life and are the only odontogenic epithelial cells that remain in the periodontium after the eruption of teeth^{80,95,96}. In pathological conditions, inflammatory stimuli and direct contact with calcified tissues seem to induce the rests to differentiate into ameloblastic cells (Hamamoto et al., 1996; Hamamoto et al., 1998).

3. Odontogenic Cysts

Epithelia of odontogenic cysts from dentigerous cyst and odontoma- this may be possible as the epithelium in the wall of the cyst and that of ameloblastoma are derived from the same embryonic source. Hypothetically, developmental cystic lesions (dentigerous, odontogenic keratocyst and lateral periodontal cyst) may give rise to ameloblastoma as a secondary phenomenon, in that they originate from the odontogenic epithelial tissue (Gold, 1991). Leider et al. proposed a pathogenic mechanism where ameloblastoma arises in dentigerous or other types of odontogenic cysts in which the neoplastic ameloblastic epithelium is preceded temporarily by a non-neoplastic stratified squamous epithelial lining (Leider et al., 1995). Numerous clinical reports have attempted to show such an association in dentigerous cysts and some authors (Leider et al., 1995; Bernier, 1964; McMillan & Smillie, 1981; Shear, 1994; Ayhan et al., 1998; Piattelli et al., 2002) believe that approximately 20% of ameloblastoma arise in dentigerous cyst.

Odontogenic keratocyst is thought to arise in place of an aborted tooth germ whose epithelial dental organ forms a cystic lesion typically lined by a relatively thin keratinized or parakeratinized epithelium, classically arranged in corrugated folds. Odontogenic keratocyst develops from the remains of dental lamina (Lucas, 1964; Piattelli et al., 2002) or from the stellate reticulum of the enamel organ (Forsell et al., 1974). Lateral periodontal cyst is also thought to be from rests of Malassez or other dental lamina residues in the periodontal ligament or adjacent alveolar bone (Standish & Shafer, 1958).

4. Oral mucosa

Jaw tumours can originate from basal cells of the oral epithelium. The reason behind this is that there is communication between the tumours and the overlying mucosal epithelium as seen in peripheral ameloblastoma. Central ameloblastomas that have penetrated their bony cortices and grown into the overlying mucosa and peripheral ameloblastoma have been seen to appear fused with the mucosa epithelium (Gadner, 1977). There are two major sources to be considered regarding the cellular origin of peripheral ameloblastoma. First, they arise from remnants of dental lamina or the Serres pearls located in the soft tissues overlying the tooth-bearing areas of the jaw bones (Gadner, 1977; Zhu et al., 1995) and secondly, the tumour may arise from the surface epithelium (Anneroth & Johansson, 1983).

5. Heterotrophic epithelium

Heterotrophic epithelium in other parts of the body especially of the pituitary can serve as source of origin.

BIOLOGICAL BEHAVIOUR

Ameloblastoma is an aggressive benign tumour of epithelial origin. The clinico-pathologic features are benign with a slow-growing pattern, but locally invasive. The clinical behavior may be regarded as lying somewhere between benign and malignant, and the high recurrence is a noted problem among clinicians. It shows various biologic behaviors, ranging from cystic expansion to more aggressive infiltration of adjacent tissues. It has a tendency to expand the bony cortices because the slow growth rate of the tumour allows enough time for periosteum to develop thin shell of bone ahead of the expanding lesion. This shell of bone cracks on palpation and this phenomenon, important diagnostic clinical feature is referred to as *egg shell crackling effect*". The mandibular and maxillary cortical bone destruction and involvement of the surrounding soft tissue is often seen in the late stage of the disease, especially if no treatment has been provided or in tumor recurrences (D' Agostino et al., 2001; Reichart & Philipsen, 2004)

When symptoms occur, they are usually due to the physical presence of the tumor and they include jaw swelling, facial deformity, pain, paraesthesia, malocclusion, mobility of teeth or ill-fitting

dentures, periodontal disease or ulceration, oro-antral fistula and nasal airway obstruction (Gardner & Pecak, 1980; Adekeye & Lavery, 1986). Ameloblastoma is often associated with the presence of unerupted teeth and bony impacted third molars. Olaitan et al. found mucosal ulceration in few patients and atypically with expansion of either the lingual or buccal cortical plate of the mandible in some patients in Nigeria (Olaitan et al., 1993). Stypułkowska, (1998) reported that most frequent reasons for referral of patients with ameloblastoma were deformity of the jaws, mal-eruption or lack of teeth or their dislocation.

CLASSIFICATION OF AMELOBLASTOMA

The classification of ameloblastoma in the past was poorly defined but the current concept is to classify ameloblastoma into three clinico-radiological groups as solid or multicystic, unicystic and peripheral tumours (Reichart & Philipsen, 2004). This classification has a direct bearing on the pathologic behavior of these variants for example solid or multicystic variants of ameloblastoma are locally aggressive, and recur if inadequately excised. However, unicystic ameloblastoma was identified as a prognostically distinct entity with less aggressive behaviour (Robinson & Martinez, 1977). Multicystic ameloblastoma is the most common variety and represents 86% of cases. Peripheral tumors are odontogenic tumors, with the histological characteristics of intraosseous ameloblastoma that occurs solely in the soft tissues covering the tooth-bearing parts of the jaws.

Unicystic ameloblastoma

It is a cystic variant of ameloblastoma which is thought to develop from dentigerous cyst and three hypotheses for the development of unicystic ameloblastoma are:

1. In the dentigerous cyst lining basal cells undergo transformation into ameloblast-like cells, which proliferate either into lumen or connective tissue forming nodules of ameloblastoma.
2. The follicles of ameloblastoma undergo degeneration leading to formation of a cavity or microcystic space, which enlarges forming large cystic space.
3. Unicystic ameloblastoma may arise de novo. It is a unilocular cystic lesion whose clinical features are of those of a non neoplastic cyst.

Lining epithelium exhibits alterations virtually identical with those described as ameloblastomatous changes in dentigerous cyst, also called mural ameloblastoma. Unicystic ameloblastoma includes cases that have been variously referred to as mural ameloblastoma, luminal ameloblastoma, and ameloblastoma arising in dentigerous cysts.

Robinson and Martinez (1977) established unicystic ameloblastoma as a clinico-pathologic entity on the basis of its unicystic radiographic appearance with emphasis that the diagnosis can only be made histologically and cannot be predicted preoperatively on clinical or radiological grounds. It is a rare type of ameloblastoma, accounting for about 6% of ameloblastoma of the jaws, usually occurring in a younger age group, with about half of the cases occurring in the second decade of life. More than 90% are located in the mandible with 50-80% occurring in association with impacted mandibular third molar.

The unicystic ameloblastoma arising in dentigerous cysts usually occurs 8 years earlier on average than the ones not arising from dentigerous cyst. Jaw swelling and facial asymmetry are the most common clinical presentations, pain is occasionally a presenting symptom while mucosal ulceration caused by continued growth of the tumour is rare. Small lesions are sometimes discovered more on routine radiographic screening examinations or as a result of local effects like tooth mobility, occlusal alterations and failure of eruption of teeth produced by the tumour.

Histologically, the minimum criterion for diagnosing a lesion as unicystic ameloblastoma is the demonstration of a single cystic sac lined by odontogenic ameloblastomatous epithelium often seen only in focal areas. Unicystic ameloblastoma should be differentiated from odontogenic cysts because the former has a higher rate of recurrence than the latter (Konouchi et al., 2006).

In a clinico-pathologic study of 57 cases of unicystic ameloblastoma, Ackermann et al.¹¹⁷ classified this entity into the following three histologic groups:

1. Luminal unicystic ameloblastoma (tumor confined to the luminal surface of the cyst).

2. Intraluminal/plexiform unicystic ameloblastoma (nodular proliferation into the lumen without infiltration of tumor cells into the connective tissue wall).
3. Mural unicystic ameloblastoma (invasive islands of ameloblastomatous epithelium in the connective tissue wall not involving the entire epithelium).

Simple unicystic lesions are less common but have a better prognosis. Simple (no nodule) variant will not be diagnosable on radiography, as it will be indistinguishable from other more common cysts. Luminal variant, has a single nodule projecting into the cyst. Mural variant has multiple nodules (often only microscopic) in the wall of the cyst. The latter has an elevated risk of recurrence.

Peripheral ameloblastoma

Peripheral ameloblastoma also known as extraosseous ameloblastoma or soft tissue ameloblastoma, is similar to solid or multicystic ameloblastoma histologically but occurs in the soft tissue outside and overlying the alveolar bone and does not invade the underlying bone (Sciubba, 1991; Philipsen et al., 2001). It originates from either the surface epithelium or remnants of dental lamina. It is common in males and on the mandibular gingiva in the molar-premolar region. Some cases are seen in buccal mucosa and maxillary tuberosity area. The patient complains of a mass which is growing in size and interfering with speech, mastication and aesthetics. Mass is mildly tender on palpation, at times ulcerated and bleeding may occur on slight touch. The lesion appears nodular on gingiva varying in size from 3mm to 2 cm in diameter. Peripheral lesion is relatively innocuous, lacks persistent invasiveness and has a limited tendency of recurrence. Prognosis of this tumor is very good.

The peripheral extraosseous ameloblastoma is rare, and usually the peripheral ameloblastoma presents as painless, usually non-ulcerated lesions on the alveolar or gingival mucosa, which can be sessile or pedunculated and demonstrate a non-aggressive benign course. In general, unicystic and peripheral lesions do not invade the bone tissue, respond better to treatment and have low recurrence rates (Martinez et al., 2008).

Malignant behaviour is seen in two forms namely ameloblastic carcinoma which is frankly malignant histologically and malignant

ameloblastoma which metastasizes despite well differentiated 'benign' histology. The literature, past and present, contains reports of ameloblastoma cases, well differentiated or not well differentiated, that have invaded the lungs or metastasized by vascular or by lymphatic routes (Cranin et al., 1987; Hayashi et al., 1997; Okada et al., 1999; Goldberg et al., 2004; Hayakawa et al., 2004). Ameloblastic carcinoma may be locally aggressive and undergoes regional lymph nodes metastasis, but it is not required to show metastasis to confirm the diagnosis whereas a malignant ameloblastoma must show metastasis to be a confirmed diagnosis. Ameloblastic carcinoma behavior is similar to that of an aggressive squamous cell carcinoma, for which they are often mistaken until histopathology identifies the pre-ameloblast cellular atypia.

RADIOLOGICAL PATTERN OF AMELOBLASTOMA

Radiographically, Ueno et al. found that among 97 cases of solid multicystic ameloblastoma, 47% were unilocular, and 37% were multilocular; 16% had soap-bubble or combination of soap-bubble and multilocular radiolucency (Ueno et al., 1986). From plain radiographs and computerised tomography (CT), ameloblastoma is classically seen as a multiloculated (80%), expansile soap-bubble lesion, with well demarcated borders and no matrix calcification. Occasionally erosion of the adjacent tooth roots can be seen which is highly specific. When the tumour is larger, it may erode through cortex into adjacent soft tissues.

CT is usually helpful in determining the contours of the lesion, its contents and its extension into soft tissues (Rampton, 1998). In a patient with a swelling in the jaw, the first step in diagnosis is panoramic radiography. However, if the swelling is hard and fixed to adjacent tissues, CT is preferred. Although the radiation dose is much higher in CT, the necessity of identifying the contours of the lesion, its contents and its extension into the soft tissues, makes it preferable for diagnosis. Plain radiographs do not show interfaces between tumour and normal soft tissue; only interfaces between tumour and normal bone can be seen. The axial view in contrast-enhanced CT images and the coronal and axial views in magnetic resonance imaging (MRI) clearly show both types of interface (Cihangiroglu et al., 2002).

Although there are no appreciable differences between MRI and CT for detecting the cystic component of the tumour, for visualising papillary projections into the cystic cavity, MRI is slightly superior. MRI is essential for establishing the exact extent of an advanced maxillary ameloblastoma and thus determining the prognosis for surgery (Kawai et al., 1998; Ziegler et al., 2002). In MRI, ameloblastoma demonstrates a mixed solid and cystic pattern, with a thick irregular wall, often with papillary solid structures projecting into the lesion.

Mclvor, (1974) stated that there are four radiographic features that are significant in ameloblastoma. These include the expansion of the cortical plate, presence of corticated scalloped margin, multilocular appearance of the lesion and the resorption of adjacent teeth.

HISTOLOGICAL PRESENTATION OF AMELOBLASTOMA

Macroscopic appearance

It is grossly characterized by a fusiform or cylindrical expansion of the bone especially involving the lingual plate of the mandible. Perforation rarely occurs. On section, it appears as a grayish yellow mass replacing bone. Some lesions are completely solid but in most, cystic spaces are present which are quite small measuring up to 1-2 cm in diameter.

Histologically, ameloblastoma exists in two main forms: follicular and plexiform patterns. Other variants which include unicystic, basal cell, granular cell, clear cell, acanthomatous and desmoplastic patterns, belong to any of these patterns (Shafer et al., 2006). Hong et al. recently showed that the histopathology of ameloblastoma is significantly associated with recurrence, while it was also shown that the follicular, granular cell and acanthomatous types have a relatively high likelihood of recurrence (Hong et al., 2007). In contrast, the desmoplastic, plexiform and unicystic types show a relatively low potential for recurrence.

Microscopic feature

In general, this tumour is unencapsulated and infiltrating, but sometimes there may be areas that may appear well demarcated. The most frequent pattern is the follicular type. The epithelial islands are present within a variable stroma, which is generally well collagenised. The

islands mimic the enamel organ. At the periphery are columnar cells, resembling preameloblasts, in which the nuclei are polarized away from the basement membrane and toward the center of the island. Within the center of the island is a loose arrangement of the epithelial cells, resembling the stellate reticulum. Within the stellate reticulum, a variety of changes may be observed. These include squamous metaplasia (acanthomatous), and spindling of the stellate cells (spindle cell ameloblastoma).

The follicular and plexiform variants of ameloblastoma possess islands and anastomosing strands of odontogenic epithelium enmeshed in a fibrous stroma. These islands and strands contain basal cells that are columnar, hyperchromatic and lined up in a palisaded fashion at the periphery. The cells have vacuolated cytoplasm and the nuclei exhibit reverse polarization away from the connective tissue. The cells in the central portions of the epithelial islands are more loosely arranged, mimicking stellate reticulum. The lesion is cytologically bland with no pleomorphism or mitotic figures noted. Acanthomatous, granular cell and basal cell patterns have central portions composed of epithelial cells with keratin formation, granular cells and uniform basal cells, respectively. The desmoplastic type of ameloblastoma is unique, as it contains small islands and cords of odontogenic epithelium with little evidence of the characteristic ameloblast-like cells. The islands and nests are found in a very dense collagenous stroma.

Follicular type

This is the most commonly encountered type of ameloblastoma. It grows mainly in form of islands, but to a smaller extent chords and strands. This type of ameloblastoma has the highest proliferative rate than any other type of ameloblastoma leading to the immature cells which have basal-like appearance. The typical cellular morphology is often altered, with ameloblast-like cells appearing low columnar and cuboidal. There is loss of reverse polarity and subnuclear vacuolation. But cells retain palisading. The most common histologic type of ameloblastoma in Nigeria is follicular ameloblastoma (Adebisi et al., 2004; Ladeinde et al., 2005).

Plexiform type

The plexiform type has epithelium that proliferates in a Fish-Net-Pattern. The plexiform ameloblastoma shows epithelium proliferating in a cord-like fashion, hence the name plexiform. There are layers of cells in between the proliferating epithelium with well-formed desmosomal junctions, simulating spindle cell layers.

Clear cell ameloblastoma

Some ameloblastoma may contain cells without eosinophilic cytoplasm and appearing clear. Clear cells are usually present in place of stellate reticulum-like cells. These cells contain high amount of glycogen, which results in clear appearance. Clear cell ameloblastomas are very aggressive tumours.

Keratoameloblastoma and papilliferous ameloblastoma

It consists of keratin filled cystic spaces and solid proliferation of epithelial cells. Cysts are lined by parakeratotic epithelium. The basal layer consists of cuboidal cells, and the rest of the layers of the epithelial lining shows loosely arranged epithelial cells. Cysts resemble odontogenic keratocyst. The stroma of the tumour consists of dense collagenous fibrous connective tissue septa. The solid components of the tumour consist of large solid masses of parakeratin and keratin, surrounded by multilayered squamous epithelium with peripheral palisaded cuboidal basal cells and the rest of the epithelium. Although the basal cells are palisaded and demonstrate nuclear polarization, they are cuboidal rather than columnar.

Keratoameloblastoma is believed to be a link between a cystic neoplasm-odontogenic keratocyst and a solid neoplasm having same origin. In few cases epithelial cells surrounding the cystic spaces show papillary projections. Such lesions are called papilliferous keratoameloblastoma. In few cases papilliferous ameloblastoma exists independent of keratoameloblastoma.

Haemangioameloblastoma

It is ameloblastoma that shows presence of spaces filled with blood or large endothelial lined capillaries. Presence of increased vascularity is not understood. Various theories have been put forward to explain the pathogenesis of the vascular component in ameloblastoma.

- It is probable that excessive stimulation of angiogenesis during the tumour development, by the inductive influences may result in the overgrowth of vascular elements.
- Alternatively, a traumatic incident such as tooth extraction may provide the stimulus for proliferation of epithelial cell rests in the periodontal ligament and subsequent tumour development. Tissue damage is usually followed by repair, involving the formation of granulation tissue. Thus capillaries become prominent part of developing tumours. It has also been suggested that this tumour represents a collision tumour.
- Another explanation is that the stroma part of plexiform ameloblastoma consists of loose myxoid tissues which can undergo degeneration, so blood vessels are left without any support. They become enlarged and rupture leading to escape of blood into empty stroma spaces.

Desmoplastic ameloblastoma

This ameloblastoma is different from other types of solid multicystic ameloblastoma, so it is thought to be a separate clinico-pathological entity of ameloblastoma and not just histologic subtype. It differs clinically, radiologically and histologically from classic ameloblastoma. This type of tumour is more common in anterior region of the maxilla. It occurs in older patients than the conventional tumour. Radiologically it appears as fibro-osseous lesion showing mixed radiopaque radioluscent appearance.

Histologically, it shows presence of large amount of collagen. These collagen fibers compress the islands leading to bizarre animal-like shapes. Peripheral cells are mostly cuboidal, columnar cells are rarely seen. Central islands show hypercellularity. Desmoplastic ameloblastoma appears to have better prognosis.

Dentinoameloblastoma

In rare cases, ameloblastoma may be associated with odontome showing inclination to form dentine and enamel. It consists of cystic and solid tissue with ameloblastic or ameloblastomous follicles. Abundant amount of eosinophilic homogenous extracellular materials interpreted as dentinoid is present. Dystrophic calcification is also seen in places.

Melanoameloblastoma

It is essentially found in infants before the age of 6 months. There is proliferation of pigment producing odontogenic epithelium.

Summary of the relative frequency of different histological patterns of ameloblastoma by Gbom and Mhaske, (2009) is thus: Follicular (33.9%), Plexiform (30.2%), Acanthomatous (11.3%), Granular cell (3.5%), Basal cell (1.4%), Desmoplastic (1.4%) and Keratoameloblastoma (0.1%).

Wu and Chan, (1985) in a study of 114 tumours of the jawbones from 204,583 surgical specimens in Chinese University Department of Pathology, Hong Kong from 1963-1982 stated the following on ameloblastoma based on pathological analysis:

1. Connection of tumour epithelium with oral mucosal epithelium suggests a better prognosis
2. Basaloid pattern in the tumour may prognostically indicate a more aggressive biological behaviour.
3. Neoplastic infiltration of the grossly normal bone surrounding the tumour mass was frequent.
4. Ameloblastoma not uncommonly contained cysts lined by innocuous-looking epithelium.
5. A significant proportion of ameloblastoma appeared grossly as thin-walled unilocular cysts.

TREATMENT FOR AMELOBLASTOMA

The management of ameloblastoma has been controversial because of the unique biological behavior of this tumor as a slow-growing, locally invasive tumor with a high rate of recurrence and possible malignant transformation when treatment is inadequate (Shatkin & Hoffmeister, 1965; Mehlich et al., 1972; Sehdev et al., 1974; Tsaknis & Nelson, 1980; Pinstolle et al., 1995). Recurrence rates of ameloblastoma are reported as high as 15% to 20% after radical treatment (Shatkin & Hoffmeister, 1965; Mehlich et al., 1972). Anatomical location, extent of disease, histological and radiological characteristics as well as patient age and compliance are among the factors that determine the selection of surgical management.

Surgery which ranges from conservative to radical surgery is the mainstay of treatment for ameloblastoma. The conservative surgical techniques include enucleation with bone

curettage (Martins et al., 1999; Sampson & Pogrel, 1999). and marsupialization followed by enucleation (Nakamura et al., 1995; Nakamura et al., 2002) as well as a combination of enucleation and Carnoy's solution or cryosurgery (Holland & Mellor, 1981; Curi et al., 1997; Lee et al., 2004). Proponents of conservative approach believe that ameloblastoma though, locally invasive, is essentially benign in nature, therefore, it should be treated as such (Ueno et al., 1989; Feinberg & Steinberg, 1996; Sammartino et al., 2007). Proponents of radical approach to the treatment of ameloblastoma are of the opinion that, though, these tumors are histologically benign in nature, they are locally aggressive and the clinical behavior may be regarded as lying somewhere between benign and malignant lesions. Enucleation and curettage of ameloblastoma results in unacceptable recurrence rates (Sampson & Pogrel, 1999). Radical surgery involves removal with a margin of normal bone by using segmental resection (Adekeye, 1980). Most investigators recommend 1.0 to 1.5cm of normal bone beyond the tumor margin (Olaitan et al., 1993; Gümgüm & Hoşgören, 2005; National Advisory Committee on Oral Health, 2004; Gardner & Pecak, 1980; Adekeye, 1980; Zwahlen & Gratz, 2002). Other authorities include 0.5cm (D' Agostino, 2001) to 3.0cm size of resection in the surrounding healthy tissue (Nakamura et al., 2002; Budhy et al., 2001). As maxillary ameloblastoma is reported to be more aggressive having the ability to metastasize (Jackson et al., 1996; Zwahlen & Gratz, 2002) ameloblastoma of the maxilla should be treated more aggressively than similar lesion in the mandible because of the proximity to vital structures and the difficulty in treating recurrences (Adebayo et al., 2011; Ueda & Kaneda, 1991). Rates of recurrence may be as high as 15% to 25% after radical treatment and 75% to 90% after conservative treatment (Gümgüm & Hoşgören, 2005).

CONCLUSION

Ameloblastoma was documented to affect individuals of all ages, gender and race. Site distributions, pathogenesis, biological behaviour, radiological pattern, histological presentation and treatment of ameloblastoma were seen to be varied.

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