**UNICYSTIC AMELOBLASTOMA: A DISTINCT CLINICOPATHOLOGIC ENTITY**

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**ABSTRACT**

Unicystic / Cystic ameloblastoma (UCA) is a single cystic cavity which shows ameloblastomatous differentiation in the lining. First introduced in 1977, it contends on being a separate clinico pathological entity than the solid ameloblastoma. The clinical and radiographic features of UCA, its differential diagnosis, histopathology and current concepts of management have been discussed. This is a review article.

**Key words:** Ameloblastoma, jaw tumours, oral pathology, maxillofacial surgery

**INTRODUCTION**

Ameloblastoma is the most clinically significant, if not the commonest odontogenic tumour to occur in the jaws.1 It is classified clinically into solid, cystic, peripheral, malignant and carcinomatous types. Generally attention has been directed on the surgical management of conventional, solid ameloblastoma with no delineated management protocols for the cystic variant. The management protocols, therefore range from the radical resection reserved for solid ameloblastomas to simple enucleation generally considered apt for a dentigerous cyst. However, recently there has been a resurgence of interest in the management of unicystic Ameloblastoma (UCA); after progress is made in determining the distinct clinicopathological behaviour of this entity.2 The concept of this tumour was first introduced by Robinson and Martinez in 1977.3 The more common term used to designate these pathological entities is UCA. However, sometimes they can present as a multilocular radiolucency, which makes the use of the term ‘cystic ameloblastoma’ more appropriate.4 However, some authors still feel that the notion that cystic ameloblastomas can have a ‘true’ clinically multicystic pattern is arguable, and contend with the use of the term ‘unicystic ameloblastoma’. They are seen to account for 10 – 15 % of all intra osseous ameloblastomas.4

Many of the lesions are chance findings after a complete histopathological examination of a pericoronal dentigerous cyst. Various studies report that between 15 to 30 % of all ameloblastomas form in the wall of a dentigerous cyst.5 However, it is not known whether they arise from a neoplastic transformation of cells from an otherwise non neoplastic dentigerous epithelium or arise de novo.2 Rosenstein et al6 found out in their case series that those lesions that experienced recurrences appeared identical histologically to...
the original lesions, making the likelihood of the development of these tumours from dentigerous cysts unlikely.\textsuperscript{6}

The pathogenesis of UCAs and cystic degeneration are not clear yet. However, it has been suggested that the reason why some ameloblastomas become completely cystic may be related to epithelial dysadhesion (e.g. defective desmosomes) or, more likely, 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.\textsuperscript{6}

Clinical and radiographic features: Unicystic versus multicystic ameloblastoma

The sex distribution is almost identical of that of multicystic ameloblastoma with the male:female ratio being 1.3:1. Both the lesions occur intraosseously in the jaws. The mandibular molar and the ascending ramus regions are the ones most often affected by both of the types. However, unlike the solid variant, UCA is seen to occur in a younger age group, with the age group of 16 – 20 years being most commonly involved. They are seen rarely in patients over 40 years of age.\textsuperscript{2} Mandible is affected more than maxilla. They are most commonly encountered in the posterior mandible, followed by the parasymphyseal region, anterior maxilla, and the posterior maxilla.\textsuperscript{7}

The most common presentation is a ‘dentigerous’ relationship with a severely displaced third molar. The next most frequent area involved is the premolar area, with them sometimes occurring in the ramus area; without a relationship with teeth; the so-called ‘non-dentigerous’ type. This pattern is seen more commonly in patients in fourth or fifth decades. They are often asymptomatic until they are seen on a routine radiograph. As the lesion slowly enlarges, a slight, nontender swelling becomes apparent on clinical examination.\textsuperscript{5} This swelling is the result of an expansion of the cortical plates of the jaw and can be identified by palpation as hard and bony.

The radiographic appearance is peculiar, with the association of a circumscribed radiolucency with the crown of a tooth.\textsuperscript{1} The margins are well delineated, with well decorticated margins present in most of the cases too. Though, the fact that the term unicystic would imply a unilocular radiographic appearance, the lesion can sometimes have a multicellular radiographic appearance. In the most comprehensive study on the radiographic aspects of UCA, it was found that the unilocular: multicellular ratio was 13:3 for cases associated with impacted teeth, against an almost equal 8:7 for the ‘non-dentigerous’ types.\textsuperscript{8}

Differential diagnosis

Dentigerous cysts, odontogenic keratocyst, other simple odontogenic cysts like residual cysts, adenomatoid odontogenic tumour, giant cell lesions and sometimes solid ameloblastoma can be the possible differential diagnoses for a unilocular lesion with or without a ‘dentigerous’ relationship occurring within the jaws. However, keratocyst seldom shows cortical expansion, residual cysts are associated with missing teeth that have been extracted, adenomatoid odontogenic tumour has a predilection for anterior maxilla, central giant cell granuloma often arises anterior to first mandibular molar and solid ameloblastoma is seen uncommonly in patients less than 30 years of age.\textsuperscript{9}

Histopathology

Ackermann et al.\textsuperscript{10} in their landmark study classified the histological subtypes into three patterns, namely lumenal (type 1), intralumenal (type 2) and mural patterns (type 3). In the lumenal type, the tumour is confined to the lumenal surface of the cyst. The lesion consists of a dense, uniformly thickened, fibrous connective tissue capsule, that consists totally or partially of ameloblastic epithelium, surrounding a solitary large fluid-filled lumen. 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. The remaining layers resemblestellate reticulum. Some lesions will contain areas in which the epithelium is thickened with papillary projections extending into the lumen. This histologic pattern is referred to as intralumenal UCA. In some of cases, the project- ing nodule demonstrates an edematous, plexiform pattern that resembles the plexiform pattern seen in conventional ameloblastomas, and therefore, these lesions are sometimes referred to as plexiform cystic ameloblastomas.\textsuperscript{1} It can be misdiagnosed occasionally as an inflamed cyst with hyperplastic epithelial lining.\textsuperscript{11} When the thickened lining (either plexiform or follicular) penetrates the adjacent capsular tissue, it is termed a mural UCA. The extent and depth of the ameloblastic infiltration may vary considerably. The mural variety is seen to be more often associated with the ‘non-dentigerous’ type of these lesions, while the intra- lumenal proliferations are more than twice as frequent in UCAs of the ‘dentigerous’ type.\textsuperscript{5}

Figure 1 reflects the significant lysis of the ameloblastic epithelium resulting in the “cyst” formation. On the right top epithelium albeit degenerated is present while in the rest of the lesion the epithelium has almost completely denuded leaving the basal layer only. There is pseudopapillae formation projecting in the lumen and lined by basal layers on the surface the
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underlying stroma. The lysis may be result of degeneration or proteases activity as mentioned above.

Ki-67 and PCNA (Proliferating cell nuclear antigen) are used to check the proliferative index of the UCA.7,12 However, Eversole13 contends that currently unaided histologic assessment for UCA remains the gold standard for diagnosis, because of a variable response of UCA to tissue markers.

The traditional surgical notion is that unless a whole dentigerous cyst is presented before histological examination, presence of ameloblastic cells cannot be ruled out. However, a case series comprising of 101 cases found that step sectioning of larger dentigerous cysts may reveal associated odontogenic cell nests in some cases but does not lead to the detection of formerly missed ameloblastic cells.14 The report concluded that UCAs are not misdiagnosed if only two slides are prepared for routine diagnosis of dentigerous cysts.

Treatment

Conventionally described treatment is based on choosing a particular treatment based on the exact histology of the UCA. In cases of the intraluminal or plexiform pattern being present (and no penetration of the fibrous tissue capsule by ameloblastic cells), enucleation generally suffices but if there is a mural component that extends into the wall to the level of the interface with the bone, bony resection is necessary to ensure adequate removal.

The treatment is decided by the clinical behaviour and which in turn is dictated by the histological pattern of the ameloblastoma. It is pertinent to mention that multiple sections through many levels of the specimen are necessary to rule out the possibility of mural invasion of tumour cells. Therefore, though an ‘ideal’ treatment in the form of simple enucleation with or without curettage for the intraluminal or lumenal types or a resection type of treatment for the mural type is difficult to determine preoperatively; it is only the postoperative careful histological typing that actually clarifies whether the tumour is wholly limited within the cystic wall or it is growing into the outer connective tissue wall. Even then it is difficult to detect unless serial sectioning of the specimen with thorough microscopic examination are performed. The whole specimen needs to be actively screened for mural invasion in every case of UCA to determine the true prevalence of histologic subtypes in any series.15 Similarly, it becomes impossible to rule out mural invasion of the fibrous tissue wall with one incisional biopsy because of the potential for taking a non-representative sample.

Rosenstein et al found that all 9 patients in their case series who experienced recurrence were initially treated with enucleation and curettage.6 Lee et al. found out that the predominance of mural lesions (Ackermann type 3) was 93% in all of his patients with UCA.15 If during enucleation a mural mass is discovered, the surgeon should flag it with sutures to enable the pathologist to concentrate on it as an area of greatest concern. Such mural mass can consist of deposits of cholesterol, fibrous tissue, granulation tissue, an area showing ameloblastic change, a mural ameloblastoma, another type of odontogenic tumour, salivary gland tumour, or rarely, a central occurring malignancy.5 An intraoperative decision can then be made to treat the bony cavity with either Carnoy’s solution or liquid nitrogen cryotherapy.

Controversy therefore exists in the further treatment of a cystic ameloblastoma that has been enucleated as a dentigerous cyst and only the postoperative histological examination shows a mural ameloblastoma. Some surgeons believe a marginal or partial resection to be a prophylactic measure; others prefer to keep the patient under close radiographic observation and delay further treatment until there is evidence of recurrence. Recurrence rates compiled from relatively small series, are approximate and probably not currently accurate. They are 18 – 25 % for intraosseous cystic ameloblastomas, when only enucleation is curettage is performed for the lesions.11 Because recurrences can frequently present very late, post treatment patients should be followed for 15 to 20 years.

Carnoy’s solution (chloroform 3 mL, absolute alcohol 6 mL, glacial acetic acid 1 mL, ferric chloride 1 g) was initially used as a sclerosing agent for treatment of cysts and fistulae,16 and is currently used as a fixative.17
The use of Carnoy’s solution in treatment of odontogenic keratocysts and central giant cell granuloma has already been studied, and was shown in an animal model to penetrate cancellous bone to a depth of 1.5 mm.

The use of Carnoy’s solution to decrease chances of recurrence after conservative surgical treatment of UCAs was initially suggested by Stoelinga and Bronkhorst in 1987, and then by Rosenstein et al. Lee et al. reported success rates with recurrence rates of 10% by using Carnoy’s solution as an adjunct to enucleation and curettage, even with a high 93% of the lesions being of the mural type. They contended that it is likely that the use of Carnoy’s solution does contribute towards a favourable result although a few limitations in the study like a short follow up period do not unequivocally prove this notion. Cryotherapy with liquid nitrogen has also been suggested after enucleation and curettage to be an effective method of treatment of these lesions.

Rational treatment of cystic lesions of jaws; the possibility of presence of UCA

Chapelle et al. have described a rational approach to treatment of cystic lesions within the jaws. Radicular and dentigerous cysts are common but the more ‘conservative’ approach of enucleation may not suffice in cases of UCAs and odontogenic keratocysts. Therefore, clinicians should always approach such lesions with caution, with emphasis on follow-ups and periodic review of the patient.

In case of a unilocular cystic lesion noted within maxilla or mandibular body, aspiration is followed by enucleation and excisional biopsy should be performed. In case of a lumenal or intralumenal UCA being found, a watch and see policy is adopted and patient is kept on a follow-up, but if a type 3 (mural type) UCA or solid ameloblastoma is reported, partial maxillectomy or marginal mandibulectomy should be performed.

In case of a unilocular cystic lesion noted within the retromolar trigone or ascending ramus area, the prior knowledge that keratocysts and UCAs have a high predisposition for this area should make the surgeon go for enucleation preceded by aspiration, excision of the overlying mucosa and treatment with either Carnoy’s solution or liquid nitrogen cryotherapy. No further treatment is needed in case of an odontogenic cyst and this treatment would also suffice for either keratocyst or Grade 1 or 2 UCAs. However, if the histology yields the diagnosis of a type 3 UCA or solid ameloblastoma, again a marginal or partial resection would most aptly reduce the chances of any recurrence.

REFERENCES