

Unicyclic Ameloblastoma – Investigation into an Enigma

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Abstract: Unicyclic ameloblastoma is a less encountered variant of ameloblastoma. Dentigerous cyst, odontogenic keratocyst, residual cyst, calcifying odontogenic cyst, adenomatoid odontogenic tumor, giant cell lesion and sometimes solid ameloblastoma can be the possible differential diagnoses for unicyclic ameloblastoma. Unicyclic ameloblastomas, differ from the solid types of ameloblastoma in that they can be enucleated with a lower risk of recurrence. Hence histopathologic examination is essential to diagnose such cases. Further, immunohistochemical examination, may be of use in small biopsies or biopsies of cystic lesions and for the identification of malignant change. Here we are reporting a case of mandibular unicyclic ameloblastoma in an older patient which was initially diagnosed as an inflammatory cyst based on clinical and radiographic findings.

Key Word: Unicyclic Ameloblastoma, Dentigerous/Non-Dentigerous variant, Calretinin

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I. Introduction

The unicyclic ameloblastoma (UA) represents an ameloblastoma variant, presenting as a cyst and has a lower recurrence rate following conservative removal. Five to 15% of all ameloblastomas are of the unicyclic type^{1,2}. It refers to those cystic lesions that show clinical, radiographic or gross features of jaw cyst, but on histologic examination show typical ameloblastomatous epithelium, lining part of the cystic cavity with or without luminal and / or mural tumor growth³. Thus, unicyclic ameloblastoma is an enigma and less encountered variant of ameloblastoma. UA also shares common clinical and radiographic manifestations with other odontogenic lesions making diagnosis difficult.

Here we are reporting a case of mandibular unicyclic ameloblastoma in an older patient which was initially diagnosed as an inflammatory cyst based on clinical and radiographic findings. We have also tried to show more evidence, to solve the dilemma during the diagnosis of this cystic tumour.

II. Case History

This case report involves a 61 year old woman with a complaint of swelling on the left lower jaw. The swelling had gradually increased in size over a period of three months with no associated pain or discomfort. The draining lymph nodes did not show signs of swelling, tenderness or lymphadenopathy. Upon examination, the patient had a partially edentulous mandible, with 45 and 46 the only teeth being present. Intra-orally, cortical expansion in relation to 34, 35 region was detected of size 3x2 cm, swelling was observed on the lingual side also [Fig 1].

Mucosa over the swelling was non-tender, and appeared to be normal in colour, texture. Radiographic analysis showed a well-defined unilocular radiolucency extending from 31 to 34 region [Fig 2]. A provisional diagnosis of residual cyst was arrived at based on the above clinical symptoms. In further investigations regarding the lesion, the FNAC (Fine Needle Aspiration Cytology) report showed compatibility with an inflammatory cystic lesion. An incisional biopsy was done and histopathological examination, revealed thin cystic lining of ameloblastomatous odontogenic epithelium. The connective tissue capsule contained follicles of odontogenic epithelium consisting of peripheral pre-ameloblast like cells and central stellate-reticulum like cells. Cystic degeneration could be seen in some of the follicles. At areas the cystic epithelium was seen proliferating into the lumen in a plexiform pattern [Fig 3]. These findings confirmed the diagnosis as a luminal, intraluminal and intramural unicyclic ameloblastoma. As part of the treatment plan, enucleation was done and the patient was kept under long-term follow-up.

III. Discussion

Histologically UA is subdivided into Subgroup 1: luminal UA; Subgroup 1.2: luminal and intraluminal; Subgroup 1.2.3: luminal, intraluminal and intramural; Subgroup 1.3: luminal and intramural⁴. It most commonly occurs in posterior mandible followed by parasymphysis region, anterior maxilla and posterior maxilla, irrespective of the histological variant^{3,5,6}.

Leider et al, proposed three plausible pathogenic mechanisms for unicystic ameloblastoma, which are⁷:

1. The reduced enamel epithelium associated with a developing tooth undergoes ameloblastic transformation with subsequent cystic development.
2. The ameloblastomas may arise in dentigerous or other type of dental cyst in which the neoplastic ameloblastic lining is preceded temporarily by a non neoplastic stratified squamous epithelial lining.
3. A solid tumour undergoes cystic degeneration of ameloblastic islands with subsequent fusion of multiple microcysts to develop a multicystic lesion.

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 development⁸.

Dentigerous cyst, odontogenic keratocyst (OKC), residual cyst, calcifying odontogenic cyst, adenomatoid odontogenic tumor, giant cell lesion and sometimes solid ameloblastoma can be the possible differential diagnoses for unicystic ameloblastoma⁹.

Most unicystic ameloblastomas resemble dentigerous cyst (DC) clinically and radiographically, but a few are not associated with impacted teeth which are called non dentigerous variant and resemble residual cyst³. In UAs which are associated with an impacted tooth, the mandibular third molar is involved most often¹⁰. This case, was not associated with any unerupted/impacted teeth and occurred in anterior mandible. When cysts are associated with teeth, several entities might be considered in the differential diagnosis, such as dentigerous cyst, calcifying odontogenic cyst, ameloblastoma, odontogenic myxoma, adenomatoid odontogenic tumor, and odontogenic fibroma^{11,2}.

Despite the term “unicystic,” radiographically the tumor not only appears unilocular but also as multilocular defect in the jaw bones⁶. The various radiographic patterns documented in UA include pericoronal unilocular, extensive pericoronal unilocular, pericoronal scalloped, periapical unilocular, inter-radicular and multilocular¹². In the case of UAs which appear as a unilocular radiolucency, it is often misdiagnosed as an OKC/a DC, especially when it develops in relation to unerupted teeth^{10,13}. In our case DC is ruled out as there is no impacted tooth present.

The clinical and radiologic presentation of UA can give a confusing picture of odontogenic cysts especially when it is seen in the inter-radicular or periapical area. Hence histopathologic examination is essential to diagnose such cases¹². Proper diagnosis goes a long way towards directing the treatment as well as predicting the prognosis for a lesion, especially if it's a neoplasm. In this case, the initial diagnosis was as a cyst, however the histopathological assessment as unicystic ameloblastoma, certainly would help in determining treatment measures towards improving the prognosis and preventing recurrence.

The diagnosis of unicystic ameloblastoma can only be made when the presence of ameloblastomatous epithelium can be established unequivocally¹⁴. One of the difficulties in routine histopathological diagnosis of oral cavity diseases is the differential diagnosis of cystic jaw lesions, including odontogenic tumours, because their lining epithelia, which are basically stratified squamous epithelia, resemble each other, especially when they become hyperplastic from inflammatory reaction¹³. The intraosseous/central calcifying odontogenic cyst (COC), also called as the gorlin cyst is usually a well-defined unilocular radiolucency, but may occasionally appear multilocular. The lining epithelium in COC is also ameloblastomatous histologically, however nests of ghost cells present within the epithelium and juxtaepithelial dentinoid differentiate this lesion from unicystic ameloblastoma¹⁵.

Even by biopsy, it would be difficult to distinguish UA from other cystic jaw lesions because its lining tends to become flat, losing typical ameloblastomatous epithelia due to cystic expansion¹³. The cystic cavities of unicystic ameloblastomas are not always uniformly characteristic and are often partly outlined with a nonspecific epithelium similar to the lining of dentigerous cysts. Biopsies consisting exclusively of such epithelium may be unable to reflect the true nature of the entire lesion, multiple areas need to be evaluated, this also confirms that the tumor does not extend beyond the cyst wall^{16,17}.

We know that, for almost all odontogenic tumors there are characteristic histological features, and the diagnosis can be made with careful attention to morphology, in conjunction with radiology and other clinical features. However, there are some problematic areas: cystic lesions, small biopsies, and the identification of malignant change for which IHC (Immunohistochemistry) may offer some help. Immunohistochemical

analysis, in conjunction with CK13, CK14, CK19, CD56 (expressed in peripheral cells) and calretinin (expressed in stellate reticulum-like cells), can be of use in such cases. Both markers ie; CD56 and calretinin are expressed, to a much lesser extent, in odontogenic keratocyst, in addition OKC will express CK1 and CK10, which are markers of cornification¹⁸.

Studies on expression of proliferating cell nuclear antigen (PCNA) and Ki-67 in unicyclic and solid ameloblastomas were done by Li et al 1995, they found that the labelling indices of solid ameloblastomas of follicular type were significantly higher than those of cystic tumour lining, intraluminal nodules and invading islands in unicyclic ameloblastoma. Their results indicate differences in proliferative potential between different areas of unicyclic ameloblastoma and between unicyclic and solid lesions¹⁹.

The development and progression of odontogenic tumors are affected by alterations of many kinds of genes and molecules. These include (a) molecules possibly associated with tumorigenesis and/or tumor cell differentiation; (b) molecules possibly associated with tumor progression. Among these, those associated with ameloblastoma include oncogenes (*P21^{Ras}*, *K-Ras*, *c-Myc*, *Fos*), tumour suppressor genes (*p53*, *MDM2*, *P14^{ARF}*), oncoviruses (HPV, EBV), growth factors (Epidermal growth factor [EGF], hepatocyte growth factor [HGF]), telomerase, cell cycle regulators (*cyclin D1*, *P16^{INK4a}*, *P21^{WAF1/Cip1}*, *P27^{Kip1}*), apoptosis related factors (*p53*), regulators of tooth development (Wnt pathway), Hard tissue - related proteins (ameloblastin), cell adhesion molecules (Eselectin, ICAM-1, VCAM-1, E-cadherin, alpha-catenin, Integrins, CD44), Matrix degrading proteinases (MMPs-1, -2 and -9, heparanase), Angiogenic factor (VEGF), Osteolytic cytokines (IL-1, IL-6, TNF- α , PTHrP, RANKL, OPG)²⁰.

Unicyclic ameloblastomas, differ from the solid types of ameloblastoma in that they can be enucleated with a lower risk of recurrence. A 10% recurrence rate 10 years after enucleation can be expected¹⁷. The most controversial type with this lesion is mural due to the higher recurrence rate with conservative treatment than with the other two types ie; luminal and intraluminal².

IV. Conclusion

To conclude, the purpose of presenting this report of UA is to emphasize the importance of histopathologic investigations of tissue specimens, even when clinical and radiological findings are innocuous.



Fig 1: Intra-oral view



Fig 2: Panoramic radiograph demonstrating well-defined unilocular radiolucency in the left mandible

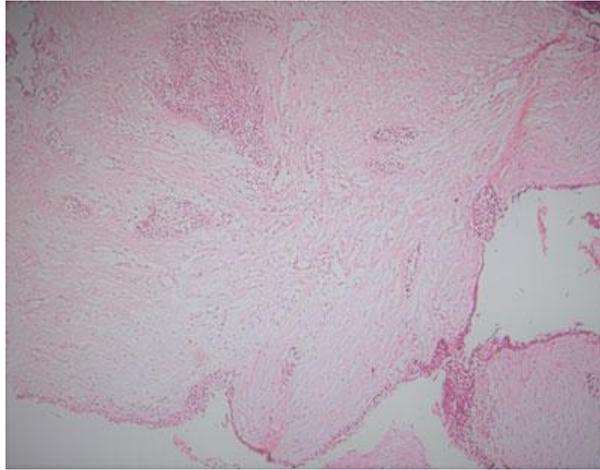


Fig 3: Photomicrograph showing cyst lined by ameloblastomatous epithelium, having intraluminal and intramural proliferation (H&E, 5X)

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