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Case Report
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WHO Reclassification of Odontogenic Keratocyst as Keratocystic Odontogenic Tumour: A Case Report

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ABSTRACT

The odontogenic keratocyst (OKC) is relatively uncommon cystic lesion of odontogenic origin which arise in the jaw bones either mandible or maxilla and has aroused much of interest because of its unusual growth pattern, aggressive clinical behavior and high rate of recurrence after surgical removal. This case-report of a 79 years old male Libyan patient presents a well-documented case of an uncommon, large and aggressive odontogenic keratocyst (OKC) with review of clinical, radiological, histopathological and surgical treatment may bring data forward for the reclassification of odontogenic keratocyst as a keratocystic odontogenic tumour (KCOT).

Keywords *- OKC; KCOT; Mandible; Maxilla; WHO; Reclassification.*

INTRODUCTION

The term odontogenic keratocyst (OKC) was first used by Philipsen in 1956 when he separated seven jaw cysts from cholesteatomas occurring in other cranial sites rather than mandible or maxilla and though that these were odontogenic and not inflammatory cysts.[1] Later in 1963 Pindborg and Hansen described the essential clinical, radiological and microscopical features of this lesion.[2]

The World Health Organization's New Classification Working Group of the year 2005 for head and neck tumours has designated odontogenic keratocyst parakeratinizing variant as keratocystic odontogenic tumour (KCOT), the change in terminology was based on the observation that the odontogenic keratocyst behaves as a benign but locally invasive tumour due to its aggressive clinical behavior, rapid growth, tendency to invade the adjacent tissue including bone, high recurrence rate and association with nevoid basal cell carcinoma syndrome (NBCCS) also called Gorlin-Goltez syndrome.[3]

Keratinizing jaw cysts are uncommon and occur over a wide age range but important because of the strong tendency of some of them unlike most other cysts to recur after surgical removal. Keratinizing cysts are divided into two main types, those with a parakeratinization and those with an orthokeratinized epithelial lining. Parakeratinized odontogenic cysts reclassified as (keratocystic odontogenic tumour) that have a high recurrence rate and may occur either sporadic or in association with multiple abnormalities in the Gorlin-Goltez syndrome.[4] Orthokeratinized cysts was previously considered as a variant of odontogenic keratocyst which has a low risk of recurrence and was classified separately.[5-8]These findings have led to extensive research on OKCs of either parakeratinized or orthokeratinized epithelial lining but the reclassification of OKC as KCOT still remain a subject of controversy.

Case Report

A 79-year old male Libyan patient presented in Oral and Maxillofacial Surgery Unit of Sabrath Tumour Institute complaining from swelling at the right side of the lower jaw associated with a slightly intermittent pain since about two months ago. The patient dental history had revealed that he visited a general dental practitioner and diagnosed as a case of dentoalveolar abscess. Antibiotic, analgesic and mouth wash gargle were prescribed and the patient asked to visit the dental clinic back after three days for extraction of the remaining root at the site of swelling which suspected to be the source of infection (Figure1).

Clinical examination revealed a bony hard swelling of approximately 2 to 3 cm in size located mostly at the premolar-molar region of the body of the mandible causing mild facial asymmetry and perforating the buccal cortical plate just posterior to the second right premolar and involved the covering soft tissue. The swelling was fluctuant on palpation indicating a cystic lesion. Clinical examination also revealed edentulous state except for lower right and left first and second premolars (Figure 2).

The patient was apparently healthy and had no clinical features of suggestive NBCCS or Gorlin-Goltez syndrome, orofacial digital syndrome, Noonan syndrome, Ehler-Danlos syndrome, Simposon-Golabi syndrome or any other syndromes. Heamatological, serological, biochemical investigations as well as cardiac and neurological consultation were within the normal limits.

Orthopantomography (OPG) revealed a well-defined mulilocular area of radiolucency with scalloped margins which extended from lower right second molar to the lower right central incisor, perforating the cortical plate in the premolar-molar region. It was noted that the primary lesion appeared to be in the molar region then extended in the

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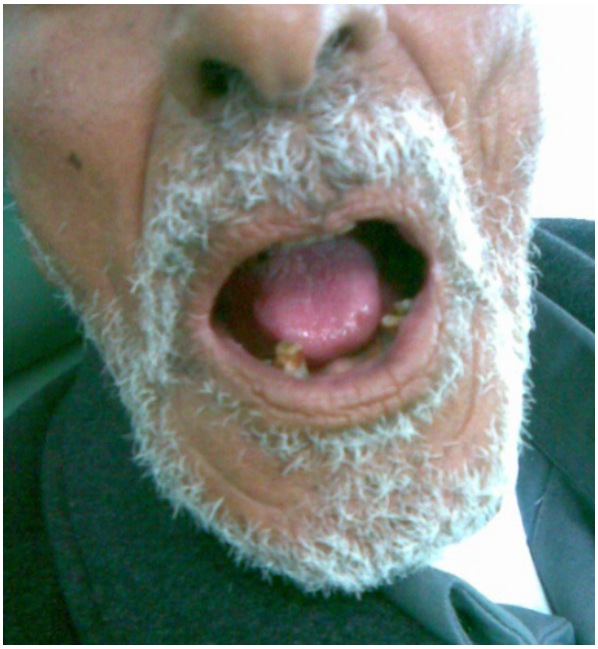

Figure 1: Shows swelling at the right of lower jaw

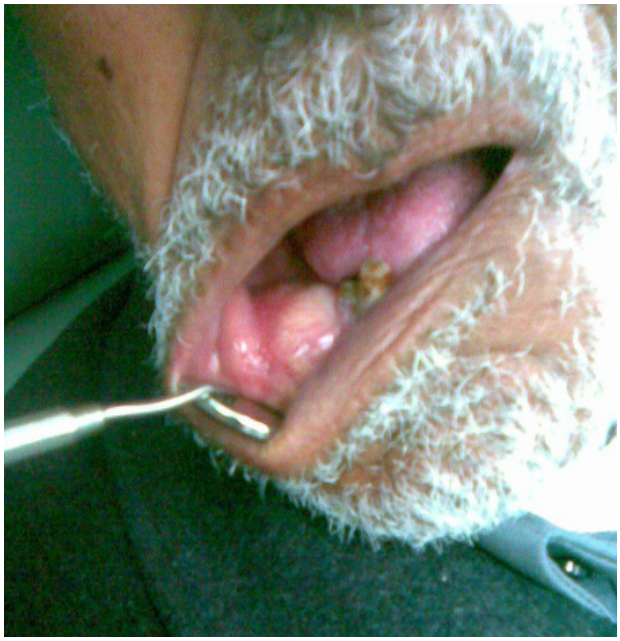

Figure 2: The swelling has perforated the cortical plate and Involve the covering soft tissue

antero-posterior direction. Resorption of roots of the first and second premolars are also the features of note (Figure 3). The differential diagnosis based on clinical and radiological features was odontogenic keratocyst or ameloblastoma.

The patient was admitted to Oral and Maxillofacial Unit, Sabrath-Tumour Institute and surgical enucleation with curettage of the lesion was performed under general anesthesia and chemically cauterized with Carnoy's solution followed by primary closure. The excised pathology was sent for microscopical examination and final histopathological diagnosis.

Macroscopical examination revealed a large lesion of about 3 to 6 cm in size containing yellowish straw fluid while microscopical examination revealed a cystic lesion consisting of a cystic cavity lined by epithelium and supported by a fibrous tissue capsule (Figure 4,5).

The epithelial lining is a parakeratinizing stratified squamous in type of some 5-10 cells in thickness and has tendency to separate from the fibrous tissue capsule. The cystic wall is corrugated with flat epithelial lining and absence of rate ridges while the basal cells are hyperchromatic and have arranged in palisaded maner.

Mitotic activity of the cystic epithelium together with a potential for budding of basal cell layer and presence of dauther cysts in the fibrous tissue cap sule are also the features of note (Figure 6, 7). The histopathological features, therefore are consistent with the diagnosis of odontogenic keratocyst. Postoperative course after a period follow-up revealed a substantial healing of bone defect.

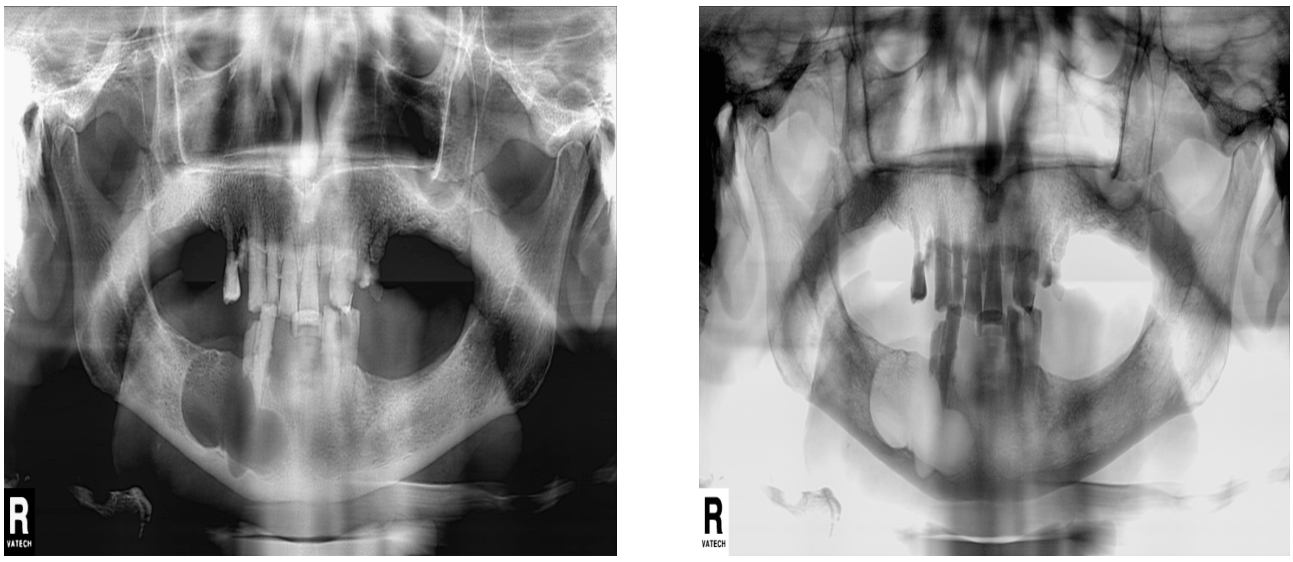

Figure 3: OPG shows well-defined multilocular area of radiolucency with scalloped margins extended from the lower right second molar to the lower right central incisor

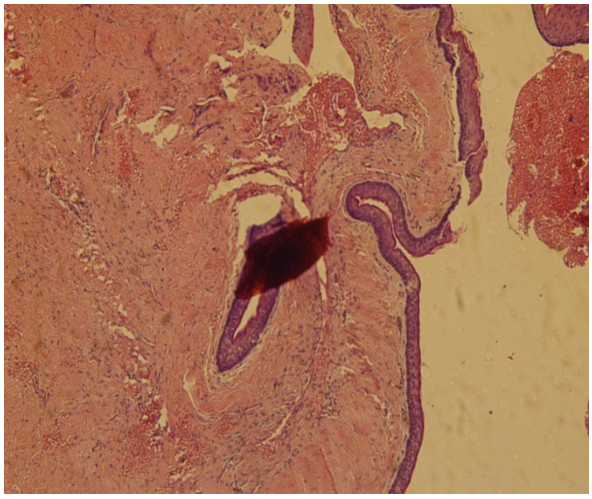

Figure 4: H & E stained section at low power showed a cystic lesion

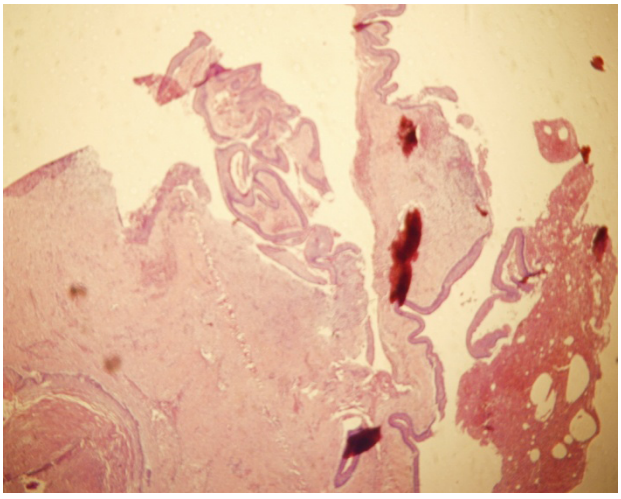

Figure 5: H& E staine section showed regular epithelialconsisting of cystic cavity lined by epithelium and supported by lining with flat epithelio-mesenchymal junction fibrous tissue capsule

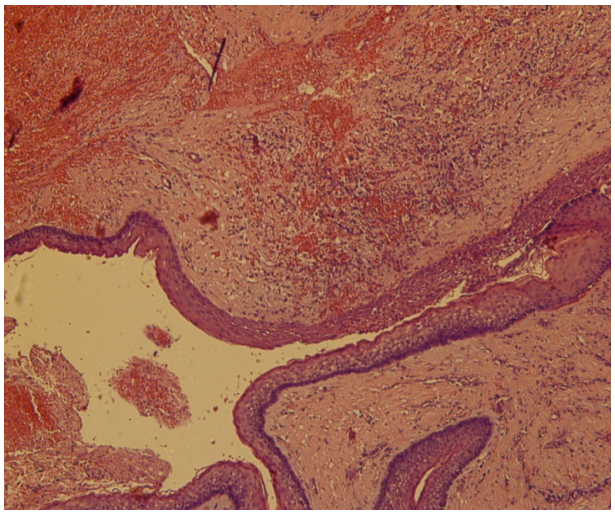

Figure 6: H & E stained section showed that the epithelial lining

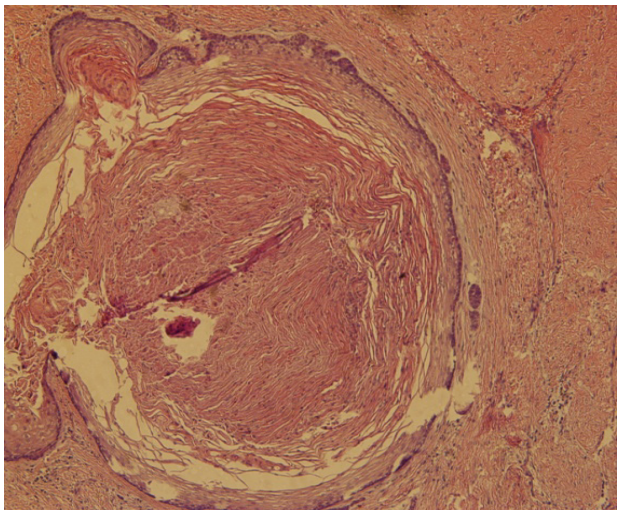

Figure 7: H & E stained section showed large daughter is corrugated and of about 5-10 cells in thickness with buddingcyst in the fibrous tissue capsule of basal cell layer

DISCUSSION

Cysts of the jaws are more common than in any other bone, and the majority of them are lined wholly or in part by epithelium. Although the pathogenesis of many of these cysts are poorly understood, they divided into two main groups depending on the origin of the epithelium lining as odontogenic cysts where the epithelial lining is derived from epithelial residues of tooth-forming organ and non-odontogenic cysts where the epithelium lining is derived from sources other than the tooth-forming organ.[9,10]

The odontogenic cysts are divided into two main groups depending on the nature of stimuli responsible for epithelial proliferation as developmental and inflammatory. Odontogenic keratocysts are developmental cysts and considered to be a significant clinical entities. The pathogenesis of these cysts are generally thought to be derived from either epithelial remnants of tooth germ such as epithelial rests or glands of Serres persisting after dissolution of the dental lamina, the basal cell layer of the surface epithelium or from the primordium of a normal or supernumerary tooth before hard tissue formation.[11-13]

Odontogenic keratocyst accounts for about 5 to 10% of all jaw cysts but is clinically important as it has an aggressive growth pattern with a high recurrence rate and, since it may be very large before becoming evident and can cause considerable surgical difficulties. The recurrence rate ranges from 5% to 62.5 % with most recurrence develop during the first 5 to 7 years after therapy.[14-16]

Browne concluded that the high recurrence rate of OKC was due to the nature of the lesion itself, namely the presence of additional remnants of dental lamina or satellite cysts (daughter cysts) left behind following surgical treatment rather than different methods of surgical treatment.[17] Several authers have attempted to correlate the behavior of OKC with the production of collagenase, prostaglandins, and high active oxidative enzymes. Sharfertter et al demonstrated both slowly and rapidly proliferating areas in different parts of epithelium and connective tissue wall.[18]

OKC involve the mandible in 70 to 80% of cases and about 50% of these are at the molar region, angle and ascending ramus. Although, it almost always occurs within the bone as a central lesion but a small number of cases of peripheral OKC have been reported. OKC occur over a wide age range, it is reported that the age incidence ranged from 6 to 78 years, but virtually a few cases have been reported in a very elderly patients. The cyst is slightly more common in males than females with a peck incidence in the second and third decade of life.[19-22]

Odontogenic keratocyst is typically symptomless only if it is secondary infected and has tendency to expand in antero-posterior direction through the cancellous bone of medullary cavity. Therefore, it can reach a large size before it can be discovered while a small sized cysts reported in the literature may represent an early chance of discovery during routine radiological examination. Lateral expansion, perforation of cortical plate, pathological fracture and teeth displacement usually represent the late clinical and radiological features.[23,24]

Radiographically, OKC usually shows a well defined scalloped area of radiolucent with or without radiopaque margin. Multilocular cysts may also the present feature which resemble ameloblastoma especially in the mandible. Some cysts appear to surround the crown of an unerupted teeth, such cysts may appear radiographically similar to dentigerous cyst. Occasionally, OKC develops on the lateral aspect of a root which resemble lateral periodontal cyst.[24-26]

Histopathologically, the characteristic microscopical feature of OKC is the structure of epithelial lining, the cyst is lined by regular layer of typically parakeratinized or occasionally orthokeratinized stratified squamous epithelium some five to ten cells in thickness supported by thin friable fibrous tissue capsule. The basal cells are intensely basophilic and may be polarized away from the basement membrane, although, mitotic figures, hyaline bodies, epithelial budding of basal cell layer and dystrophic calcification have been reported.[25-27]

The cyst wall is frequently corrugated with flat epitheliomesenchymal junction and the epithelial lining may show tendency to separate from the fibrous tissue capsule. Another characteristic feature is the presence of daughter cysts in the fibrous tissue capsule. Some OKC lining may have the characteristic feature of epithelial dysplasia that may posses the potential to evolve into ameloblastoma or squamous cell carcinoma.[25-27]

Multiple OKCs usually occurs as a component of NBCCS or Gorlin-Goltz syndrome, orofacial digital syndrome, Noonan syndrome, Ehler-Danlos syndrome, Simpson-Golabi-Behmel syndrome or other syndromes. The Gorlin-Goltz syndrome (NBCCS) is inherited as an autosomal dominant trait and consisted essentially triad of multiple naevoid basal cell carcinoma, multiple OKCs of the jaws and skeletal abnormalities. The occurrence of multiple OKCs may be the first and only manifestation of NBCCS and may remain hidden in the early years of life, therefore the dentist may will be the first to detect this syndrome.[28-33]

In 1967, Toller proposed that the OKC may best regarded as a benign tumour rather than a cystic lesion based on its clinical behavior.[34] In 1984, Ahlfors and others suggest that if the OKC was recognized as a true benign cystic epithelial tumour, the question of modified treatment would be raised. 35

Several reports and recent studies have provided valuable additional parameters to distinguish between OKC and KCOT. Therefore, these new scientific data have influenced the WHO to redesign OKC as KCOT based on the following scientific factors.

Clinical behavior: OKC is a locally invasive with high recurrence rate and has tendency to expand in antero-posterior direction unlike other jaw cysts that have a unicentric ballooning way of expansion.[24-27]

Histopathologically: OKC shows increase of mitotic activity in the cystic epithelium particularly in the suprabasal cell layer together with a potential for budding of basal cell layer and presence of daughter cysts in the cystic wall.[23-27]

Genetic mutation and chromosomal abnormalities that are reported to be in consistent with neoplastic proliferation rather than cystic formation: Evidences have shown that the pathogenesis of naevoid basal cell carcinoma syndrome (NBCCS) is associated with multiple OKCs, adding to that sporadic cases of OKC are both involve mutation of PTCH (patched) gene. PTCH gene is a tumour suppressor gene present on the long arm of chromosome nine (9q22) which controls the normal growth and development process of normal tissue and encodes for a protein involves in the signaling and function of Sonic Hedgehog (SHH) pathway. PTCH gene forms a receptor complex with the oncogene SMO (smoothened) for the SHH (sonic hedgehog) ligand. PTCH binding to SMO inhibits growth signal transduction while PTCH binding to SHH releases this inhibition. Therefore if the normal function of PTCH gene is lost, the proliferation-stimulating effect of SMO predominates.[36-41]

Loss of heterozygosity (LOH): It have been reported in OKC that LOH leads to abnormal regulation of oncoproteins cycline D1 and P53 similar to that of basal cell carcinoma, squamous cell carcinoma and transitional cell carcinoma.[42]

Higher levels of biologic proliferative markers: Ki67 and proliferating cell nuclear antigen (PCNA) are observed in OKC compared to dentigerous cyst and radicular cysts, suggesting that proliferation of the epithelial lining is important in the pathogenesis of OKC. CD105 (a marker for newly formed blood vessels), is also expressed at higher levels in OKC, providing evidence that angiogenesis within the cyst wall may also contribute to its growth potential and aggressive clinical behavior, adding to that immunohistochemical detection has shown that cytokeratins CK17 and CK19 are over expressed in OKC.[43-44]

In light of these evidences which scientifically support that OKC has neoplastic origin, the World Health Organization officially reclassified odontogenic keratocyst as keratocystic odontogenic tumour. But many oral and maxillofacial diagnostic pathologists who are not familiar with keratocystic odontogenic tumour continue to use the term odontogenic keratocyst in their histopathological reports. Therefore to minimize the confusion and for clinical practice, the new term KCOT and previous term OKC may be used as a synonymous.

Morgan and colleagues categorized surgical treatment

methods for OKC as conservative or aggressive. Conservative treatment is a cyst oriented which including enucleation with or without curettage or marsupialization. This process is generally used for large cysts in order to preserve bone, teeth, and other vital structure, while aggressive treatment addresses the neoplastic nature of OKC and include peripheral ostectomy, chemical curettage with Carnoy's solution or en block resection.[45-46]

Clinically, the term OKC matters less than how it can be managed more accurately as KCOT in the surgical unit and up to date the final histopathological diagnosis still using the traditional methods of hematoxylin and eosin stained microscopical slides. However, continued scientific study and research may hel pathologists and surgeon determine which lesion is more likely to behave aggressively and thereby assist in guiding the treatment of each case.

This case-report is a well documented KCOT diagnosed by us and treated in Sbrath Tumour Institute. The lesion showed the diagnostic criteria that used by WHO Working Group in their reclassification, and in accordance with the findings that described before.

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