Multiple Recurrent Odontogenic Keratocysts with Malignant Transformation Occurring in a Non Syndromic Setting

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Introduction
Keratocystic odontogenic tumor (KCOT) are epithelial developmental cysts showing aggressive behaviour and high recurrence rate as compared to other odontogenic cysts. Multiple cysts are usually associated with Nevoid Basal Cell Carcinoma Syndrome (NBCCS), which is caused by mutation of patched (PTCH), a tumour suppressor gene that has been mapped to chromosome 9q22.3-q31. We present non syndromic case of multiple KCOTs in a male patient with one of the cyst lining showing transformation into squamous cell carcinoma which is very rarely seen.

KCOT is a cyst with specific histopathological features and clinical behavior. It arises from the rests of dental lamina. These tumours show aggressive behavior because of their tendency to invade the adjacent tissues. KCOTs have recurrence rate varying from 5% to 62%. Peak incidence of occurrence is from second to fourth decade of life. Majority of the lesions appear in mandible, mainly in posterior body and ascending ramus followed by maxillary 3rd molar area and cuspid region. The common clinical features of KCOTs include pain, soft tissue swelling, expansion of bone and paraesthesia of lip. KCOT demonstrate a well defined radiolucent area with smooth and often corticated margin. Histologically KCOTs show a thin cyst wall lined by stratified squamous epithelium, six to eight cells thick. There is keratinized corruate layer on the surface of the epithelium. The wall of the cyst frequently shows satellite/daughter cysts. KCOT is usually treated by enucleation and curettage. Multiple KCOTs are often reflected as being a component of Nevoid Basal Cell Carcinoma Syndrome (NBCCS). At other times these multiple KCOT are rarely observed.

Case Report
A 31 yr old patient initially reported to department of oral and maxillo facial surgery in December, 2011 with the complaint of right sided discharging maxillary oroantral fistula. The patient was operated and histopathology report revealed a cyst showing keratinized stratified squamous epithelium with flat connective tissue and epithelium interface without any rete pegs. The underlying connective tissue showed multiple daughter cysts. Diagnosis of KCOT of right side of maxilla was made.

In March, 2012 the same patient developed acute episodes of pain, bilateral swelling of the lower jaw and associated numbness in the lower lip. On clinical examination, there was no obvious swelling or abnormality in facial symmetry. Intraoral examination revealed a prominent swelling in the buccal mucosa in relation to the right posterior region of mandible, with paraesthesia of the lower lip. There was no discharge from the lesion with normal tongue and jaw movements. The patient had no history of smoking and systemic diseases. The findings from the remainder of the head and neck examination were within normal limits. Radiographic examination revealed multiple well defined radiolucent lesions with smooth cortical borders in association with the roots of left maxillary lateral incisor and canine, left mandibular molars, right mandibular premolars and molars (Figure 1). Dermatologist was consulted to rule out the NBCCS. The examination revealed no clinical manifestation of cutaneous abnormalities such as epidermal cyst of the skin and palmer or planter pits. On the basis of clinico-radiographic findings the case was provisionally diagnosed as non syndromic multiple recurrent KCOT. The lesions were enucleated along with the curettage in a single operation. Three of the specimens taken from the both sides of the mandible and left side of the maxilla revealed cyst walls lined by keratinized stratified squamous epithelium with the surface of keratin layer showing corrugation (Figure 2). The microscopy was consistent with the diagnosis of KCOT with no evidence of malignancy. Another biopsy from the right side of mandible revealed a cystic lining along with a tumour with atypical squamous cells, showing nuclear pleomorphism, high nuclear/cytoplasm ratio, atypical mitosis, hyperchromatic nuclei along with some areas of keratin pearl formation(Figure 3 and 4). The intervening areas showed dense infiltration by
lymphocytes and plasma cells. Tumour was reaching up to the biopsy margins. The case was diagnosed as a cyst with the lining showing malignant transformation to squamous cell carcinoma. Immunohistochemistry was applied to rule out the possibility of ameloblastoma. The results showed 34-B12 and p63 positivity and calretinin negativity. In the case of malignant lesion, complete surgical excision of involved margins along with adjuvant chemotherapy or radiation therapy was advised. Due to the aggressive nature of the KCOTs and malignant nature of the squamous cell carcinoma, regular follow up of patient was advised.

Discussion

Non-syndromic multiple KCOTs have been known to occur but in very rare instances. Multiple KCOTs are thought to be the first manifestation of the NBCCS or otherwise they may be because of the multifocal nature of KCOTs. They may occur as a component of other syndromes as well such as orofacial digital syndrome, Noonan syndrome, Ehler-Danlos syndrome and Simpson-Golabi-Behmel syndrome. 67\textsuperscript{9} KCOTs have a biologic behavior similar to a benign neoplasm.\textsuperscript{3} NBCCS is associated with a triad of multiple basal nevi, multiple OKCs and skeletal abnormalities. This triad of symptoms may be associated with other manifestations involving skeletal, craniofacial, neurological, skin, sexual, ophthalmic and cardiac anomalies.\textsuperscript{8,9}

Radiographically, KCOT usually appears as a unilocular, radiolucent lesion with smooth, corticated borders, mostly associated with an impacted tooth. KCOT are more likely to show aggressive growth than other odontogenic cysts and may have undulating borders and a multilocular appearance. These characteristics make KCOT\textsuperscript{s} indistinguishable from ameloblastomas.\textsuperscript{10} KCOT may cause cortical thinning, tooth displacement, and root resorption.\textsuperscript{11}

Histologically, cyst is lined by orthokeratinised or parakeratinised stratified squamous epithelium, with corrugated surface and absence of rete pegs. The columnar or cuboidal basal cells have palisaded nucleus. The presence of satellite cysts and odontogenic epithelial islands in the cyst wall is another feature.\textsuperscript{3} The possibility that the epithelial cells lining an odontogenic cyst may undergo malignant transformation to a squamous cell carcinoma has been recognized but is rare, with very few documented cases.\textsuperscript{2}\textsuperscript{3} Treatment options for KCOT are marsupilization, simple enucleation with the use of carnoy’s solution or cryotherapy, marginal, or radical section.\textsuperscript{4,13}

References