Bilateral Odontogenic Keratocyst of the Mandible

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Received: 5 March 2010 / Accepted: 14 October 2010 / Published online: 25 March 2011
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Abstract Odontogenic keratocyst (OKC) is a cyst of dental origin with an aggressive clinical behavior, having high recurrence rate. Multiple cysts are associated with bifid-rib basal cell nevus syndrome (Gorlin syndrome). We present a case of bilateral odontogenic keratocyst in a cleft lip patient.

Keywords Keratocyst · Mandible · Maxilla · Odontogenic · Recurrence

Introduction

The odontogenic keratocyst (OKC) was first described in 1876, named by Phillipsen in 1956 and has been associated with a tendency to recur [1]. According to the new histological classification of WHO, odontogenic keratocyst is considered a odontogenic tumour [2]. OKC represent a more aggressive form of odontogenic cyst. The parakeratinized

variant (previously called a primordial cyst) is thought to have a high recurrence rate than the orthokeratinized variant. Because of these features, a more aggressive treatment than simple enucleation has been advised [3]. Recommended treatment include curettage with peripheral Osteotomy [4], curettage plus liquid nitrogen cryotherapy [5], curettage plus application of Carnoy's solution [6], localized en bloc resection [7] and, occasionally, mandibular segmental resection [8]. Some authors recommend that OKC should be considered as benign cystic neoplasm and treated accordingly [9]. Nevroid basal cell carcinoma syndrome (NBCCS), Gorlin syndrome, Gorlin–Goltz syndrome and Basal Cell Nevus syndrome (BCNS) are synonyms to each other.

In the reported case, patient had complaint of pain, swelling and discharge of pus from left retromolar region. Radiological examination showed impacted mandibular third molar teeth with radiolucent area circumscribed by radio opaque margins surrounding crown of impacted teeth on both sides. Histopathological examination revealed 6–8 cells layer thick parakeratinized stratified squamous epithelium with superficial corrugated surface and palisaded layer of basal columnar cells. The cystic wall was made of thin layer of fibrous connective tissue. Cystic lining along with impacted crown was removed and osteotomy was done.

Case Report

A 16 year old female patient reported to the Department of Oral and Maxillofacial Surgery, CSM Medical University, Lucknow with complaints of pain, swelling and discharge of pus from the left retromolar region of the mandible since 1 month. Three year back she had pain in left lower molar

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tooth which was managed with antibiotics by a dental surgeon. Symptoms relieved temporarily and reappeared after 3 months.

Extra-oral examination showed slight facial asymmetry with flattening of nose and scar mark on right side of the lip (Fig. 1). A submandibular lymph node was palpable on left side. No obvious abnormality was observed on systemic examination. Intra-oral examination showed absence of mandibular and maxillary 3rd molar teeth on both (right and left) side of the jaw, right maxillary lateral incisor was also invisible, left deciduous maxillary canine was retained, and permanent left maxillary canine was absent. Maxillary right canine was partially erupted.

Radiological examination of maxilla showed both maxillary 3rd molar teeth in impacted position and right maxillary 3rd molar was in unusual position. Left maxillary canine was impacted and a radiolucent shadow was attached at the tip of crown. Right maxillary lateral incisor was missing, right maxillary canine tooth was partially erupted and almost horizontally placed. Radiological examination of mandible showed both mandibular 3rd molars in impacted position. A radiolucent shadow was seen around the crown of the impacted molars circumscribed by radio opaque border around them. Roots of the molars were resorbed (Fig. 2).

On the basis of radiological findings, patient was operated on 6 October, 2008. Cystic lining along with circumscribed mandibular third molars was removed. Osteotomy was done with trimmer (Fig. 3). Histopathological examination showed 6–8 cells layer thick parakeratinized stratified squamous epithelium with superficial corrugated surface and palisaded layer of basal columnar cells. The cystic wall was made of thin layer of fibrous connective tissue. On the basis

Fig. 1 Pre-operative photograph of patient, showing scar mark of cleft lip

Fig. 2 Preoperative radiograph showing bilateral OKC with impacted molars

Fig. 3 Postoperative radiograph, after removal of lesion of right side

Fig. 4 Histopathology of the lesion (H&E stain)

of histopathological examination the diagnosis of odontogenic keratocyst was made (Fig. 4). Second operation was done on 25 May 2009 to remove the radiolucent mass on the right side of mandible circumscribing the right sided molar (Fig. 5) the diagnosis was same as diagnosed by the previous histopathological examination. After one year of follow up no recurrence was observed (Fig. 6).

Fig. 5 Postoperative radiograph, after removal of lesion on both sides

Fig. 6 Post operative radiograph after one year follow up

Discussion

OKC are relatively common developmental odontogenic cysts and account for 10–12% of all jaw cysts [8, 10]. An OKC usually occurs as a single lesion. Multiple lesions are associated with the nevoid basal cell syndrome (Gorlin–Goltz syndrome) [11]. The OKCs originate either from epithelial remnants of tooth germ in the mandible and maxilla [10] or the basal cell layer of the overlying surface epithelium [12].

The peak incidence is in the second and third decades of life with a gradual decline thereafter [13–15]. Peak incidence in both sexes occur in the third decade [5] frequency of occurrence is higher in male than female [11, 13, 14]. Though it can occur in any part of mandible and maxilla, but in 70% of the cases, arise in the posterior body and 6.9% at the symphyseal region of the mandible [16]. The mandible is the more favoured site than the maxilla, 65 vs. 35% [11] and 78 vs. 22% [14]. Ramus and the molar area are the most favoured sites [15].

In approximately 50% of patients, lesion is asymptomatic. In other cases pain, swelling, expansion, drainage, and bone perforation are reported [8]. These lesions grow to sizes larger than any other odontogenic cyst. They more often penetrate the bone rather than expand it and grow in an anterior to posterior direction [13]. Despite this aggressive growth, they often remain asymptomatic [16]. It

may displace the root of teeth, extend into the maxillary sinus, or result in pathologic fracture of mandible.

An OKC has a fibrous wall lined by epithelium with a thin layer of stratified squamous epithelium on histopathological examination. This epithelium has a basal cell layer of six to eight cells thick and a lining of flattened keratotic epithelial cells. The formed keratin lines the luminal surface of the epithelial cells in a slightly wavy or corrugated pattern [10]. The luminal content can have different consistencies as a “straw-coloured fluid”; “thick pus like” material; or a caseous, thick, cheesy, milk white mass [17]. The varying consistencies reflect various densities of keratinaceous debris. Histologically OKCs have been classified into parakeratotic and orthokeratotic subtypes [8]. These types refer to the histological characteristics of the lining and the type of keratin produced. Compared with the parakeratotic subtype, the orthokeratotic subtype produces keratin closely resembling the normal keratin produced by the skin. The keratin (orthokeratin) does not contain nuclei. The parakeratotic subtype has a more disordered production of keratin. The keratin contains nuclei and is referred to a para keratin. The parakeratotic type is the most frequent (80%) and has a more aggressive clinical presentation than the orthokeratinized variant [18]. Immunohistochemical studies have shown higher levels of interleukin-1 α (an inflammatory multifunction cytokine) in OKC compared with dentigerous cyst [19]. Interleukin-1 α is thought to play a crucial role in expansion of OKCs by inducing the secretion of keratocyte growth factors from interactive fibroblasts [20]. Nature of the cyst lining before and after decompression with cytokeratin stains have reported positive cytokeratin-10 staining in pre-decompression biopsy and negative cytokeratin-10 stain in post-decompression specimen indicating a return to more normal oral epithelium [21]. Bcl-2, is an anti-apoptotic protein and has been shown to be strongly and consistently expressed by all basal cells of OKCs but not in other odontogenic cysts [22]. Hence it was likely that bcl-2 could be used to differentiate keratocyst lining from normal epithelium [20].

Radiologically lesion characteristically presented as an extensive well defined area of bone destruction. The border of these lesions appears to be thinly sclerosed [17]. Characteristic radiographic features of OKCs are an intinctly corticated, often scalloped, border, expansion toward the lingual side, and growth along the length of the mandibular bone, displacement of developing teeth and/or separation of resorption of the roots of erupted teeth and extrusion of erupted teeth, a radiolucent lumen, and occasionally a cloudy or milky appearance of the lumen on the panoramic radiograph. Multiple or bilateral cysts are suggestive of basal cell nevus syndrome [8, 18]. CT provides additional information about the contents of the lesion. The high attenuation is thought to the result of a high protein concentration in the dense keratin filling the lumen. Other

possibilities include hemorrhage or calcification. If the high attenuation represent calcification rather than simple high protein content, the differential diagnosis would include a Gorlin cyst (calcifying odontogenic cyst), Pindborg tumor (calcifying odontogenic tumor), and adenomatoid odontogenic tumor [8, 18], hemorrhagic bone cyst (simple bone cyst), vascular lesion of malformation with calcification. However, with a vascular lesion, a change in attenuation should occur when a contrast-enhanced CT scan is compared with a non enhanced CT scan [23]. OKC do not expand the bone to the same degree as dentigerous cysts and are less likely to produce teeth resorption [24]. OKC are more likely to have scalloped periphery but dentigerous cysts have smooth periphery. It is not possible to differentiated OKC, dentigerous cysts and unicystic ameloblastomas by clinical and radiographic examination [25]. On MR images, an OKC typically has low to intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images. This pattern may be caused by fluid containing a low concentration of protein, which results in intermediate signal intensity on T1-weighted images [23].

Multiple keratocysts are frequently associated with the bifid-rib basal cell nevus syndrome (Gorlin syndrome) [16]. Gorlin and Goltz in 1960 defined the condition as a syndrome comprising the triad of multiple basal cell naevi, jaw keratocyst and skeletal anomalies [26]. A wide range of neurological, endocrine, ophthalmic and genital manifestations [26] are known to be variably associated with this syndrome. The prevalence of the NBCCS (nevoid basal cell carcinoma syndrome) has been estimated to range from 1 in 57 000 to 1 in 164 000 [27] but now considered that the prevalence is about 1 in 60 000 [28]. Both sexes are equally affected [29]. WHO has re-classified odontogenic keratocysts as keratocystic odontogenic tumour (KCOT) [30]. KCOT associated with NBCCS (nevoid basal cell carcinoma syndrome) is usually observed in younger patients with presentation at multiple sites. Heparanase expression is correlated with the invasive properties of NBCCS associated KCOT [6] there is association of cytokeratin-17 expression with this syndrome [31].

Transformation of OKC into squamous cell carcinoma and ameloblastomas has been reported in the literature [3]. Ameloblastomatous transformation of the OKC is very rare but has been reported by Holmlund et al. [32].

There are different opinions regarding the management of OKC. These cysts are most aggressive forms of odontogenic keratocysts because of the high recurrence rates due to the presence of epithelial remnants of satellite cysts in the osseous margins. The parakeratinized variant has a higher recurrence rate than the orthokeratinized variant. For this reason a more aggressive treatment has been advocated [3]. The recommended treatment is; curettage with peripheral Osteotomy, [5] cryosurgery (curettage with liquid nitrogen

therapy) [3], curettage plus application of Carnoy's solution [6], localized en bloc resection [7] and occasionally, mandibular segmental resection [7], enucleation with post-operative intra-oral suction [33] and rinsing the bone defect with 3% hydrogen peroxide in order to detect and remove eventual remains of the capsule [33]. The goal of using Carnoy's solution and cryosurgery is to kill epithelial remnants and dental lamina in the osseous margins. Use of liquid nitrogen maintains the osseous structure and facilitates new bone formation. Carnoy's solution is a tissue fixative that penetrates bone to a depth of 1.54 mm and decreases risk of recurrence, by killing the epithelial remnant or satellite cysts [34]. Cyclopamine, a plant-based steroidal alkaloid, blocks the activation of sonic hedgehog (SHH) pathway, therefore makes it a potential "mechanism-based" therapeutic agent for those human tumours whose pathogenesis involves excess SHH pathway activity. Antagonists of SHH signalling factors could also be effectively used to treat KCOT [35]. The suggested strategies include re-introduction of a wild-type form of PTCH (a tumour suppressor gene), inhibiting SMO molecule (an oncogene) by synthetic antagonists and suppressing the downstream transcription factors of the SHH pathway. Intracystic injection of an SMO protein-antagonist has the greatest potential as a future treatment option [35].

The most important feature of OKC is its high recurrence rate ranging from 5 to 62.5% [5]. Recurrence is documented even after 10 years of follow up [27]. Recurrence is usually characterized radiologically by evidence of further bone destruction with or without clinical evidence of infection [15].

In the case under reporting, we have done enucleation with peripheral osteotomy followed by iodoform dressing for 6 months. Second operation for right sided lesion was done after 8 months of the first surgery. Same procedure was done for right side also. There was no sign of recurrence on a follow up of 10 months following the first surgery on left side. Patient is asymptomatic and under regular follow-up.

OKCs are frequent benign jaw tumor but bilateral OKC are relatively rare. Many cases of single OKCs have been reported in the literature. Bilateral or multiple cysts are rare and may be associated with syndromes like Gorlin syndrome. To the best of our knowledge, none of them presented bilaterally in a cleft lip patient without having any syndrome, as was seen in this patient.

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