Syndromic odontogenic keratocyst: A case report and review of literature

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Abstract

Odontogenic keratocysts (OKCs) may occur in two different forms, either as solitary (nonsyndromic OKCs) or as multiple OKCs (syndromic OKCs). Multiple OKCs usually occur as one of the findings in Gorlin–Goltz syndrome with other features such as skin carcinomas and rib, eye, and neurologic abnormalities. We report a rare case of Gorlin–Goltz syndrome in a 20-year-old male patient who presented with a slow growing swelling on lower right and left back teeth region since 2 months. Apart from these, other findings were frontal bossing, depressed nasal bridge, ocular hypertelorism, prominent supra orbital ridge, and mild mandibular prognathism. Excision was done and microscopic study revealed OKC and the follow-up could not be carried out for the complete management. We also presented a review of its pathogenesis, criterion, and differences between syndromic and nonsyndromic OKCs and suggest to thoroughly examine any patient who presents with multiple OKCs to rule out syndromic variety.

Key words: Basal cell carcinoma, bifid ribs, odontogenic keratocyst, spina bifida

INTRODUCTION

Odontogenic keratocysts (OKCs) are developmental cysts that arise from remnants of dental lamina.[1] They may appear either as single entity or as multiple cysts associated with syndromes like Gorlin–Goltz syndrome.[2] Jarish and White (1984) first reported this syndrome. Later, Gorlin and Goltz illustrated this lesion in detail with features such as multiple nevoid basal cell carcinomas (BCCs), bifid ribs, jaw cysts, and other features; hence, this lesion is called Gorlin–Goltz syndrome or basal cell nevus syndrome or jaw cyst bifid rib syndrome, or multiple nevoid BCC syndrome.[3] This lesion is inherited in autosomal dominant manner characterized by total penetrance and variable expressivity.[1,3]

Various treatment modalities have been suggested by different authors for OKCs. For small lesions enucleation is preferred and for larger ones marsupialization is preferred. After surgical enucleation, the application of Carnoy’s solution has been suggested to prevent recurrences. Complete treatment of syndromic OKCs involve a team of dental, medical, and genetics specialties. A periodic follow-up is recommended for these lesions due to their high recurrence rates.[4,5] We are presenting a case of Gorlin–Goltz syndrome and briefly talk about its...
pathogenesis, diagnostic criteria, and differences between syndromic and asyndromic OKCs.

CASE REPORT

A 20-year-old male came to the oral medicine department with a chief complaint of swelling on lower right and left back teeth region since 2 months. The swelling was initially smaller in size and gradually increased in size to attain the present dimensions. The history of present illness revealed that there was swelling in the upper front teeth region 2 years back for which he consulted a dentist and the upper front teeth were extracted. But the complaint persisted. Again he visited the same dentist and during the check-up the other two swellings were diagnosed on right and left back teeth region and adjacent to extracted teeth. The patient’s past medical history revealed a history of epileptic attack 2 months back. He is under medication. He did not have significant family history.

Complete clinical examination was carried out. Extraorally, frontal bossing, depressed nasal bridge, ocular hypertelorism, prominent supra orbital ridge, and mild mandibular prognathism were found. There were two diffuse swellings seen on right and left side of the face at the junction of body and angle of the mandible measuring about 1 cm × 1 cm in size. There were no signs of any perforation and pus discharge. On palpation it was hard and nontender.

Two diffuse swellings were evident on intraoral examination in the retromolar region of the left side from 37 region to retromolar area and on right side distal to 48 region at the level of occlusion. Mucosa over the swellings was normal with no discharge. On palpation, all the inspection findings were confirmed and the swellings were hard and nontender with diffuse borders. Missing teeth were 13, 23, 18, and 28, whereas 38 and 48 were impacted.

A radiographic examination was carried out that comprised of a panoramic and periapical films, computed tomography (CT) scan of brain, and chest x-ray along with ultrasound of abdomen and pelvis. On evaluation of radiographs, it was observed that there were three unilocular radiolucencies of various sizes located at the lower right (adjacent to 48), left mandible (38), and upper left maxilla (21–24) [Figure 1].

Chest x-ray revealed splaying of ribs 8–9, 9–10, and 10–11 [Figure 2]. CT scan of brain revealed calcification of falx cerebri and tentorium cerebri [Figure 3]. There was thinning of body of corpus callosum, which was evident. Ultrasound abdomen and pelvis showed small right renal calculi.

With a provisional diagnosis of multiple dentigerous cysts, an enucleation of the cyst was performed. Gross examination revealed multiple bits of soft tissue specimens and cystic lining, together measuring about 0.5 cm × 2 cm, which are whitish to creamish in color and leathery in consistency [Figure 4]. Microscopic examination showed a cystic lining that is thin, folded, and collapsed. The cystic lining appeared as parakeratinized corrugated stratified squamous epithelium that was about 3–4 layer thick without any rete ridges. Basal layer showed intensely basophilic palisaded arrangement of nuclei. Underlying connective tissue stroma exhibited an odontogenic island that was undergoing keratin formation. Diffuse chronic inflammatory cells were also seen [Figures 5 and 6]. Based on the histopathological findings, a diagnosis of keratinizing cystic odontogenic tumor in relation to lower right and left posterior teeth region and upper right anterior teeth region was made. After correlating clinical, radiological, and histopathological features, a final diagnosis of Gorlin–Goltz syndrome was given.

We decided to carry on the treatment of the patient after the taking medical opinion. We planned for removable prosthetic rehabilitation after the excision of the lesions. The patient was referred to a medical hospital to seek opinion but the patient did not turn up later.

DISCUSSION

Gorlin–Goltz syndrome is a uncommon entity with multiple OKCs as its first manifestation; hence, dentists have an important role in its early detection thereby achieving proper management of this syndrome.[6] Studies have shown that it has an incidence of about 1 in 50,000–150,000.[7] Apart from Gorlin–Goltz syndrome, multiple OKCs are seen in other syndromes

Figure 1: OPG
Arshad: Gorlin-Goltz syndrome

The lesion is inherited in a dominant pattern. The review of the literature about its pathogenesis revealed mutation of the protein patched homolog (PTCH) gene, which is mapped to 9q21-23 chromosome. These genetic studies suggest that in this syndrome there is an abnormal hedgehog signaling pathway. PTCH acts as a receptor for sonic hedgehog gene, which has a primary role in embryogenesis. PTCH is shown to have two constituents. Smoothened (Smo) has a role in cell growth and differentiation and in hedgehog signaling pathway. Hh binds to the other component Patched (Ptc) and releases Smo. In this case, the mutated PTCH gene results in abnormal hedgehog, which will not bind to PTC, which in turn inhibits Smo thus affecting cell growth and differentiation and may result in abnormalities such as neoplasms and others.\(^7,8\)

Gorlin-Goltz syndrome shows a spectrum of clinical manifestations that can be broadly put in six categories [Table 1]. These clinical manifestations are categorized into major and minor diagnostic criteria. Evans et al. and Kimonis et al. suggest that to diagnose a patient to have Gorlin–Goltz syndrome, two major or one major and two minor criteria should be present [Table 2]. In case of our patient, the diagnosis was confirmed as he matched three major criteria (multiple OKCs, splayed ribs, and calcified falx cerebri) and five minor criteria (frontal bossing, nasal bridge depressed, ocular

Figure 2: CT scan showing bilateral falx cerebri calcification

Figure 3: Chest x-ray exhibiting splayed ribs

Figure 4: Gross specimen showing multiple soft tissue thin cystic lining

such as Ehlers-Danlos syndrome, orofacial digital syndrome, and Noonan syndrome.\(^9\)
Literature review of clinical features showed that Gorlin–Goltz syndrome is usually seen in younger age group ranging in between 10 years and 30 years. Our patient was 20 years old. Generally, females are predominantly affected, whereas ours was a male patient. The commonest site of OKCs for Gorlin–Goltz syndrome is maxillary molar area; our case presented with multiple cysts bilaterally at posterior mandible and ramus area and at maxillary incisor canine area.

Radiologic characteristics of OKCs show unilocular, well-defined radiolucent lesions, usually associated with unerupted tooth. Our case showed unilocular radiolucency in relation to an unerupted right and left third molars along with upper anterior teeth. Generally, “multiple cysts” means the presence of more than one cyst at a time, whereas in this case multiple cysts means presence of more than one cyst in one’s life time.

Histologically, OKCs show corrugated para- or orthokeratinized surface, almost equal uniform thickness of the epithelium, basal cells showing tomb stone or picket fence arrangement. Few cases show the presence of daughter or satellite cells in the underlying connective tissue and these cysts show more recurrence rate. Parakeratotic OKCs are more common and more aggressive than orthokeratotic OKCs. In case of Gorlin–Goltz syndrome, parakeratotic OKCs are seen. The major differences between OKCs associated with Gorlin–Goltz syndrome and solitary OKCs are listed in Table 3. Our case showed three to four layered thick parakeratinized corrugated stratified squamous

Table 1: Clinical manifestations of Gorlin–Goltz syndrome

| Anomalies | Manifestations |
|-----------|----------------|
| Cutaneous | Basal cell nevi, basal cell carcinomas, benign dermal cysts and tumors, dermal calcinosis, and palmar and plantar keratosis |
| Dental    | Multiple OKCs, mild mandibular prognathism |
| Osseous   | Frontal bossing, bifid ribs, spina bifida, kyphoscoliosis, and brachymetacarpalism |
| Eye       | Hypertelorism, congenital blindness, and internal strabismus |
| Neural    | Dural calcification, mental retardation, and medulloblastoma |
| Sexual    | Hypogonadism, ovarian tumors |

Table 2: Major and minor diagnostic criterion of Gorlin–Goltz syndrome

| Major criteria | Minor criteria |
|----------------|----------------|
| Multiple basal cell carcinomas or one BCC below 20 years | Macrocephaly (adjusted for height) |
| Multiple OKCs | Congenital malformation: Cleft lip or palate, frontal bossing, and moderate or severe hypertelorism |
| Three or more palmar or plantar pits | Other skeletal abnormalities: Sprengel’s deformity, marked pectus deformity, marked syndactyly of the digits |
| Bilamellar calcification of the falx cerebri | Radiological abnormalities: Bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands, and feet or flame shaped hands or feet |
| Bifid, splayed, or fused ribs | Medulloblastoma |
| Close relative having syndromic OKCs characteristics | Ovarian fibroma |

OKCs: Odontogenic keratocysts

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Figure 5: Parakeratinized palisaded corrugated epithelium

Figure 6: Islands invading in connective epithelium
Table 3: Differences between syndromic OKCs and solitary OKCs

| Feature            | Syndromic OKCs                  | Solitary OKCs                  |
|--------------------|---------------------------------|---------------------------------|
| Age                | Younger individuals             | Middle or older aged individuals|
| Cysts              | Multiple in number              | Single                          |
| Site               | Maxillary posterior region commonly | Mandibular posterior region      |
| Recurrence rate    | Higher (82%)                    | Lower (61%)                     |
| Epithelium         | Less thickness                  | More thickness                  |
| Odontogenic islands| More frequent                   | Less                            |

OKCs: Odontogenic keratocysts

epithelium and presence of odontogenic island in underlying connective tissue.

The treatment of OKCs is usually carried out by either enucleation or marsupialization. Carnoy’s solution is used to prevent the recurrence of these cysts. We treated cysts by enucleation with adjuvant application of Carnoy’s solution. The studies have shown that multiple OKCs are detected almost 10 years before the appearance of other symptoms of Gorlin–Goltz syndrome. Hence, a dentist has a very important role in treating this syndrome as he will be the first person to detect oral findings and predict occurrence of syndrome in future. Comprehensive treatment of this syndrome requires a dental and medical opinion as well as genetic counseling.[13,15]

CONCLUSION

A rare case of Gorlin–Goltz syndrome that showed its uniqueness in that it was seen in a male patient and the site of the cysts was bilaterally at posterior mandible and ramus area and in maxillary incisor canine area not at its usual location of maxillary molar area as seen in majority of patients.

We suggest that patients with multiple OKCs should be thoroughly evaluated as they are the major component of Gorlin–Goltz syndrome and early findings of this syndrome. These patients should be followed for a long time with proper medical care and genetic counseling so as to prevent the development of other complications such as malignancies.

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Conflicts of interest

There are no conflicts of interest.

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