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Case Report

Multiple 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 (non syndromic OKCs) or as multiple OKCs (syndromic OKCs). Multiple OKCs are usually associated with Gorlin–Goltz syndrome with features like skin carcinomas and bifid ribs, eye, and neurologic abnormalities. We report a rare case of Gorlin–Goltz syndrome in a 35-year-old male patient who presented with a swelling in lower left back teeth region since 1 week. Apart from these, other findings observed in the patient were frontal bossing, depressed nasal bridge, ocular hypertelorism, prominent supra orbital ridge, and mild mandibular prognathism. On the basis of clinical and radiological evaluation, Enucleation was planned in all the three quadrants and histopathological evaluation revealed multiple OKC's. Patient was followed-up multiple times for the duration of six months. This case report highlights the important findings and presentation of a rare case of Gorlin Goltz syndrome along with its review of literature.

1. Introduction

Odontogenic keratocysts (OKCs) are cysts of developmental origin arising 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 and later, Gorlin and Goltz documented other features such as multiple jaw cysts, nevoid basal cell carcinomas (BCCs), bifid ribs, 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 as autosomal dominant trait and is characterized by total penetrance and variable expressivity. Diagnosis is based upon established major and minor clinical and radiological criteria and ideally should be confirmed by DNA Analysis[1,3].

Various treatment modalities have been suggested in literature for multiple OKCs. For small lesions enucleation is preferred and for larger lesions marsupialization is preferred. After surgical enucleation, the application of Carnoy's solution has been suggested to prevent recurrences. Complete treatment of syndromic OKCs involves 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] This paper is presenting a rare case of Gorlin–Goltz syndrome with a brief discussion about its pathogenesis, diagnostic criteria, and differences between syndromic and asyndromic OKCs.

2. Case Report

A 35-year-old male patient reported to the department of Oral Medicine and Radiology with a chief complaint of swelling in the left mandibular posterior region since 1 week. The swelling was initially smaller in size and gradually increased to attain the present dimensions. The history revealed that patient had undergone extraction of 37 due to deep caries from a dentist 1week before, which was

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followed by a swelling in the same region. The patient's past medical history is not associated with any relevant findings. All the vital signs were in normal range.

On Extra oral examination; frontal bossing, depressed nasal bridge, ocular hypertelorism, prominent supra orbital ridges and mild mandibular prognathism were observed (Figure 1). Intra-orally, there was a diffuse swelling noticed involving the vestibular sulcus extending from mesial aspect of 33 till the mesial aspect of 36 tooth; measuring about 1.5 cm × 2 cm in size. There were no signs of any perforation and pus discharge. On palpation, all the inspectory findings were confirmed; swelling was firm and tender with normal overlying mucosa. On Intraoral examination no other areas showed evidence of swelling but mild vestibular tenderness was observed in the 2^{nd} and 4^{th} quadrant on palpation. Based on clinical examination, a provisional diagnosis of benign odontogenic cyst was given. (Figure 1).

A radiographic examination was carried out that comprised of a panoramic and specialized imaging Cone Beam Computed Tomography (CBCT) scan. On evaluation, OPG revealed multiple well defined radiolucencies in the mandibular and maxillary region. A large well defined, corticated, multilocular radiolucency with curved septa and scalloped borders was noticed in the mandibular anterior region crossing the mid-line wrt 41, 31,32,33,34, 35and 36. Second, well defined radiolucent lesion can be appreciated at the left angle of the mandible in 38 region of approx 1x1.5cm in size. Third well defined, corticated radiolucent lesion of approx 2X2.5cm in size can be appreciated in #48 region involving anterior aspect of ramus. (Figure 2). Fourth, a mixed radiolucent and radiopaque lesion of approx 1x1.5cm in size can also be appreciated on the left posterior region of maxilla wrt 27 and 28.

3. CBCT Report: (Figures 3 and 4)

3.1. Right ramus

1. A well-defined ovoid unilocular radiolucent non-expansile lesion is noted in right
2. Inferior - ascending ramus regions. Margins are distinct and corticated.
3. The lesion measures approx. 1.7cm x 0.9cm x 1.4cm in greatest antero-posterior, transverse and supero-inferior dimensions.
4. There is thinning of adjoining mesial – lateral cortices of right ramus.
5. The internal structure is radiolucent without internal calcifications or septae

3.2. Left symphysis – parasymphysis of mandible

1. A well-defined ovoid corticated unilocular non-expansile osteolytic radiolucent lesion is noted from mandibular midline till the #35 region .
2. Lesion extends from mesial peri-radicular & apical peri-radicular region of #31 till the distal peri-radicular & periapical region of #35 with distinct – corticated margins.
3. The lesion measures approx. 2.9cm x 1.0cm x 1.9cm in greatest antero-posterior, transverse and supero-inferior dimensions.
4. There is thinning-scalloping of adjoining labio-buccal-lingual cortices with intermittent effacement of the labio-buccal cortex in #31 – 33 regions.
5. The internal structure is radiolucent without internal calcifications or septae.
6. Obvious root divergence of #32 & 33 noted; however, associated teeth show largely intact root outlines.
7. Acute disto-buccal dilaceration of apical third of #35 root also seen.

3.3. Left body of mandible

1. A well-defined ovoid corticated unilocular non-expansile osteolytic radiolucent lesion is noted in #36 region from mesial peri-radicular & apical peri-radicular region of #36 till the distal periradicular & periapical region of #36, with distinct – corticated margins.
2. The lesion measures approx. 1.8cm x 1.1cm x 1.3cm in greatest antero-posterior, transverse and supero-inferior dimensions.
3. Focal contiguity of the lesion to anterior left parasymphysis-symphysis lesion is noted in distal #35 areas.

3.4. Left body-ramus

1. A partially well-defined irregular shaped, unilocular radiolucent non-expansile lesion is noted in left posterior body-ramus regions with an elongated superior partially corticated part and a small ovoid inferior corticated part.
2. The medial – superior margins of the superior elongated part of lesion are deficient or indistinct.
3. Lesion extends from lingual peri-radicular area of #37 socket & pericoronal region of #38 till inferior – ascending left ramus regions of mandible, measuring app. 3.5cm x 0.9cm x 3.0cm in greatest antero-posterior, transverse and supero-inferior dimensions.
4. Thinning-effacement of the lateral cortex of left IAN and lateral displacement of the IAN noted in relation to the corticated inferior component of the lesion.
5. The internal structure is radiolucent without internal calcifications or septae.

Radiographic Diagnosis of Multiple OKCs with presence of Odontome in left posterior region of maxilla was made. After the radiographic evaluation,, patient was advised to go for chest and skull x-rays.

With a provisional diagnosis of multiple odontogenic cysts, an enucleation of the cysts was performed under General Anesthesia. Microscopic examination showed a parakeratinized corrugated stratified squamous epithelium cystic lining that is thin, folded, and collapsed. The cystic lining appeared 3–4 layer thick without any rete ridges. Basal layer showed intensely basophilic palisaded arrangement of nuclei. Underlying connective tissue stroma reveals presence of odontogenic island 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 was made. After evaluating clinical, radiological, and histopathological confirmation, a final diagnosis of Gorlin–Goltz syndrome was given.

It was decided to carry on the treatment of the patient after seeking the medical opinion. We planned for removable prosthetic rehabilitation after the excision of the lesions. The patient was referred to Department of oral surgery for further treatment.

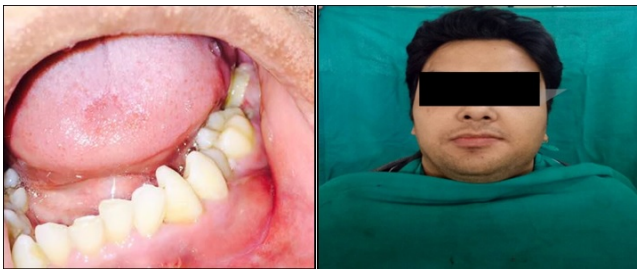

Fig. 1: Profile and intraorally

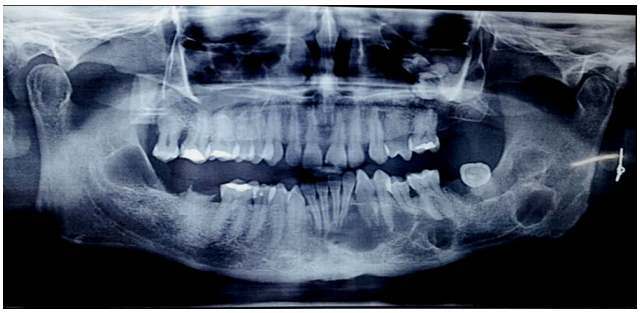

Fig. 2: OPG

4. Discussion

Gorlin–Goltz syndrome is usually associated 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 been documented with an incidence of about 1 in

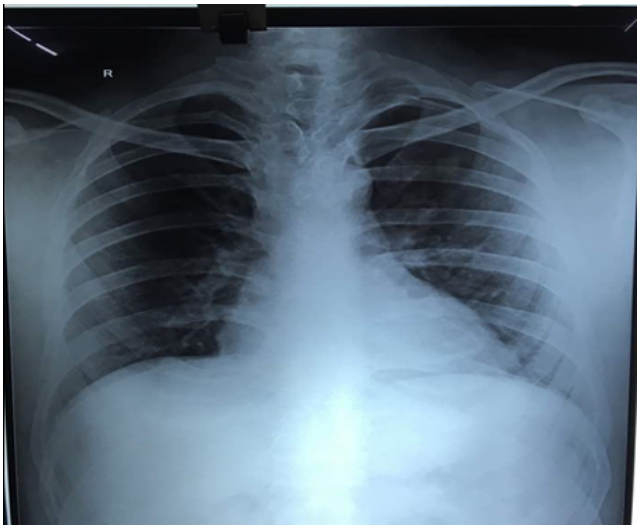

Fig. 3: Chest X-ray

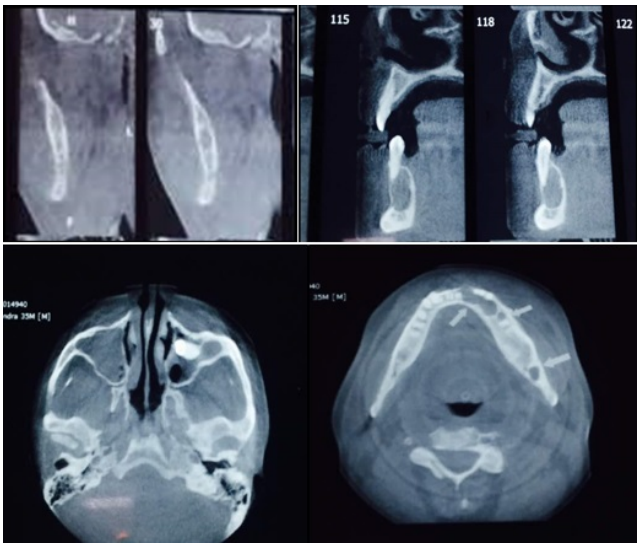

Fig. 4: CBCT Images

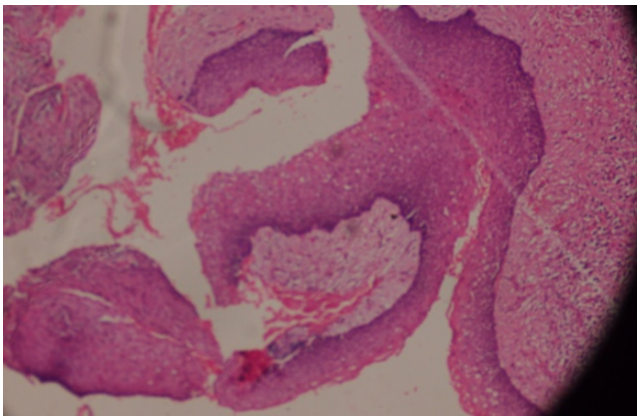

Fig. 5: Parakeratinized palisaded corrugatede pithelium

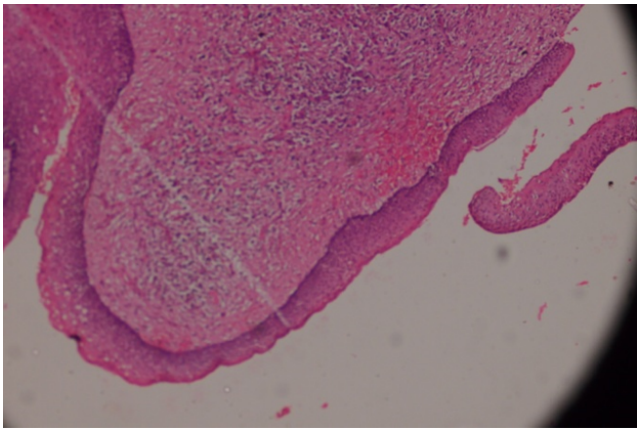

Fig. 6: Islands invading in connective epithelium

50,000–150,000.[7] Apart from Gorlin–Goltz syndrome, multiple OKCs are seen in other syndromes. The lesion is inherited in a dominant pattern. The pathogenesis revealed mutation of the protein patched homolog (PTCH) gene, which is mapped to 9q21-23 chromosome. The genetic studies show that in this syndrome there is an abnormal hedgehog signaling pathway. PTCH acts as a receptor for sonic hedgehog gene, having 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 (etc) and releases Smo. PTCH gene mutation results in abnormal hedgehog signalling, which is unable to bind to PTC, thus inhibiting Smo thereby 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.

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

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.

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

In our patient, the diagnosis was confirmed as he matched two major criteria (multiple OKCs, splayed ribs,) and five minor criteria (frontal bossing, nasal bridge depressed, ocular hypertelorism, prominent supra orbital ridge, and mild mandibular prognathism).[8–10]

Gorlin–Goltz syndrome is usually seen in younger age group with a range between 10-30 years. Our patient was 35 years old. Generally, females are predominantly affected, whereas ours was a male patient. The multiple OKCs for Gorlin–Goltz syndrome is frequently found in maxillary molar area; our case presented with multiple cysts bilaterally at posterior mandible, ramus area and maxillary molar area.[9,11]. Radiologic characteristics of OKCs show unilocular, well-defined radiolucent lesions, usually associated with unerupted tooth. But, Our case showed unilocular radiolucency in relation to right and left mandibular third molars region along with ramus area and maxillary left posterior region. 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.[1,11,12] Histologically, OKCs show corrugated para- or orthokeratinized surface, almost equal uniform thickness of the epithelium, basal cells showing tomb stone or picket fence arrangement. The presence of daughter or satellite cells in the underlying connective tissue can be seen which shows 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). [12,13]

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

Our case showed three to four layered thick parakeratinized corrugated stratified squamous epithelium and presence of Odontogenic Island in underlying connective tissue. OKCs are usually removed 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 plays an important role in documenting this syndrome as he will be the first person to observe the oral findings and predict occurrence of syndrome in future. An interdisciplinary approach is required for the comprehensive treatment of this syndrome as well as genetic counseling. [12,14]

5. 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 which is not commonly seen. 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.

6. Source of Funding

None.

7. Conflict of Interest

None.

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