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CASE REPORT

GORLIN GOLTZ SYNDROME: CASE REPORT

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ABSTRACT

Gorlin Goltz syndrome involves multiple organ system. The most common findings include odontogenic keratocysts in the jaws, basal cell carcinomas, skeletal, dental, ophthalmic and neurological abnormalties, intracranial ectopic calcifications of the falx cerebri, and facial dimorphism. The authors report a case of Gorlin Goltz syndrome in a 21-year-old male presenting with multiple odontogenic keratocysts in the jaws, bifid ribs, basal cell nevi on the trunk and soft tissue cysts.

INTRODUCTION

Gorlin Goltz syndrome is also known as nevoid basal cell carcinoma syndrome or nevus epitheliomades multiplex, basal cell nevus syndrome, multiple basal cell carcinoma syndrome, Gorlin syndrome, or hereditary cutaneomandibular polyonocosis, multiple nevoid basal cell epithelioma-jaw cysts or bifid rib syndrome.[1,2] Almost 60% of the patients with Gorlin-Goltz syndrome have no known affected family members, 35-50% of these representing new mutations. [1,3] This is a hereditary disease with autosomal dominant trait, characterized by high penetration and variable expressiveness, even if sporadic cases have been described. [4,5,6] The estimated prevalence varies from 1/57,000 to 1/256,000 among various studies, with a male-to-female ratio of 1:1. [6,7]

Often these patients first visit a dental hospital with jaw swelling where the diagnosis of this syndrome is generally made. Hence a dental clinician should be aware of this rare syndrome especially in young patients to establish proper and early diagnosis and provide opportunity for better prognosis. [4] There have been a very few reported cases from India. Over a period of 34 years only 17 cases have been reported.[8] We present a case of Gorlin Goltz syndrome in a 21-year-old patient having multiple odontogenic keratocysts in the jaws and bifid ribs with basal cell nevi on the trunk.

Case description

A 21-year-old male reported with the complaint of restricted mouth opening since birth, which progressively increased, to the present stage. Medical and dental history were non-significant. On general physical examination, the patient was moderately built with normal gait and satisfactory vital signs. Painless fluctuant swelling 1-2 cm was present on the inner aspect of the left ankle. (Figure 1) Multiple pigmented nevi were seen on the chest with a focal nevus like lesion on the skin of the right wrist. (Figure 2) On extra-oral examination, face appeared asymmetrical due to limitation of the mandible on the right side. (Figure 3) A bony hard mass was palpated in the right coronoid region. TMJ movements were absent on the right side and reduced on the left side. Prominent antegonial notch was palpated on the right side. Mouth opening was limited to 0.5 cm. On intra-oral examination, anterior teeth showed bimaxillary proclination, anterior deep bite with maxillary diastema. (Figure 4)

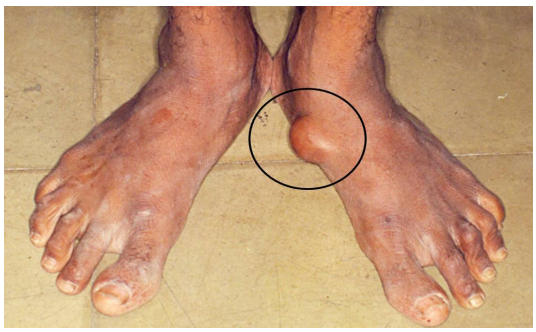

Figure 1 Presence of Soft Tissue Cyst on Left Ankle

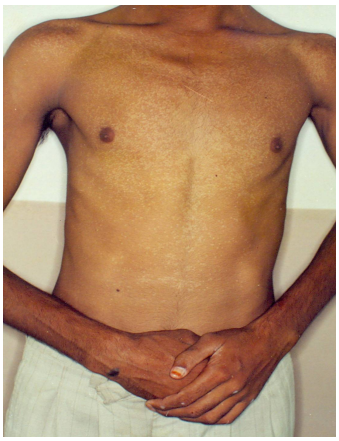

Figure 2 Basal Cell Nevi on The Trunk And Focal Nevus On Hand

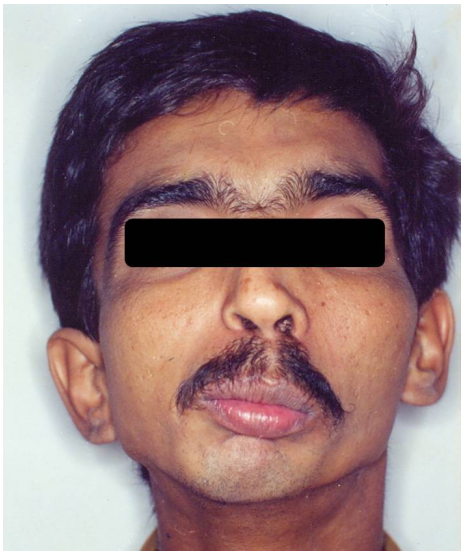

Figure 3 Asymmetry of Face

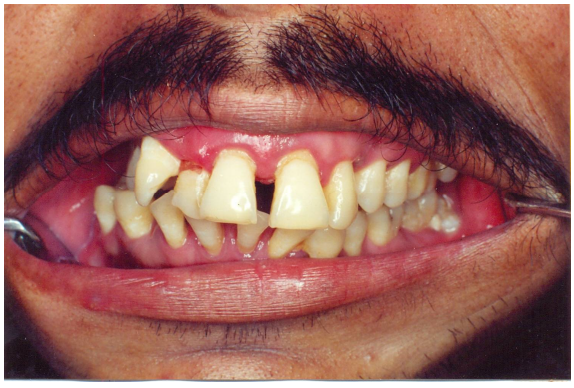

Figure 4 Malocclusion

Posterior cross bite was evident on the right side with shift of the midline to the right side. (Figure 4) On the basis of history and clinical examination, a diagnosis of fibrous/bony ankylosis of the right TMJ was given.

Panoramic radiograph (Figure 5) showed hypoplastic flattened right condyle. Obliteration of the sigmoid notch with the superior part of the ramus in close proximity with the articular eminence also was noted. Coronoid process showed an impacted third molar 48 with a pericoronal cystic radiolucency around it due to which coronoid process appeared expanded. Prominent right antegonial notch also was seen. Symphysis region showed cystic well corticated radiolucency extending from the distal of 45 to the mesial of 35 associated with impacted 43, 33 within the lesion. The inferior border of the mandible appeared to be expanded but intact. Well defined cystic corticated unilocular radiolucencies were seen near left angle of the mandible in connection with 38, left anterior maxilla where in 23 appeared obliquely displaced and impacted within the lesion and in connection with 18 which was partially encroaching upon the maxillary sinus.

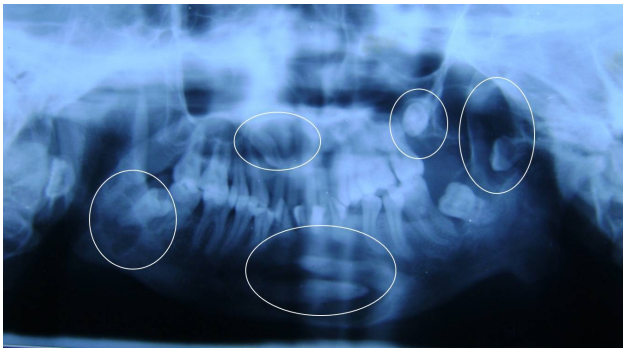

Figure 5 Panoramic Radiograph Showing Multiple Radiolucent Lesions In Maxilla And Mandible With Impacted Teeth

Considering the possibility of Gorlin Goltz syndrome due to the presence of multiple cysts, further evaluation was done with P.A chest and CT scans. PA chest (Figure6) revealed a bifid left 4^{th} and 5^{th} rib and right 5^{th} rib.

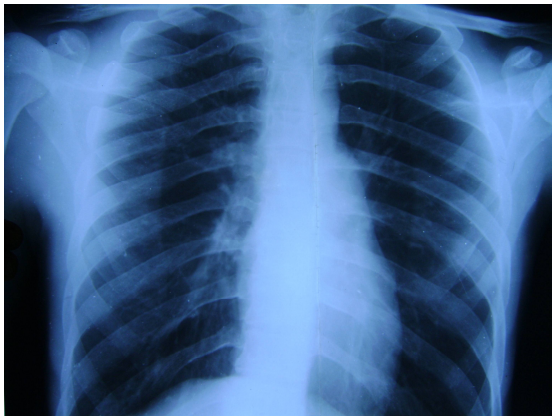

Figure 6 PA Chest Radiograph Showing Bifid 4^{TH} And 5^{TH} Rib

CT images (Figure 7-10) showed well defined hypodense expansile lesion in the right coronoid with irregular sclerosis in the right condylar region. The right coronoid showed an impacted third molar within the well- defined hypodense expansile lesion. The impacted third molar also was seen encroaching the maxillary sinus. Reconstructed sagittal sections of the right side showed well-defined expansile hypodense lesion in the coronoid process with the condyle being malformed and irregular. Sigmoid notch appeared to be entirely obliterated.

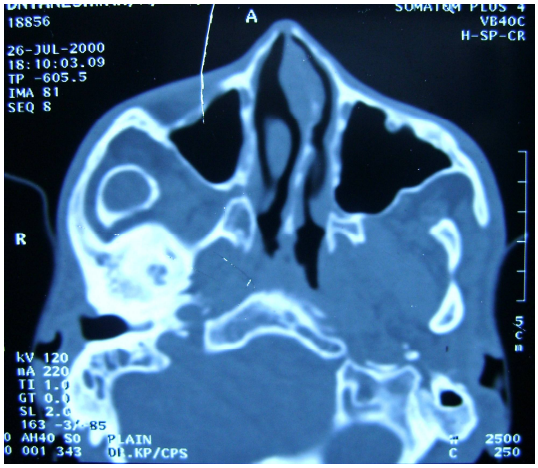

Figure 7 CT Axial View Showing Ankyloses On Right Side With Cystic Lesion In Maxilla

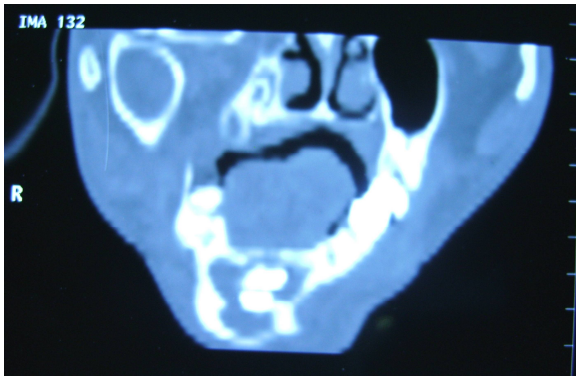

Figure 8 CT Coronal Section Showing Impacted Mandibular Canines In Symphysis Region

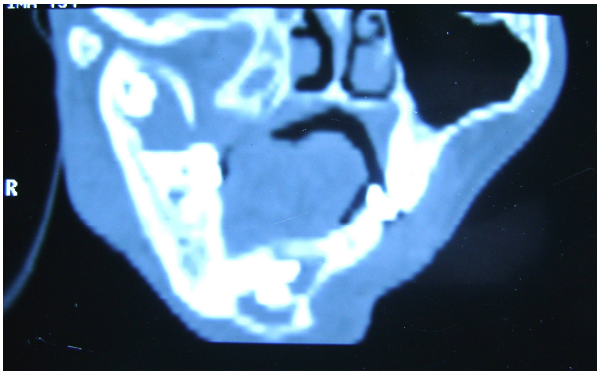

Figure 9 CT Coronal Section Showing Impacted Third Molar Surrounded By Cystic Radiolucency

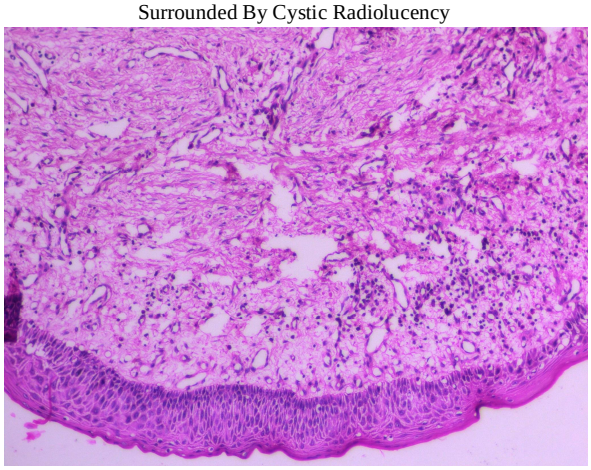

Figure 10 Para Keratinized Odontogenic Epithelium with Tombstone Appearance of Basal Cells

Thin joint space was seen. Reformatted coronal sections (Figure 8) showed the presence of two teeth in a well-defined cystic lesion in the symphysis region surrounded by a hyperdense cortex. (Figure 9) showed an impacted third molar 48 within well defined pericoronal cystic radiolucency. An incisional biopsy (Figure 10) of the lesion was carried out and it was histologically diagnosed as parakeratinized Odontogenic Keratocyst.

Thus, a final diagnosis of Gorlin Goltz syndrome was made based on the presence of multiple odontogenic keratocysts, bifid ribs and basal cell nevi on the trunk associated with TMJ ankylosis. Appropriate management of the ankylosis and surgical enucleation of the cystic lesions were done. The case was followed up for 1 year and there was no recurrence of lesion.

DISCUSSION

Gorlin Goltz syndrome existed during Dynastic Egyptian times, as shown by findings compatible with the syndrome in mummies dating back to 1,000 b.c. [8,9] It probably presents itself in all ethnic groups [10], but most often seen in whites [2,3,10] and affects both men and women in the same way. [2,9] This syndrome was first reported by Jarish and White in 1894, who described a patient with multiple basal cell carcinomas, scoliosis and learning disability. Howell and Caro were the first to associate the basal cell nevus with other cutaneous disorders and anomalies, while Gorlin and Goltz defined the condition as a syndrome comprising the principal triad of multiple basal cell nevi, jaw keratocysts, and skeletal anomalies. This triad was later modified by Rayner *et al.*, who established that for giving the diagnosis; at least cysts had to appear in combination with calcification of the falx cerebri or palmar and plantar pits. [2,3,7,11]

Incidence of the Gorlin-Goltz syndrome is estimated at 1 in 50,000 to 150,000 in the general population. [2,10] Farndon *et al.* reported a minimum prevalence of 1 in 57,000 people. Shanley *et al.* in Australia, and Lo Muzio *et al.* in Italy estimated the prevalence as 1 per 64,000 and 256,000, respectively. Evans *et al.*, reported that the prevalence rate in the United Kingdom was 1 per 560,000.[12]

It is also called as fifth phakomatosis due to the presence of a wide spectrum of other cutaneous, skeletal, neurological, ophthalmic, endocrine, and genital manifestations are now known to be variably associated with this triad.[4,5,10,13] The tumor suppressor gene called Patched (PTCH), a human analogue of Drosophilia gene mapped on the long arm of 9q22.3 chromosome, has been identified as cause of Gorlin Goltz syndrome.[2,6,9,10] Mutation of this gene produces dysregulation of several genes involved in organogenesis and carcinogenesis. Consequently, the syndrome includes a wide spectrum of defects involving the skin, eyes, central nervous and endocrine systems and bones.[11]

Diagnostic criteria

The diagnostic criteria were put forth by Evans and colleague in 1993 and modified by Kimonis *et al.* in 1997.[8,10] According to them, diagnosis of Gorlin Goltz syndrome can be established when two major or one major and two minor criteria as described below are present.

Major criteria

1. More than two basal cell carcinomas (BCC) or one BCC under the age of 20 years.
2. Histologically proven odontogenic keratocysts of the jaw.
3. Three or more cutaneous palmar or plantar pits.
4. Bifid, fused or markedly splayed ribs.
5. First degree relative with Gorlin-Goltz syndrome.

Minor criteria

1. Macrocephaly.
2. One of several orofacial congenital malformations: cleft lip or palate, frontal bossing, 'coarse' face, moderate or severe hypertelorism.
3. Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
4. Radiological abnormalities: falx calcifications, bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modelling defects of the hands and feet, or flame shaped lucencies of the hands or feet.
5. Ovarian fibroma.
6. Medulloblastoma. [3,6,9]

Odontogenic keratocysts (OKC's) occur in 75 % of patients and are the hallmark of the disease and may represent the initial manifestation of the disease. [7, 14] OKC's related to Gorlin-Goltz syndrome are often multiple, occur at an early age, are larger and have a more aggressive behavior. Particularly when OKC's occur in children under the age of eight, Gorlin-Goltz syndrome should be suspected.[14] Until the age of 30 there may be a continuous development of new and recurring cysts. They are locally destructive and in young children they cause displacement of the developing teeth, delayed dental development and root resorption. [1, 14] Despite this aggressive growth, they often remain asymptomatic.[14] Peak incidence of cysts is in the second and third decade of life. [1,11]

The OKC's associated with this syndrome are of the parakeratinized variety, although a single case of orthokeratinized odontogenic keratocyst has been reported in this syndrome by Bolbaran *et al.* in 2000. [8,15] The odontogenic keratocyst was first described by Philipsen in 1956 and he renamed it keratocystic odontogenic tumor (KCOT) in the 2005 edition of the World Health Organization's histologic classification of odontogenic tumors. This edition reclassified the parakeratinized odontogenic keratocyst as KCOT and the orthokeratinized variant is now recognized as a separate entity and called an orthokeratinized odontogenic cyst.[4,5,8,15] KCOT's represent 3-15% of all odontogenic tumors and appear in 65-75% of cases in this syndrome.[15] Multiple keratocystic odontogenic tumors (KCOTs), ranging from 1 to 30 that tend to appear in first to second decade of life, have been of interest among dentists due to their biological aggressiveness and great amount of recurrence.[8,11,12,15] The KCOT is locally destructive, despite its bland histological features.[12] Also they may be complicated by the development of pathologic fractures, ameloblastoma and squamous cell carcinomas.[11]

Less than 10% of the patients with multiple OKCs have other manifestations of this syndrome. It has therefore been suggested that multiple OKCs alone may be confirmatory of the syndrome. [4,5] Our case too presented with multiple cystic lesions involving the mandible, which were histopathologically diagnosed as a parakeratinized odontogenic keratocyst.

The Gorlin-Goltz syndrome has equal predilection for either sex.[1] Male to female ratio is 1:0.62 for odontogenic keratocyst not associated with Gorlin Goltz syndrome, and 1:1 for odontogenic keratocyst in Gorlin Goltz syndrome, that is, simple keratocysts are more common in males, but more females with Gorlin Goltz syndrome develop OKCs.[13] OKCs associated with Gorlin Goltz syndrome have 2-3 times greater predilections for the mandible than the maxilla, with 69% occurring in the mandible and 31% in the maxilla. In the mandible 43% occurs in the molar ramus region followed by 18% in the incisor-canine area, and 7% in the premolar area. In the maxilla, 14% occurs in the incisor and canine region followed by 12% in the molar tuberosities, and 3% in the premolar region. [9,12,13,14]

There are however no distinctive radiological features between isolated keratocysts and those seen in Gorlin-Goltz syndrome.[14] McDonald-Jankowski reported that orthokeratinized odontogenic lesions occurred with an unerupted tooth significantly more than parakeratinized ones. This may indicate a different pathogenesis for lesions associated with impacted teeth and probably a different keratin content which is reflected in magnestic resonance and ultrasound studies.[15]

According to the neoplastic and biologic potential Katase *et al.* found KCOT associated with the Gorlin Goltz syndrome showed intense gene and protein expressions as compared to the sporadic ones.[12]

The presence of bifid ribs is the most characteristic musculoskeletal manifestation of the disease. Rib anomalies are found in 49% of patients consisting of synostosis, splaying, bifid and cervical ribs that are predominantly seen in the first to forth ones.[11] In the present case, the PA chest radiograph revealed the presence of bifid left 4^{th} and 5^{th} rib and right 5^{th} rib.

KCOTs appear as uni/multilocular radiolucent lesions that may have a smooth or scalloped border associated with impacted/displaced teeth and tendency to grow along the internal aspect of the jaws causing minimal expansion. Cortical expansion and thinning and rarely a hazy lumen has been reported in the previous reports. The lesions sometimes occur around an impacted tooth. [6,8,15] The radiological differential diagnosis for unilocular lesions would include dentigerous cyst, lateral periodontal cyst, and residual cyst, whereas the multilocular variety will have to be differentiated from ameloblastoma, odontogenic myxoma, simple bone cyst, and aneurysmal bone cyst.[8]

Thus, in the present case the diagnosis of Gorlin-Goltz syndrome was done on the the presence of two major criteria i.e the presence of multiple odontogenic keratocysts and bifid ribs.

Early recognition of the disease, a detailed family history and a thorough evaluation of signs and symptoms are the cornerstones for an appropriate management. Because of the different systems affected and the diversity in clinical picture, once diagnosis is established, a multidisciplinary approach team of various specialists is required for a successful treatment. Survival in Gorlin-Goltz patients is not noticeably

altered, however morbidity from complications can be considerable.[6]

Once the diagnosis of Gorlin Goltz syndrome is made, then screening for the syndrome must be carried out in other family members and genetic counseling must be offered.[8] The managemet of these lesions varies in aggressiveness from simple enucleation with or without curettage and marsupialization or peripheral ostectomy, chemical curettage with Carnoy's solution and cryosurgery to kill epithelial remnants and dental lamina within osseous structures to prevent recurrence or to osseous resection in block .[4,5,7,13] Radical interventions as enucleation with shaving of surrounding bone or sometime resection might contribute to preventing recurrences and to improve the prognosis. [9]

In order to decide which technique must be employed, the following factors have to be taken into account: lesion size, lesion extension, location, possible cortical and soft parts damage, the age and whether it is a primary or recurrent lesion. It is also important to detect if it is an isolated keratocyst or if it is associated with the syndrome, [10,15] as Forsell *et al.* have suggested- the recurrence rate is of 63% in keratocysts associated to the syndrome, and of 37% in the isolated ones.[7] Crowley *et al* stated the recurrence rates of KCOTs (42.6 %) and OOCs (2.2%). Therefore, it is also important from the treatment aspect, since the parakeratinized lesions had more aggressive behavior to decrease the recurrence rate. [5,15]

CONCLUSION

Gorlin-Goltz syndrome is rare in the Indian population or may be underreported owing to the lack of awareness. It must be considered as a possible diagnosis in all patients with odontogenic cysts. Early recognition is useful to reduce morbidity and mortality since multiple features have a malignant potential or aggressive behaviour, the latter including multiple and recurrent OKC's which may become large and cause oromaxillofacial deformation and destruction as well as nevoid basal cell carcinomas and cerebral malignancy. (especially medulloblastoma).[11,14]

This case highlights the importance of the awareness of this rare syndrome, especially in young patients so that diagnosis is established and therefore the chances of better overall survival rate.

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