Gorlin-Goltz syndrome: A rare case report

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Abstract

Gorlin-Goltz syndrome is an uncommon autosomal dominant inherited disorder characterized by numerous basal cell carcinomas, odontogenic keratocysts (OKCs) and musculoskeletal malformations. A rare case of this syndrome observed in a 13-year-old male patient is presented in which multiple OKCs were causing disfigurement of the lower jaw as well as displacement and malocclusion of the teeth. Early diagnosis and treatment of this syndrome is important to reduce the severity of complications including cutaneous and cerebral malignancy and oromaxillofacial deformation and destruction due to jaw cysts.

Keywords: Calcification of falx cerebri, Gorlin-Goltz syndrome, nevoid basal cell carcinoma syndrome, odontogenic keratocyst, Palmar pits

Introduction

Gorlin-Goltz syndrome (GGS) also known as nevoid basal cell carcinoma syndrome (NBCCS) is an autosomal dominant inherited disorder.[1] The incidence of this disorder is estimated to be 1 in 50,000-1,50,000 in the general population, varying by region.[2] It appears in all ethnic groups, but most often in whites; males and females are equally affected.[3]

The pathogenesis of GGS is attributed to abnormalities linked to the long arm of chromosome 9 (q22.3-q31). It has been reported that loss of human patched gene (PTCH1 gene), which is a tumor suppressor gene, could be the molecular origin of the syndrome.[4] Human patched gene (PTCH1 gene) is significant for embryonic structuring and cellular cycle and thus its mutation comprises a key event for the development of this syndrome.[4]

GGS is characterized mainly by the presence of multiple basal cell carcinomas (BCC), odontogenic keratocysts (OKCs) of the jaw, palmar pits and ectopic calcifications of the falx cerebri. More than 100 minor criteria have been described. The presence of two major and one minor criteria or one major and three minor criteria are necessary to establish a diagnosis.[5]

GGS has rarely been reported from India. We report here one such patient diagnosed at our hospital.

Case Report

A 13-year-old boy visited our hospital with a chief complaint of swelling on lower anterior region of the jaw since 10 days. Swelling was approximately 2 cm × 1 cm in size, soft to firm in consistency and tender on palpation. Intraoral examination revealed his deciduous teeth were still present and few permanent teeth were missing [Figure 1].

The orthopantomogram was advised, which revealed three cystic lesions in the mandible and two involving the maxillary sinus on either side with the displaced permanent teeth [Figure 2]. Owing to the presence of multiple cysts like lesions in the jaw, GGS was suspected and further investigations were carried out.

The radiograph of the skull showed bilamellar calcification of the falx cerebri [Figure 3]. Physical examination revealed macrocephaly with a head circumference of 92 cm (normal for a 13-year-old boy is 54-57 cm), frontal bossing, depressed nasal bridge, hypertelorism and mandibular prognathism [Figure 4]. Palmar pits were brown coloured and measuring 1-3 mm in diameter [Figure 5]. No other anomalies of the skeletal, cardiovascular, or central nervous system were present. On the basis of clinical findings, diagnosis of GGS was made. Prior to the surgical procedure, an arch bar was placed on the lower jaw to prevent fracture of the mandible as well as to splint the unsupported permanent teeth. The cyst enucleation was done under general anesthesia via intraoral approach. After the cystic lesions enucleated, large areas of bone loss were seen and the displaced permanent teeth were visible on the floor of the cystic cavity [Figure 6]. The enucleated cystic lining was sent for histopathological examination.

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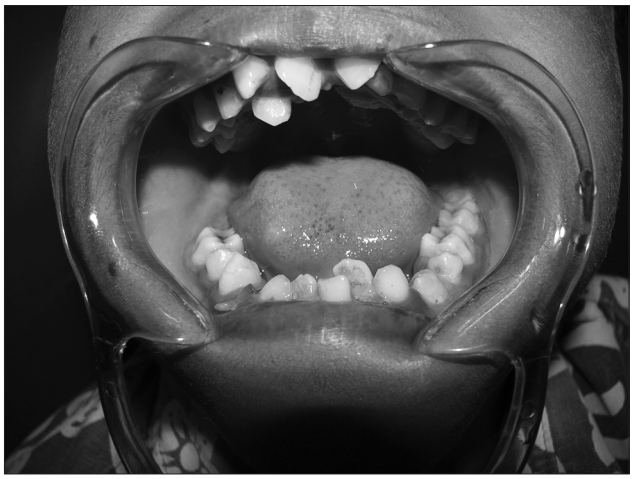

Figure 1: Intraoral photograph showing missing permanent teeth and deciduous teeth were still present

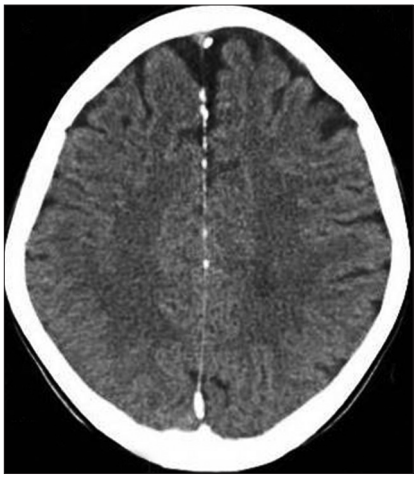

Figure 3: Axial computed tomography brain image showing bilamellar calcification of the falx cerebri

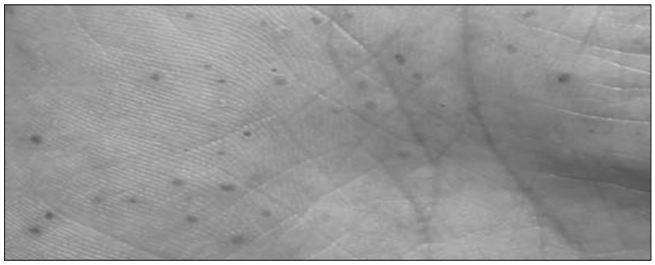

Figure 5: Numerous palmar pits

Carnoy's solution was then applied using cotton rolls for a period of 5 min. The excess solution was then irrigated using saline and the cavity was packed with bismuth iodine paraffin paste. The pack was removed after 7 days and regular irrigation of the cavity was done.

The histopathological examination of the enucleated tissue showed parakeratinized uniform squamous epithelial lining, five to eight cells thick with fairly flat base. The epithelium

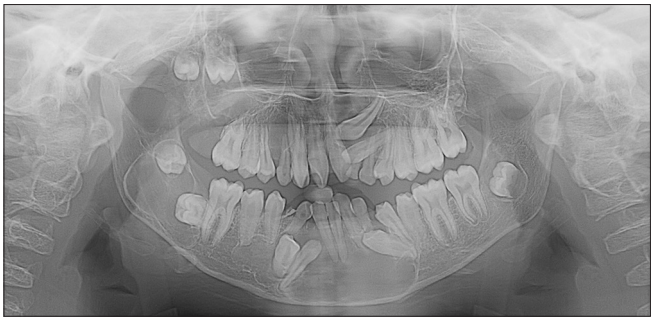

Figure 2: Orthopantogram showing three cystic lesions in the mandible and two involving the maxillary sinus on either side with the displaced permanent teeth

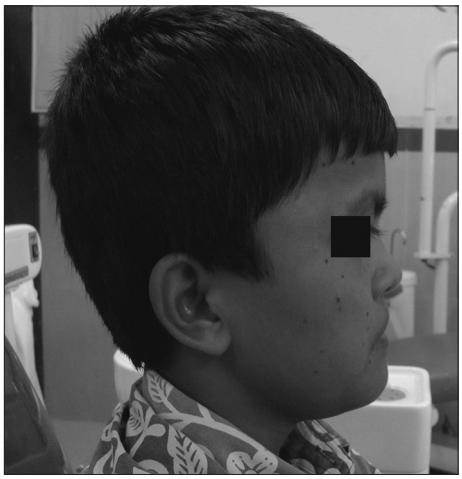

Figure 4: Side profile photograph showing mandibular prognathism (Class III jaw relationship)

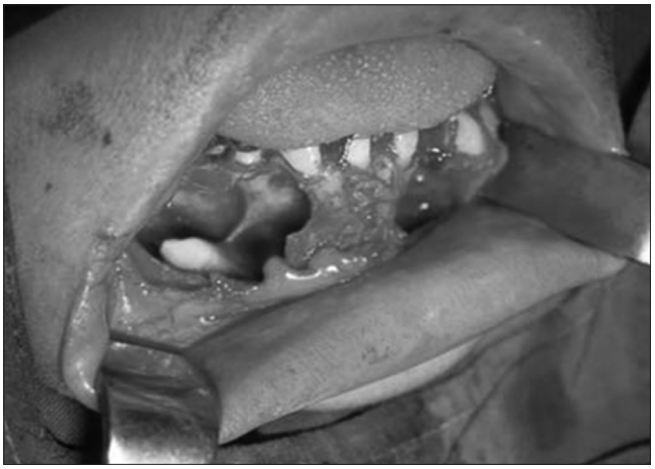

Figure 6: Very thinned out labial cortical plate and displaced right permanent canine were seen

demonstrated a well-developed basal layer of palisaded columnar cells with polarized hyperchromatic nuclei. Multiple satellite and daughter cysts were seen in the connective tissue wall [Figure 7]. The histopathological examination confirmed the diagnosis of OKC.

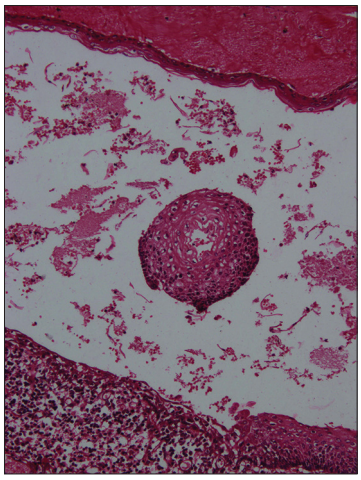

Figure 7: Histopathological photomicrograph showing uniform parakeratinized epithelial lining with satellite cyst in the connective tissue wall (H and E, ×10)

The parents of the patient were examined and underwent radiological evaluation; neither of them had any features of the GGS.

Discussion

NBCCS was first described by Jarish and White in 1894 and was later establish as a unique syndrome by Gorlin-Goltz in 1960. The syndrome initially consisted of triads of BCC, jaw cysts and skeletal anomalies.[6]

Evans *et al*.[7] first established major and minor criteria for diagnosis of this rare entity, later modified by Kimonis *et al*.[3] According to them diagnosis of GGS can be established when two major or one major and two minor features are present.

The major criteria are:
- Multiple BCC or one occurring under the age of 20 years
- Histologically proven OKCs of the jaws
- Palmar or plantar pits (three or more)
- Bilamellar calcification of the falx cerebri
- Bifid, fused or markedly splayed ribs
- First-degree relative with NBCCS.

The minor criteria are:
- Macrocephaly (adjusted for height)
- Congenital malformation: Cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism
- Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactily of the digits
- 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
- Ovarian fibroma
- Medulloblastoma.

Our patient had three major features, namely Palmar pits, multiple OKCs in the jaw and lamellar calcification of the falx cerebri and minor features such as macrocephaly, fontal bossing and hypertelorism, thus suggesting it to be a case of the GGS.

In general, OKCs are more common in the adult life, the peak incidence being the third decade of life.[8] However, in the GGS, OKC occurs at a much younger age.[9] Lo Muzio *et al*.,[10] observation showed that OKCs were often the first sign of GGS in 78% of the cases and they could be detected in patients younger than 10 years of age.

OKCs, which are relatively common in GGS, are diagnosed with dental panoramic radiography. Keratocysts may show a uni - or multilocular pattern and the cystic spaces may have a smooth or scalloped border.[11] Woolgar *et al*.[12] and Dominguez *et al*.[13] found significant differences between syndrome keratocysts and non-syndromic keratocysts. Syndrome keratocysts were found to have a markedly increased number of satellite cysts, solid islands of epithelial proliferation, odontogenic rests within the capsule, and mitotic figures in the epithelial lining of the main cavity. In our patient, the lining of the OKCs revealed the presence of parakeratinized uniform squamous epithelial lining with multiple satellite and daughter cysts in the connective tissue wall, thus indicating the association with GGS.

Removal of cystic lesions, similar to the one seen in our case, weakens the remaining bony integrity and places it at risk of pathologic fracture. This can be managed with intermaxillary fixation or placement of reconstruction plate. In our case, an arch bar was attached to the lower teeth to splint them as well as to support the remaining bone structure to prevent any fracture of the jaw.

Early recognition of the disease, a detailed family history and a thorough evaluation of signs and symptoms are the cornerstones for appropriate management. Because of the different systems affected and diversity in the clinical picture, once diagnosis is established, a multidisciplinary approach team of various specialists is required for a successful treatment.

Conclusion

The GGS is a well-known syndrome with a variety of findings in and outside the head and neck region. The OKC is the most common manifestation of this syndrome.

Early diagnosis of this syndrome is important to reduce the associated complications, which are life-threatening and also to provide genetic counselling to the parents.

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