

CASE REPORT

Gorlin-Goltz syndrome

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ABSTRACT

Gorlin-Goltz syndrome is an autosomal dominant inherited disorder characterized by the presence of multiple odontogenic keratocysts along with various cutaneous, dental, osseous, ophthalmic, neurological, and sex organ abnormalities. Early diagnosis is essential as it may progress to aggressive basal cell carcinomas and neoplasias. Gorlin-Goltz syndrome has rarely been reported from India. We report here one such patient, diagnosed at a rural hospital.

Key words: Diagnosis, Gorlin-Goltz syndrome, odontogenic keratocyst

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INTRODUCTION

Gorlin-Goltz syndrome is an autosomal dominant disorder with a high degree of penetrance^[1] and variable expressivity.^[2] It is characterized by basal cell carcinomas, odontogenic keratocysts, palmar and/or plantar 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. Early diagnosis and treatment of Gorlin-Goltz syndrome, as well as family screening and genetic counseling are essential as it may be associated in 10% of the patients with aggressive basal cell carcinomas and malignant neoplasias.^[3] We report here a patient with Gorlin-Goltz syndrome.

CASE REPORT

A 13-year-old male patient reported to the outpatient wing of the D.J. College of Dental Sciences and Research, Modinagar, Uttar Pradesh, India. He presented with insidious onset swelling of the left side of his face since two months, and pus discharge since 10 days from a sinus on the left side of his face, in the region overlying the third lower molar. The swelling was mildly painful since last 10 days. Pain was continuous, but dull in nature, with no radiation, aggravation, or relieving factors. He was born after a full-term pregnancy and thereafter had an unremarkable medical and dental history.

His weight was 30 kg and height was 163 cm, which were normal for his age. Although the face was bilaterally symmetrical, the frontal view revealed flattening of the nasal bridge. Head circumference was 56 cm, whereas, the normal for a 13-year-old boy is 54 -57 cm.^[4] Painless, soft fluctuant swellings 1 – 2 mm in size were found over the middle finger of the left hand [Figure 1] and 1 cm away from the midline over the dorsal spine region [Figure 2]. These swellings were

present since birth. Fine Needle Aspiration Cytology (FNAC) from these lesions reported them to be sebaceous cyst type lesions. Examination of extremities showed an accessory toe with syndactyly with the fifth digit of the right foot [Figure 3].

Presence of a discharging sinus tract on the left side of the face was noted. On intraoral examination there were no carious teeth related to the external swelling and no intraoral swelling. The Orthopantomogram (OPG) of the patient revealed bilateral radiolucent lesions associated with an unerupted third molar tooth in the ramus of the mandible [Figure 4]. The chest radiograph showed a bifid fifth rib on the right side [Figure 5]. The radiograph of the skull showed bilamellar calcification of the falx cerebri as well as hypertelorism. No skin lesions in the form of basal cell nevus, palmar or plantar pits, or keratosis were present. No other anomalies of the skeletal, cardiovascular, or central nervous system were present. A diagnosis of Gorlin Goltz Syndrome was made.

The parents of the patient were examined and underwent radiological evaluation; neither of them had any features of the Gorlin-Goltz syndrome.

Both cystic lesions of the jaw were enucleated surgically. The histopathological examination of the enucleated tissue showed an odontogenic keratocyst on the right side [Figure 6] and an odontogenic keratocyst with secondary infection on the left side.

DISCUSSION

The Gorlin-Goltz syndrome is an autosomal dominant inherited syndrome manifested by multiple defects involving the skin, nervous system, eyes, endocrine system, and bones. It is also known as 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.



Figure 1: Sebaceous cyst over middle finger of the left hand



Figure 2: Sebaceous cyst on the back



Figure 3: Accessory toe with syndactyly with 5th digit of right foot

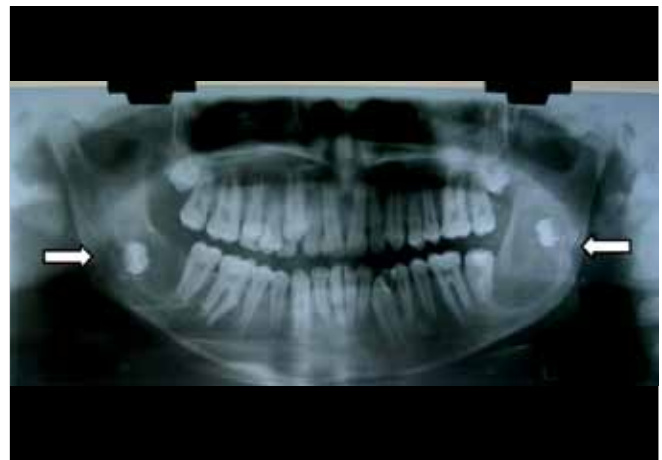


Figure 4: Orthopantomogram showing bilateral cyst with unerupted teeth



Figure 5: Chest X-ray showing bifid rib



Figure 6: Biopsy from right mandibular lesion showing odontogenic keratocyst showing characteristic cystic epithelial lining (H and E, ×10)

It was first reported by Jarisch and White in 1894, and later in detail by Gorlin and Goltz.^[5] Clinical manifestations of the syndrome are grouped into the following five categories.^[5]

(A) *Cutaneous anomalies:* Basal cell nevus, other benign

dermal cysts and tumors, palmar pitting, palmar and plantar keratosis, and dermal calcinosis.

(B) *Dental and osseous anomalies:* Multiple odontogenic keratocysts (OKC), mild mandibular prognathism, frontal

and temporoparietal bossing, kyphoscoliosis or other vertebral defects, bifurcated ribs, spina bifida, and brachymetacarpalism.

(C) *Ophthalmic anomalies*: Hypertelorism, wide nasal bridge, dystopia canthorum, congenital blindness, and internal strabismus.

(D) *Neurological anomalies*: Mental retardation, dural calcification, bridging of sella, agenesis of corpus callosum, congenital hydrocephalus, occurrence of medulloblastoma.

(E) *Sexual anomalies*: Hypogonadism, ovarian tumor-like fibrosarcoma.

Clinically this condition is characterized by different signs and symptoms. Diagnosis is based on the most frequent and specific features of the syndrome as given by Evans *et al.* in 1993.^[6] Diagnosis of Gorlin-Goltz syndrome can be established when two major or one major and two minor criteria are present.

The major criteria are:

1. Multiple basal cell carcinoma or one occurring under the age of 20 years.
2. Histologically proven OKCs of the jaws.
3. Palmar or plantar pits (three or more).
4. Bilamellar calcification of the falx cerebri.
5. Bifid, fused or markedly splayed ribs.
6. First-degree relative with Nevoid Basal Cell Carcinoma syndrome.

The minor criteria are:

1. Macrocephaly (adjusted for height).
2. Congenital malformation: cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism.
3. Other skeletal abnormalities: sprengel deformity, marked pectus deformity, marked syndactily of the digits.
4. 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.
5. Ovarian fibroma.
6. Medulloblastoma.

In our patient the diagnosis of the Gorlin-Goltz syndrome was established by the presence of three major criteria (*viz.*, multiple odontogenic keratocysts, bifid rib, and calcified falx cerebri) and three minor criteria (*viz.* hypertelorism, other cysts on the body and syndactily).

Incidence of the Gorlin-Goltz syndrome is estimated at 1 in 50,000 to 150,000 in the general population.^[3] Farndon *et al.* reported a minimum prevalence of 1 in 57,000 people.^[7] Shanley *et al.* in Australia, and Lo Muzio *et al.* in Italy estimated the prevalence as 1 per 64,000 and 256,000, respectively.^[8,9] Evans *et al.*, reported that the prevalence rate in the United Kingdom was 1 per 560,000.^[6]

The reported review revealed that, to date, there are only seven cases of the Gorlin-Goltz syndrome reported from India, out of which only two were from North India,^[10,11] and five were from South India.^[12-16] This most probably represents under-recognition due to inadequate dental facilities, especially in the vast rural regions of India, outside big cities.

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.^[17] Our case too presented with multiple cystic lesions involving the mandible, which was histopathologically diagnosed as an odontogenic keratocyst.

Generally OKCs are not associated with *Nevoid Basal Cell Carcinoma Syndrome* (NBCCS), which are more common in the adult life, the peak incidence being the third decade of life.^[18] However, in the Gorlin-Goltz syndrome, OKC occurs at a much younger age.^[19] Lo Muzio *et al.*, observed OKCs were often the first sign of NBCC in 78% of the cases and they could be detected in patients younger than 10 years of age.^[9]

The Gorlin-Goltz syndrome has equal predilection for either sex.^[20] Male to female ratio is 1:0.62 for odontogenic keratocyst not associated with NBCCS, and 1:1.^[21] for odontogenic keratocyst in NBCCS, that is, simple keratocysts are more common in males, but more females with NBCCS develop OKCs.^[22]

OKCs associated with NBCCS have greater predilections for the mandible than the maxilla, with 69% occurring in the mandible and 31% in the maxilla.^[9,15] In the mandible 43% occurs in the molar ramus region followed by 18% in the incisor-canine area, and 7% in the premolar area.^[22] In the maxilla, 14% occurs in the incisor and canine region followed by 12% in the molar tuberosities, and 3% in the premolar region.^[22] In our case both the OKCs were in the molar ramus area of the mandible.

Although benign, the recurrence rate after excision of OKC is high, ranging from 12 to 62.5% and multiple recurrences are not unusual.^[23]

The OKC is now termed as 'keratocystic odontogenic tumor' (KCOT).^[24] It may be associated with the Gorlin-Goltz syndrome in the form of multiple cystic lesions. The KCOT is locally destructive, despite its bland histological features.

Katase *et al.*, analyzed the neoplastic nature and biological potential of sporadic and NBCCS-associated KCOT.^[25] Heparanase is an endo-d-glucuronidase enzyme that specifically cleaves heparan sulfate and the increase of its level in tumors promotes invasion, angiogenesis, and metastasis. In the study, all odontogenic cysts have shown positive immunoreaction for the heparanase protein in various intensities. Interestingly, intense gene and protein expressions have been observed

in the KCOT associated with NBCCS, as compared to the sporadic ones and the dentigerous cyst. Their results imply that heparanase expression may be correlated with the neoplastic properties of KCOT, particularly in NBCCS-associated cases.

Currently there are new lines of investigation based on biomolecular studies, which aim at identifying the molecules responsible for these cysts and thus allowing an early diagnosis of these patients. Pruvost-Balland *et al.* carried out a clinical and genetic study in 22 patients with basal cell nevus syndrome.^[26] The PTCH 1 gene, the human homolog of the *Drosophila* segment polarity gene, has been seen to be involved in the development of the NBCCS. PTCH 1 is mapped to chromosome 9q22.3. PTCH 1 mutations have been identified in 13 patients: six familial cases, three sporadic cases, and for four patients, it was not possible to conclude if they were familial or not. Thus genetic analysis allowed molecular confirmation of diagnosis in about half of all patients.

The Gorlin-Goltz syndrome is a well-known syndrome with a variety of findings in and outside the head and neck region. Early diagnosis is essential for detection of clinical and radiological manifestations in young patients and for provision of advice concerning protection of the skin from sunlight. In its clinical management and follow up, the pedodontist, oral pathologist, maxillofacial surgeon, and several other medical specialists are involved. Interdisciplinary cooperation is mandatory for the diagnosis and follow-up control of patients with the Gorlin-Goltz syndrome.

CONCLUSION

The Gorlin-Goltz syndrome is an autosomal dominant disorder with numerous diagnostic criteria, but only two major and one minor criteria or one major and three minor criteria are required to arrive at a diagnosis. The odontogenic keratocyst is frequently the presenting manifestation of this syndrome. As this condition requires early diagnosis to prevent clinical progression and complication, the onus for this often lies with the dental teams.

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