CASE REPORT

Gorlin-Goltz Syndrome

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ABSTRACT

Gorlin-Goltz syndrome also known as nevoid basal cell carcinoma syndrome (NBCCS) is an infrequent multisystemic disease inherited in a dominant autosomal way, which shows a high level of penetrance and variable expressiveness. It is characterized by keratocystic odontogenic tumors (KCOT) in the jaw, multiple basal cell carcinomas and skeletal abnormalities. This syndrome may be diagnosed early by a dentist by routine radiographic examination in the first decade of life, as KCOTs are usually one of the first manifestations of the NBCCS syndrome. This article reports the case of a 12-year-old girl with Gorlin-Goltz syndrome, emphasizing its clinical and radiographic manifestation. This study highlights the importance of health professionals in the early diagnosis of this syndrome and a multidisciplinary approach to provide a better diagnosis and prognosis.

Keywords: Gorlin-Goltz syndrome, Keratocystic odontogenic tumor, Basal cell nevus syndrome.

INTRODUCTION

Gorlin-Goltz syndrome is an autosomal dominant disorder principally characterized by triad of abnormalities, like multiple basal cell carcinoma, odontogenic keratosis in the jaw and bifid ribs. Other common features of this syndrome included calcification of the falx cerebri, spine and rib anomalies. Palmar and plantar epidermal pits, facial milia, frontal bossing, ocular malformations, medulloblastomas, cleft lip and cleft palate.1

Gorlin-Goltz syndrome is caused by a tumor suppressing gene called ‘patched’ gene. Found in the long arm of a chromosome 9q22.3-q31 which controls growth and development of normal tissues.2 Mutations of a single point of the patched allele cause malformations. Deactivation of both allele causes formation of tumors and cysts, like KCOT, basal cell carcinoma and medulloblastoma.

Early diagnosis, family screening and genetic counseling of the patient’s family are required as it is inherited as an autosomal dominant disorder.3 The following case report describes a 12-year-old female patient with some classical features of this syndrome.

CASE REPORT

A 12-year-old girl reported to our OPD with a chief complaint of swelling in the posterior part of the lower left jaw with an insidious onset since 2 months (Fig. 1). She was born after normal gestation and delivery. The case history revealed no significant medical and dental history. Her general physical examination showed her weight and height to be normal for her age. The face showed asymmetry at the mandible, increased intercanthal distance, mandibular prognathism, wide nasal bridge. Extraoral examination revealed swelling extending from

Fig. 1: Extraorally swelling extending from symphysis to angle of mandible
symphysis to angle of mandible on the left side. The swelling was firm, nontender and smooth on palpation. Intraorally, it extended from deciduous canine to permanent first molar, irregular and on palpation was firm and nontender. Anterior crossbites were also seen.

The orthopantomogram (OPG) of the patient revealed multiple multilocular radiolucency with multiple unerupted teeth and resorption of the roots of 36, 74 and 75 (Fig. 2). Considering the differential diagnosis of Gorlin-Goltz syndrome, further evaluation was done with chest radiograph, radiographs of the skull and jaw, computed tomography and MRI. The chest radiograph showed bifid ribs (Fig. 3). Skull radiograph showed lamellar calcification of falx cerebri (Fig. 4). Routine blood investigations were done and found to be normal. FNAC revealed thin straw-colored fluid with cholesterol crystals. The patient’s parents and family had no history of the syndrome; they were examined and radiologically evaluated too.

The tumor was surgically removed through enucleation and marsupialization technique. The histopathological examination showed epithelium with palisade basal cell layer with dark staining nuclei and corrugated surface with parakeratin. Areas of dense keratin whorls, inflammatory infiltrate with loss of lining epithelium were also seen (Fig. 5). Based on the clinical, radiographic and histological data, the diagnosis of Gorlin-Goltz syndrome was established.

**DISCUSSION**

Gorlin-Goltz syndrome is also known as nevoid basal cell carcinoma (NBCCS) and Gorlin syndrome. The history of this disorder dates back to Egyptian mummies of 1000 BC who showed similar findings. In 1894, it was first reported by Jarrish and White. In 1961, Binkley and Johnson also reported this syndrome, however in 1960, Goltz and Gorlin first described the classical triad of multiple basal cell carcinomas, KCOT in jaw and bifid ribs that characterized the diagnosis of the syndrome. As more and more cases were reported, more findings...
were included which can be broadly classified as clinical manifestations of Gorlin-Goltz syndrome.5

1. Cutaneous anomalies: Basal cell nevus, other benign dermal cyst, palmar pitting, palmar keratosis and dermal calcinosis.

2. Dental and osseous anomalies: Multiple odontogenic keratocyst (OKC), mild mandibular prognathism, frontal and temperoparietal bossing, kyphoscoliosis, vertebral bifurcated ribs, spina bifida and brachymetacarpelism.

3. Ophthalmic anomalies: Hypertelorism, wide nasal bridge, congenital blindness and internal strabismus.

4. Neurological anomalies: Mental retardation, dural calcification, bridging of sella, agenesis of corpus callosum, congenital hydrocephalus, occurrence of medulloblastoma.


Diagnosis is based on more specific features of the syndrome as given by Evans et al.6 Diagnosis of Gorlin-Goltz syndrome can be established when two major criteria or one major and two minor criteria are present.

The major criteria are as follows:

- More than two basal cell carcinomas (BCC), or one BCC at younger than 30 years of age; or more than 10 basal cell nevi
- Any odontogenic keratocyst (proven on histology) or polyostotic bone cyst
- Three or more palmar or plantar pits
- Ectopic calcification: Lamellar or early—at younger than 20 years of age—falk calcification
- Positive family history of NBCCS

The minor criteria are as follows:

- Congenital skeletal anomalies: Bifid, fused, splayed or missing rib or bifid, wedged or fused vertebra
- Occipital-frontal circumference, more than 97% with frontal bossing
- Cardiac or ovarian fibroma
- Medulloblastoma
- Lymphomesenteric cysts
- Congenital malformations, such as cleft lip or palate, polydactyly or eye anomaly (cataract, coloboma, microphthalmos).

Clinical protocol followed to diagnose Gorlin-Goltz syndrome is detailed family history with medical and dental history should be taken.6 Clinical examination includes examination of oral cavity, skin, central nervous system, head circumference, interpupillary distance, eye, genitourinary system, cardiovascular system, skeletal system and respiratory system. Radiographic examination of chest, anteroposterior and lateral skull, spine panoramic radiograph, hands, pelvic (female) should be evaluated. Ovarian ultrasound (female), cranial magnetic resonance imaging or computed axial topographic scan and echocardiogram (children) should also be advised.

The patient in our report had three major criteria, like KCOT, calcification of falk cerebi, bifid rib confirming the diagnosis of Gorlin-Goltz syndrome. Lo Muzio et al6 reported the prevalence of Gorlin-Goltz syndrome as one in 64,000. Odontogenic keratocyst is now called as keratocystic odontogenic tumor (KCOT) and is defined as ‘a benign intraosseos neoplasm of odontogenic origin with characteristic lining of parakeratinized squamous epithelium’ (WHO 2005). Lorenzo et al6 suggested that KCOTs are often the first sign of NBCCS and can be detected in patients younger than 10 years of age. The KCOTs associated with NBCCS are more common in mandible with 69% involvement and 31% in maxilla.7 Around 43, 18 and 7% KCOTs were found to occur in molar ramus region, incisor-canine area and premolar region respectively. In maxilla 14, 12 and 3% were seen in incisor-canine area, molar tuberosity area and premolar region respectively. The male to female ratio was 1:1.22 for KCOT associated with NBCCS. Whereas others as Gomez et al10 have shown KCOT in NBCCS occurring at an average age of 28 years (range from 14 to 60 years). The male to female ratio being 4:1. Common site being maxilla 53 and 47% in mandible. The recurrence rate was 38.5%. Other studies have reported recurrence rate of 12 to 62.5%8 and also multiple recurrences.11,12 The high recurrence of KCOT can be because of invasive growth due to active growth of the connective tissue wall. Other possible regions are increased mitotic activity, epithelial proliferation and connective tissue and residual dental lamina with subsequent new cyst formation.13 However, the exact mechanism of the recurrence is still unclear. Katase et al12 showed that the heparanase and endo-D-glucuronidase enzyme, that specifically cleaves heparan sulfate, increase its level in the tumors and promotes invasion, angiogenesis and metastasis. This gene and protein showed intense expression in KCOT associated with NBCCS compared to sporadic KCOT. Kolar et al13 showed NBCCS KCOTs have a different immune phenotype than sporadic KCOTs. The former had higher expression of Bcl-2, P 27 and C-erb B-2. Lu Muzio et al14 found higher expression of P 53 and cyclil D 1 in NBCCS KCOTs.

Early diagnosis leads to better prognosis. Diagnosis of NBCCS in at-risk infants can be made radiographically by detection of calcification of falk cerebi, ribbed anomalies and calcification of ovarian fibromas. Definitive presymptomatic diagnosis can also be made by molecular genetic linkage.2 NBCCS is caused by mutations in a tumor suppressor gene PTCH located in chromosome 9q22.3.4 For a tumor suppressor gene to be inactivated two mutagenic hits are required. The first hit causes mutation in one allele. The second hit causes loss of heterozygosity and is seen in NBCCS KCOTs and medulloblastomas. Various physical anomalies of the brain, rib, vertebrae, limbs apparently need only one hit. The first hit that is present in a germ cell can be dominantly inherited. This accounts for the malformation and the variability in NBCCS patients.4

The results from several studies have indicated that the risk of developing basal cell carcinoma has a strong positive relationship with exposure to UV radiation from the sun. Therefore, these patients need to avoid excess sun exposure.
Marotto et al\textsuperscript{15} suggested that radiographs taken routinely for orthodontic treatment are important sources to determine the clinical findings of this syndrome. The Gorlin-Goltz syndrome is an uncommon disorder. A multidisciplinary approach of not only dental specialties, like oral medicine, oral pathology and pedodontics, are required for early diagnosis but reference to other medical specialists is mandatory for further evaluation.\textsuperscript{16} The patient and the family should be well informed of the disorder and importance of follow-up.

**CONCLUSION**

Gorlin-Goltz syndrome is a dominant autosomal genetic process with multiple findings. The major and minor criteria are easily identifiable both on clinical and radiological examinations. Awareness among the dental specialists helps in correct diagnosis and treatment of affected patients.

**REFERENCES**