Case Report

JRAD Journal of Research and Advancement in Dentistry

J Res Adv Dent 2018;9:1:300-303.

Gorlin-Goltz Syndrome: A Case Report

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ABSTRACT

Background: In Indian scenario, Gorlin–Goltz syndrome (nevoid basal cell carcinoma syndrome [NBCCS]) has been rarely reported. The clinical, radiological, and histopathological findings and major and minor criteria in five cases of NBCCS in North Indian population have been presented along with a discussion of the role of gene mutation analysis in early diagnosis of syndrome. It is an infrequent multisystemic disease with an autosomal dominant trait, with complete penetrance and variable expressivity, though sporadic cases have been described. This article includes a case report and an extensive review of the GGS with regard to its history, incidence, etiology, features, investigations, diagnostic criteria, keratocystic odontogenic tumor and treatment modalities.

Keywords: Goltz-Gorlin syndrome, keratocystic odontogenic tumor, odontogenic keratocyst.

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. Pathogenesis of the syndrome is attributed to abnormalities in the long arm of chromosome 9 (q22.3-q31) and loss or mutations of human patched gene (PTCH1 gene). More than 100 minor criteria have been described. Diagnosis is based upon established major and minor clinical and radiological criteria and ideally confirmed by deoxyribo nucleic acid analysis. 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 counselling are essential as it may be associated in 10% of the patients with aggressive basal cell carcinomas and malignant neoplasia's.[3] The frequency of the syndrome varies according to the country where the study has been carried out. On an average, the incidence of Gorlin-Goltz syndrome has been reported to be 1 in 50,000 to 150,000 in general population. The review of literature reveals that only seven cases of this syndrome are reported from India. We report here a patient with Gorlin-Goltz syndrome.

CASE REPORT

A 13-year-old boy presented to the Department of Oral and Maxillofacial surgery in Goenka Dental College and Hospital, Gandhinagar, with complaint of swelling in the upper posterior region of right side of jaw since the last six months. Swelling had increased and the puss discharge was evident since 15 days and mild pain was associated with it.

CT Scan was advised. It showed well defined oval expansile lytic lesion with partially corticated margins involving the body of left maxillary bone, with evidence of an impacted tooth within. It showed mixed density content within. It caused mass effect in the form of compression over the left maxillary sinus which is hypoplastic and filled with soft tissue density. It measured 3.7 × 3.1 × 2.4 cm in

Received: Mar. 17, 2018: **Accepted**: June. 10, 2018
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pISSN 2278-0076
eISSN 2321-9270

size. Other two well defined oval shaped mildly expansile lytic lesions with partially corticated margins and impacted tooth within are seen at the level of angle of mandible on both sides, measuring 25 × 21 × 17 mm on right side and 26 × 20 × 12 mm on left side. Agenesis (hypogenesis) of left frontal sinus was observed. Due to the presence of multiple cyst-like lesions in the jaws, Gorlin-Goltz syndrome was suspected and further investigations were carried out.

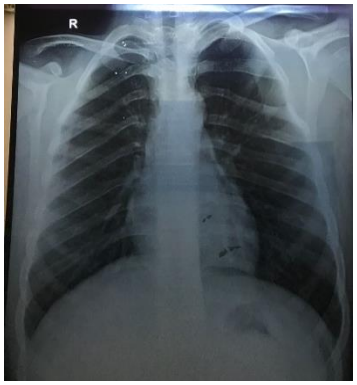

Fig 1: Chest X-ray showed bifid ribs.

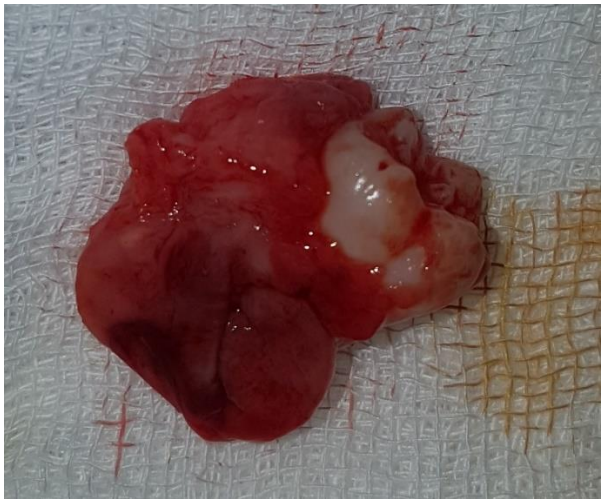

Fig 2: Excised tissue with tooth from the left mandible.

An X-ray of the skull revealed calcification of falx cerebri and a chest X-ray showed bifid ribs (Figure 1). All the cystic lesions of the jaw were enucleated surgically. Intraoperative photographs and photographs of excised tissue are shown in Figures 2 and 3, respectively. The histopathologic examination of enucleated tissue was done. The cystic lining was made up of uniformly thick, stratified squamous epithelium of 5 to 6 layers thick, flat with corrugated parakeratin surface. The basal cell layer was cuboidal to columnar with well-polarized nuclei. Underlying connective tissue capsule was loose fibrocellular, with supporting vasculature, extravasated blood elements, strands, and nests of odontogenic epithelium. In all four cysts, histopathologic features were suggestive of OKC. Ki 67 immunohistochemical staining was done which was positive (25%).

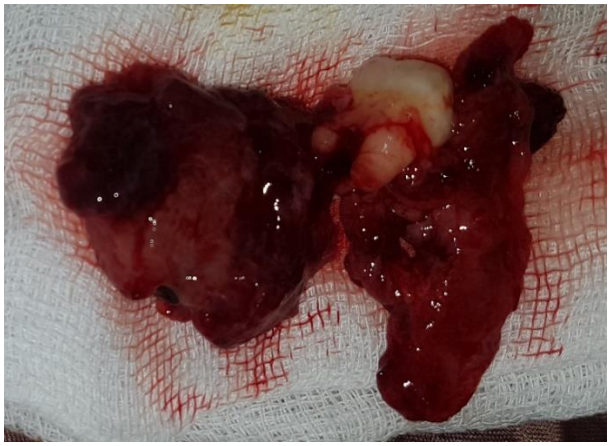

Fig 2: Excised tissue with tooth from the Right mandible.

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 epethelioma-jaw cysts or bifid rib syndrome.

It was first reported by Jarisch and White in 1894, and later in detail by Gorlin and Goltz.[4] Clinical manifestations of the syndrome are grouped into the following five categories.[4]

(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.

In order to make a diagnosis of the Gorlin-Goltz syndrome, some diagnostic criteria have to be taken into account. The most important criteria to make a diagnosis for this syndrome are the presence of pigmented basocellular carcinomas, OKC, palmar and/or plantar pits, and ectopic calcifications of the falx cerebri.[5, 6] Together with these major features, more than 100 minor features have been described. The more relevant are the following: cardiac or ovarian fibroma, macroencephaly, bifid ribs, kyphoscoliosis, cleft palate, medulloblastoma, alterations in the sella turcica, mandibular prognathia, lateral displacement of the inner canthus, frontal and biparietal bossing, imperfect segmentation of the cervical vertebrae, linfomesenteric cysts that tend to calcify, meningiomas, fibrosarcoma, rhabdomyosarcoma, short fourth metacarpal, ocular hypertelorism, congenital blindness, high arched eyebrows and palate, narrow sloping shoulders, immobile thumbs, low pitch voice in women, renal anomalies, and hypogonadism in men.

Evans *et al*.[7] first established major and minor criteria for the diagnosis of the syndrome and later were modified by Kimonis[8] *et al*. in 2004. The presence of two major and one minor or one major and three minor criteria are necessary to establish diagnosis.[7,8]

Major criteria

- Multiple basal cell carcinomas or one occurring under the age of 20 years.
- Histologically proven OKCs of the jaws.
- Palmar or plantar pits (three or more).
- Bilamellar calcifications of the falx cerebri.
- Bifid, fused, or markedly splayed ribs.
- First degree relative with nevoid basal cell carcinoma syndrome.

Minor criteria

- Macrocephaly (adjusted for height).
- Congenital malformation: Cleft lip or cleft palate, frontal bossing, coarse face moderate or severe hypertelorism.
- Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
- Radiological abnormalities: Bulging of sella turcica, vertebral anomalies such as hemi vertebrae, fusion or elongation of vertebral bodies, modeling defects of the hands and feet, or flame-shaped hands or feet.
- Ovarian fibroma.
- 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 two minor criteria (viz. hypertelorism 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.[9] Shanley *et al*. in Australia, and Lo Muzio *et al*. in Italy estimated the prevalence as 1 per 64,000 and 256,000, respectively.[10,11] Evans *et al*., reported that the prevalence rate in the United Kingdom was 1 per 560,000.[7]

This reported case showed that, till date, only 8 cases have been reported from India. 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. Our case too

presented with multiple cystic lesions involving the mandible, which was histopathologically diagnosed as an odontogenic keratocyst.

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.[12] 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.

This investigation prompts an early verification of the disease, which is very important to prevent recurrence and better survival rates from the existent diseases. OKC of the jaws which can cause disfigurement of the face, mobility and even loss of teeth can be avoided by early detection and treatment of the same.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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