Case Report

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Gorlin – Goltz Syndrome: A Hidden Diagnosis

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ABSTRACT

Background: Goltz Gorlin syndrome is a rare autosomal disorder with strong penetrance and extremely variable expressivity that is often missed in diagnosis and treated for multiple odontogenic keratocysts. Early diagnosis of the syndrome is important due to susceptibility to carcinomas, and the syndrome can become destructive as age advances. Most often, the syndrome will be rarely diagnosed due to a lack of proper investigations. Here we present a case report of a patient with multiple odontogenic keratocysts diagnosed with Goltz Gorlin syndrome.

Keywords: Goltz Gorlin syndrome, multiple odontogenic keratocysts, Nbcc syndrome.

INTRODUCTION

Gorlin -Goltz syndrome, which is also known as nevoid basal cell carcinoma (NBCC) Syndrome, is a rare autosomal dominant disorder with strong penetrance and extremely variable expressivity. This syndrome is also named Gorlin syndrome, multiple nevoid basal cell epithelioma, jaw cyst bifid rib syndrome, or multiple nevoid basal cell carcinoma syndromes. Gorlin and Goltz [1], in the year 1960, described the triad, which includes multiple basal cell carcinoma, odontogenic keratocysts and bifid ribs characteristic of the syndrome. Rayner et al. [2] in the year 1977 added additional characteristics to the syndrome such as falx cerebral calcification and palmar or plantar epidermal pits. Multiple OKC'S are the first ones to get diagnosed as they are almost present in 80% of NBCC syndromes. Incidence is 1in 57000 to 1in 256000. The male to female ratio is 1:1. It is mainly caused due to mutations in the patched tumour suppresser gene (Ptch), a human homologue of the Drosophila gene mapped to chromosome 9 q22.3- q31 [3]. Early diagnosis of the syndrome is important due to susceptibility to carcinomas, and the syndrome can become destructive as age advances. Most often, the syndrome will be rarely diagnosed due to a lack of proper investigations. Here we present a case report of a patient with multiple OKC's diagnosed with Goltz Gorlin syndrome.

CASE REPORT

A 25-year-old female patient reported to the Department of Oral and Maxillofacial Surgery, MNR dental college and hospital with a chief complaint of swelling and pain in the left upper and lower back regions of the jaw for two months and also associated with pus discharge from the same region. Family history revealed similar swelling in her elder sister. The patient was moderately built and nourished. Extraoral examination revealed a soft swelling extending anteriorly from the corner of the mouth posteriorly to the angle of the mandible, inferiorly from the lower border of the mandible till the tragus of the ear (Fig1). The patient also presented with frontal bossing, increased inter canthal distance of 40mm, and a broad nasal bridge

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(Fig 2). A panoramic radiograph revealed a multilocular radiolucency involving the left angle and ramus of the mandible, which is extending from the distal aspect of 37 teeth to the angle of the mandible and ascending ramus superiorly till sigmoid notch of the mandible (Fig 3). Erupting 38 teeth is seen within the radiolucent region.

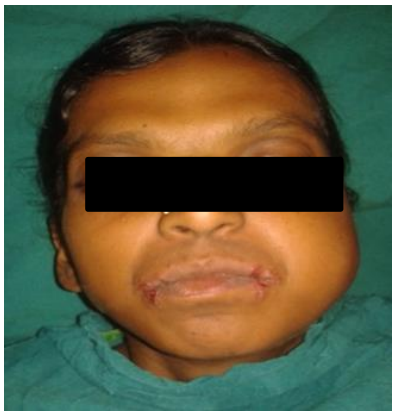

Fig 1: Showing extra oral swelling in left angle region and frontal Bossing.

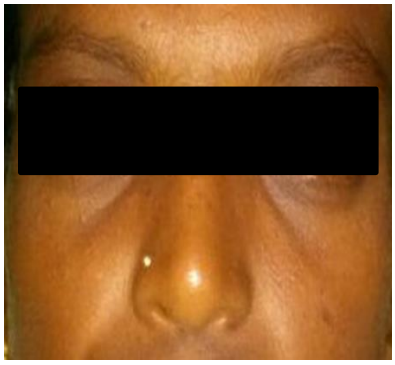

Fig 2: Facial photograph showing hypertelorism

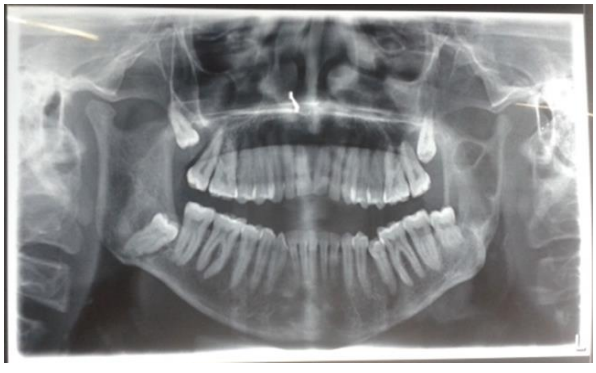

Fig 3: OPG showing multiple impacted teeth and multiple radiolucent lesions with radiopaque border in left ramus, angle of the mandible and left posterior maxilla.

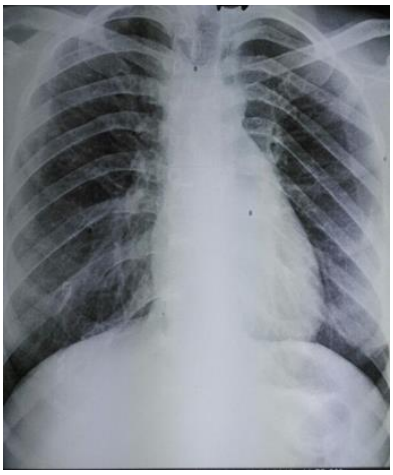

Fig 4: Chest radiograph showing bifid ribs.

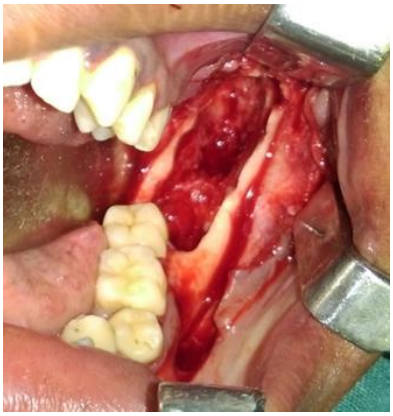

Fig 5: Enucleation of mandibular cyst.

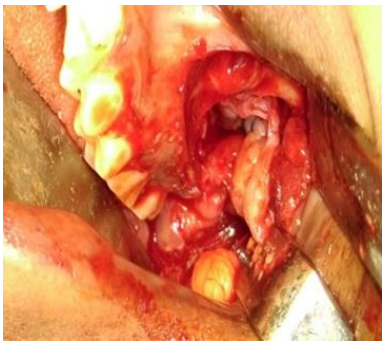

Fig 6: Enucleation of maxillary cyst.

Periapical radiolucency is seen in relation to the 26 and 27 teeth of the maxilla. Multiple impacted teeth in relation to 18,28,48 are seen. No pathological migration of teeth and no definitive root resorption of teeth are present. Chest radiograph revealed the presence of bifid ribs (Fig 4). Aspiration of the cystic lesions showed cheesy white keratin like material

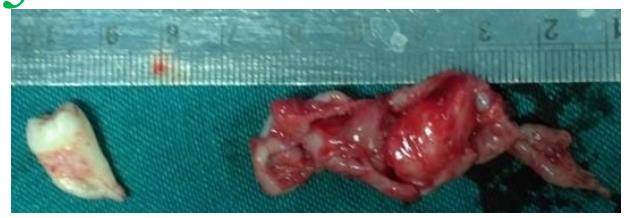

Fig 7: Excised cystic lining with impacted teeth.

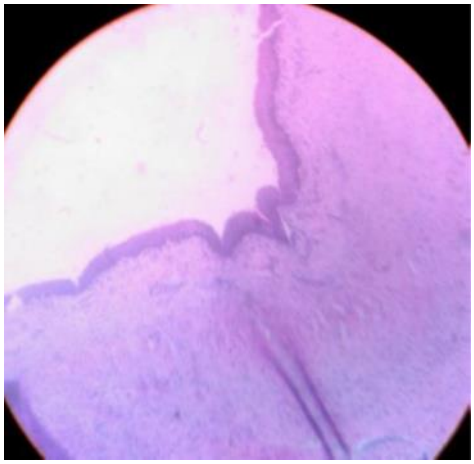

Fig 8: Histopathological slide confirming OKC.

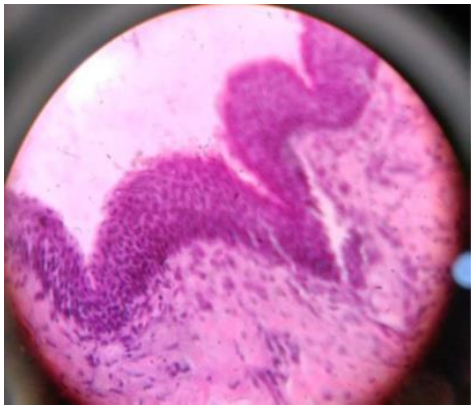

Fig 9: Histopathological slide confirming OKC.

An incisional biopsy was done and sent for histopathological examination, which revealed stratified squamous parakeratinised epithelium with a palisading pattern of basal cells, confirming the diagnosis of odontogenic keratocyst (fig 8,9).

Correlating the presence of all clinical features such as multiple odontogenic keratocysts, bifid ribs, multiple impacted teeth, macrocephaly, frontal bossing, high arched palate, broad nasal bridge, increased intercanthal distance and familial history, it was diagnosed as "Gorlin-Goltz syndrome" according to the Kimonis et al. diagnostic criteria.

Under general anaesthesia, surgical removal of multiple impacted teeth and enucleation of the multiple cystic lesions, followed by chemical cauterization with Carnoy's solution, was done in both maxilla and mandible as shown in (fig 5,6). The entire cystic specimen from maxilla and mandible, as shown in (fig 7) were sent for histopathological examination confirming the diagnosis of OKC. The patient was put on a soft diet for one month postoperatively

DISCUSSION

Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin-Goltz [1] syndrome, is an autosomal dominant disorder characterized by a predisposition to neoplasms and other developmental abnormalities. Gorlin & Goltz [1] described the classical triad composed of multiple basal cell carcinomas, multiple odontogenic keratocysts (OKC's) in the jaws and bifid ribs that characterized the diagnosis of this syndrome. In addition to this triad, calcification of the falx cerebri, palmar and plantar epidermal pits, spine and rib anomalies, relative macrocephaly, frontal bossing, ocular malformation, medulloblastomas, cleft lip and/or palate, and developmental malformations were also established as features of the syndrome [1,2].

It is caused by mutations in the patched tumor suppresser gene (Ptch), a human homologue of the Drosophila gene mapped to chromosome 9 q22.3-q31. Chromosomal mapping and genetic studies suggested that the underlying basis of this disease is an abnormality in the Hedgehog (Hh) signalling pathway. The role of this pathway in embryogenesis is well known. In the drosophila model, the primary receptor for Hh signalling pathways has two transmembrane protein components: patched (Ptc) smoothened (Smo). Normally PTCH forms a receptor complex with the oncogene SMO (smoothened) for the SHH (sonic hedgehog) ligand. PTCH binding to SMO inhibits growth signal transduction. SHH binding to PTCH would release this inhibition. If the normal functioning of PTCH lost, the proliferation – stimulating effect of SMO are permitted to predominate[3-11].

Evans et al. [12] first established major and minor criteria for the diagnosis of the syndrome and later were modified by Kimonis [13] et al. in 2004. The

presence of two major and one minor or one major and three minor criteria are necessary to establish the diagnosis of Goltz Gorlin syndrome [12,13].

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 hemivertebrae, fusion or elongation of vertebral bodies, modelling defects of the hands and feet, or flame-shaped hands or feet.
- Ovarian fibroma.
- Medulloblastoma.

Medulloblastomas are seen in syndromic patients in the first two years of life. Molecular genetic studies for PTCH1 gene mutation may be helpful in early diagnosis. Ovarian fibromas and cysts associated with the syndrome are usually seen in 16-45 years age group

The absence of all the manifestations of the syndrome may be due to variability of the PTCH gene expression, as mentioned by Hahn H et al. [3]. According to the literature review in the Indian population, the features of the Goltz Gorlin syndrome are in descending order, such as Impacted or ectopic tooth -100% , Multiple odontogenic keratocysts -95.8%, Rib anomalies - 71%, Hypertelorism – 54% , Frontal bossing - 45.8%, Basal cell carcinoma – 41.6%, Bridging of sella turcica – 29%, Macrocephaly – 25%, polydactyly -21%.

The present case report showed a female patient presenting with both major and minor features of the syndrome, such as multiple OKC's in the maxilla and mandible, rib anomalies, ocular Hypertelorism, frontal bossing, high arched eyebrows and palate and with a familial history of multiple odontogenic kerato cysts which confirmed the diagnosis of NBCCS or Gorlin-Goltz syndrome.

CONCLUSION

In conclusion, the present case report highlights Gorlin-Goltz syndrome as an uncommon multi-systemic disease, which may be underdiagnosed and requires a multidisciplinary approach (maxillofacial surgeon, neurologist and dermatologist). A complete clinical, radiological and histopathological analysis must be performed to detect any features associated with this syndrome and ideally confirmed by DNA analysis. It is the responsibility of the oral and maxillofacial surgeon to rule out the presence of any associated features of the syndrome and start adequate treatment as soon as the diagnosis is made. As Goltz Gorlin syndrome is mainly due to a defect in tumor suppressor gene, the patients are more susceptible to malignancy when exposed to carcinogens. Therefore proper counselling should be given to the patient regarding expected complications of the syndrome. The follow-ups of these patients should be managed regularly according to scientific protocols.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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