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Gorlin – Goltz Syndrome – A Case Report

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Abstract

The Gorlin-Goltz syndrome is a rare autosomal dominant condition caused by mutations in the *PTCH* (patched) gene, shows a high level penetrance and variable expressiveness, characterized by multiple basal cell nevi or carcinomas, odontogenic keratocysts, palmar and / or plantar pits, calcification of the falxcerebri, and is occasionally associated with internal malignancies. Awareness about the syndrome plays a significant role in diagnosis. An early diagnosis is essential for early management of neoplastic lesions and that results in a better prognosis. Hence, present a case report and a review of Gorlin - Goltz syndrome.

Keywords: Gorlin- Goltz syndrome, odontogenic keratocyst, PTCH gene

Introduction

Gorlin - Goltz syndrome, also known as Nevoid basal cell carcinoma (NBCC) Syndrome is a rare autosomal dominant disorder with strong penetrance and extremely variable expressivity[1,2]. Other names for this syndrome include Gorlin Syndrome, Multiple Nevoid Basal Cell Epithelioma, Jaw Cyst Bifid Rib Syndrome, and Multiple Nevoid BCC syndrome.

In 1894 **Jarisch** and **White** were the first to describe about this syndrome highlighting the presence of multiple basocellular carcinomas in their patients[3,4]. Later, in 1939 **Straith** described a with family history of case in which multiple basocellular carcinomas and cysts [5].In 1953, **Gross et al** suggested some additional associated signs of the syndrome such as synostosis of the first left rib and bilateral bifurcation of the sixth ribs[6].Bettley (1953) and Ward(1960) reported the association of palmar and plantar pits with the syndrome. [7,8]Nevertheless, it was not until 1960, when Robert J .Gorlin and Robert W Goltz established a classical triad that characterizes the diagnosis of this syndrome which include (multiple basocellular epitheliomas, keratocysts in the jaws and bifid ribs)[9]. Rayner et al noted two additional characteristics to the syndrome which were falxcerebri calcification and palmar or plantar pits[10]. The reported incidence of this disorder is 1 in 50,000 to 150,000 in the general population.Both genders are equally affected and the clinical features usually seen in the first to third

decade of life. In this paper we report a case of Gorlin-Goltz syndrome a with a brief review of literature.

Case Report

A 25 year old female patient was referred to the Department of Oral and Maxillofacial Surgery, MNR dental college and hospital with a complaint of swelling on the left lower jaw since 2 months. She also complained pain and pus discharge at lower left intra oral region since 15 days.History revealed that the intra oral swelling started 2 months back, which gradually increasing in size and attained to the present size. Pain was started since 15 days, which was sudden in onset localised in nature and aggravated while eating. Except for family history,which revealed similar swelling in her elder sister, other parts of the history are non contributory. Extra - orally it was noted as a soft swelling extending anteriorly from corner of the mouth posteriorly to the angle of the mandible , inferiorly from lower border of the mandible to superiorly till the tragus of the ear (Fig1). Frontal bossing, increased intercanthal distance (40mm) and broad nasal bridge (Fig3) was documented on the patient. Intraoral examination revealed a swelling extending from distal aspect of lower left first molar tooth to involving the ramus region and expansion of cortical plates on buccalside. No mobility and no carious lesions associated with other adjacent teeth . Lower left third molar tooth is partially erupted and mild obliteration of left lower buccal vestibule was noted. Palate was deep and high. Based on the history and clinical examinations it was provisionally diagnosed as cystic lesion with a differential diagnosis of benign odontogenic tumor in left lower molar region. Blood investigation revealed a normal hemogram except the raised ESR.Radiographic examination consisting of occlusal, orthopantanogram and chest radiograph was done. Panoramic radiograph revealed a multilocular radiolucency involving left side of the angle and ramus of the mandible extending from distal aspect of lower left second molar tooth to angle of the mandible and ascending ramus superiorly till sigmoid notch of the mandible (Fig 2). Erupting lower left third molar tooth was observed within the radiolucent region.

Periapical radiolucency is seen in relation to the upper left first and second molar teeth. Impacted maxillary right and left third molars and mandibular third molar were seen. No pathological migration and no definitive root resorption of teeth were evident .Chest radiograph revealed bifid ribs in relation to second and third ribs (Fig.4). Aspiration and the incisional biopsy of the lesion performed showed a white cheesy keratin like material. Histopathological examination showed cystic areas lined by a discontinuous, parakeratinized, folded, corrugated odontogenic keratocyst epithelium and cuboidal palisaded basal cell layer conforming diagnosis of ‘keratocystic odontogenic tumor”.Along with the histopathological details and all the 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. Considering the size of the cysts, enucleationof the lesions, removal of the impacted teeth in maxillary and mandibular cystsand chemical cauterization with carnoy's solution was done under general anaesthesia. [fig 5-8] .

All the excised cystic linings [fig9] were subjected to histopathological examination, which revealed stratified squamous parakeratinised epithelium with palisading pattern of basal cells, confirming the diagnosis of KCOT [fig 10,11].

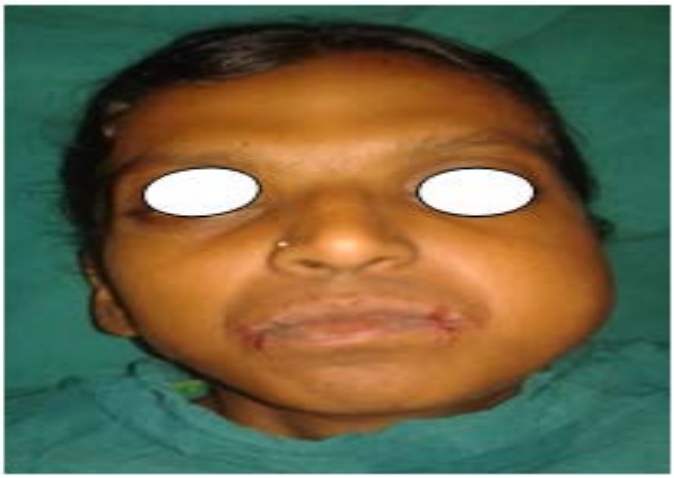

Fig. 1: Facial photograph showing, hypertelorism, with extraoral swelling in the left angle region

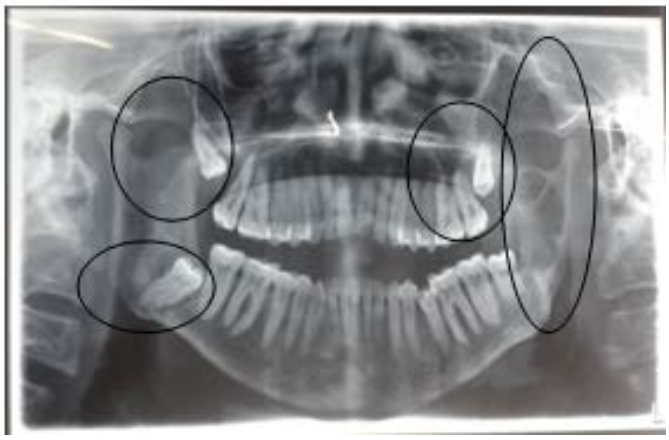

Fig. 2: Panoramic radiograph showing ill-defined radiolucencies and impacted teeth in the maxillary and mandibular region.

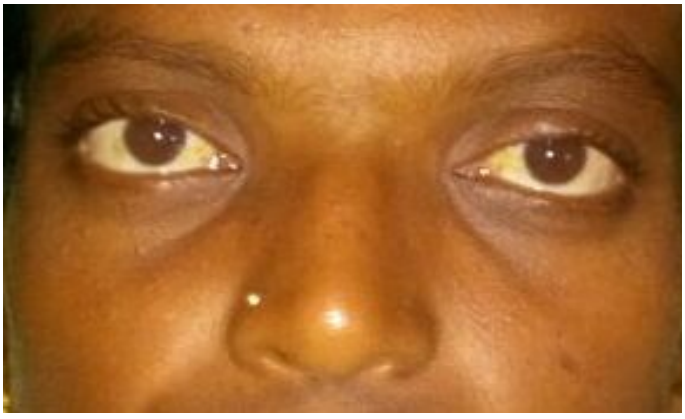

Fig. 3:Facial photograph showing hypertelorism

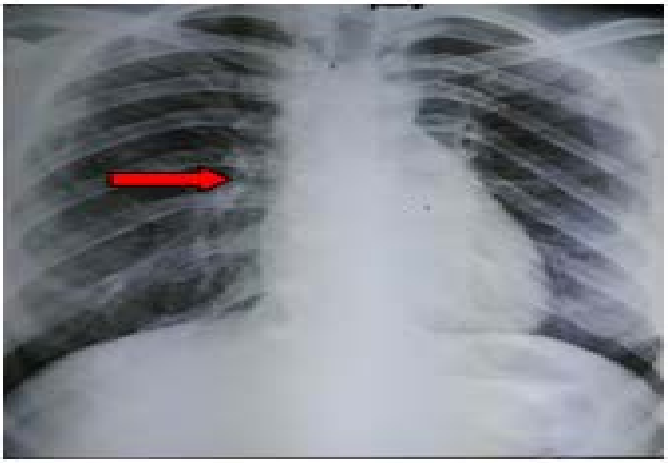

Fig. 4:Chest radiograph showing bifid ribs

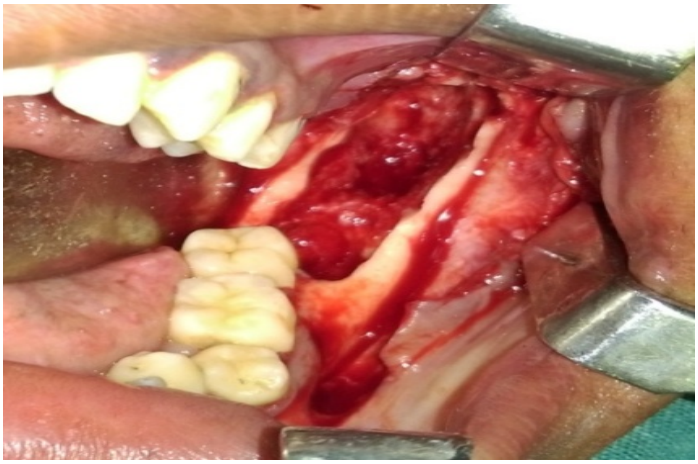

Fig.5:Enucleation of mandibular cyst

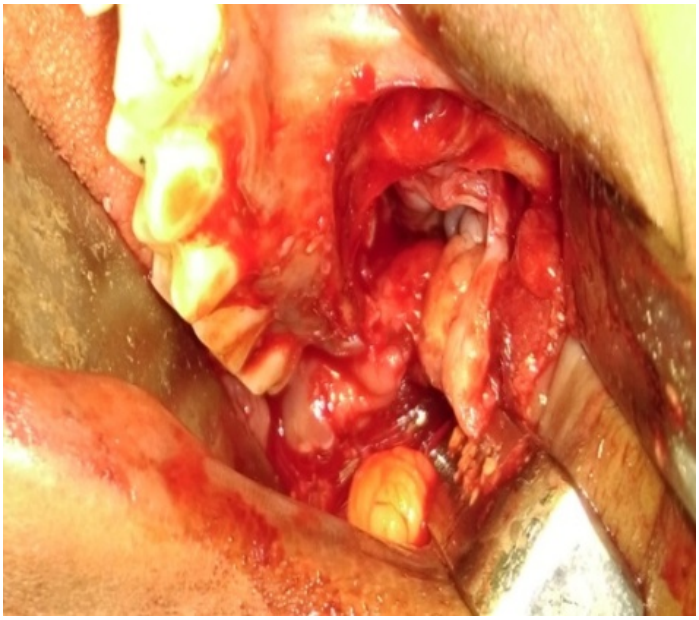

Fig. 6: Enucleation of maxillary cyst

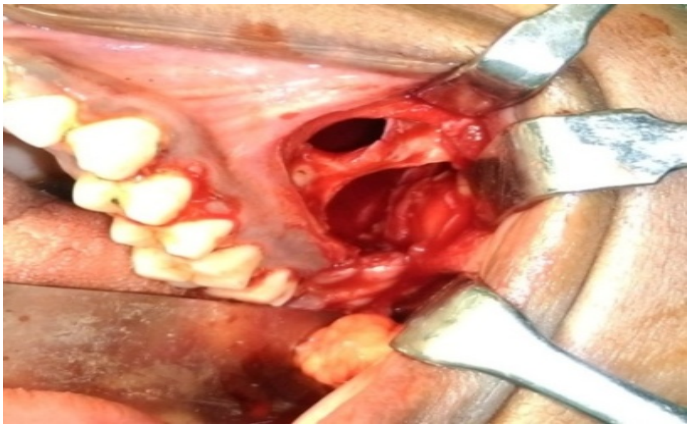

Fig. 8: Maxillary cystic defect

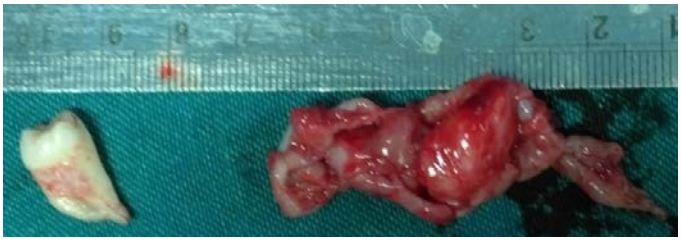

Fig. 9: Excised cystic linig

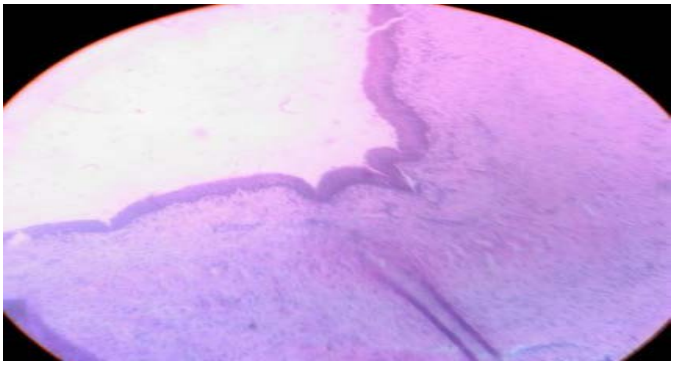

Fig. 10: Photomicrograph showing KCOT

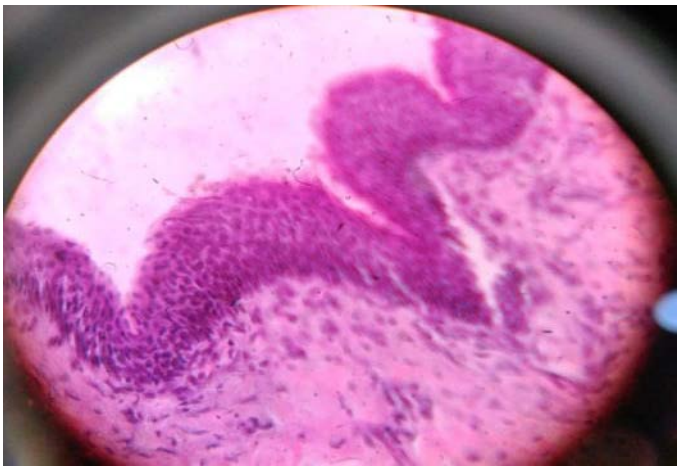

Fig. 11: Photomicrographshowing KCOT

Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin-Goltz syndrome, is an autosomal dominant disorder characterized by a predisposition to neoplasms and other developmental abnormalities[11]. Gorlin & Goltz described the classical triad composed of multiple basal cell carcinomas, keratocysticodontogenictumors (KCOTs) in the jaws and bifid ribs that characterized the diagnosis of this syndrome. In addition to this triad, calcification of the falxcerebri, 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[12,13].

It is caused by mutations in the patched tumor suppresser gene (Ptch), a humanhomologue 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) signaling pathway. The role of this pathway in embryogenesis is well known. In the Drosophila model, the primary receptor for Hh signaling pathways has two transmembrane protein components: patched (Ptch) 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[14-19] . SHH binding to PTCH releases this inhibition[20]. If normal functioning of PTCH lost, the proliferation – stimulating effect of SMO are permitted to predominate.

Evans *et al.*[21] first established major and minor criteria for the diagnosis of the syndrome and later were modified by **Kimonis[22] *et al.*** in 2004. The presence of two major and one minor or one major and three minor criteria are necessary to establish diagnosis.

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 falxcerebri.
- 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.

The absence of all the manifestations of the syndrome may be due to variability of the PTCH gene expression as mentioned by Auluck et al. According to the literature review in Indian population the features of the syndrome in descending order[23]Impacted or ectopic tooth - 100%,Multiple odontogenickeratocysts -95.8%,Rib anomalies -71%, Hypertelorism – 54% ,Frontal bossing - 45.8%, Basal cell carcinoma – 41.6% ,Bridging of sellaturcica – 29%, Macrocephaly – 25%, polydactyly/ syndactyly -21%. The present case report showed a female patient presenting, among others, some of these features, such as multiple KCOTs in the maxilla and mandible, rib anomalies, ocular hypertelorism ,frontal bossing and high arched eyebrows and palate and with a familial history of multiple keratocysistic odontogenic tumors which confirmed the diagnosis of NBCCS or Gorlin-Goltz syndrome.

Conclusion

The present case report highlights Gorlin-Goltz syndrome as an uncommon multi-systemic disease, which may be underdiagnosed and requires a multidisciplinary approach (dermatologist, surgeon, dentist, maxillofacial surgeon and neurologist). A complete clinical , radiological and histopothological analysis must be performed to detect any features associated with this syndrome and ideally confirmed by DNA analysis . It is the responsibility of the dentist and of the oral surgeon to rule out the presence of any associated syndrome and start the adequate treatment as soon as the diagnosis is made. The follow-ups of these patients should be managed regularly according to the scientific,protocols.

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