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GORLIN GOLTZ SYNDROME –A CASE SERIES

Dr. Nalini Aswath MDS, Dr. Sankar Narayanan MDS
Head of the department, Department of Oral Medicine and Radiology, Sree Balaji Dental College and Hospital, Bharath University, Chennai.
Reader, Department of Oral Medicine and Radiology Sree Balaji Dental College and Hospital. BIHER, Chennai.
Corresponding author:

ABSTRACT:
Gorlin goltz syndrome, is a rare autosomal dominant inherited condition caused by the mutation in patched (PTCH),a tumor suppressor gene. It is clinically characterized with frontal and temporoparietal bossing results in the increased cranial circumference, multiple basal cell carcinomas, odontogenic kerotocysts, epidermal cysts of the skin, ocular telorism ,kyphoscoliosis, and various skeletal abnormalities. Here we present a case series of Gorlin goltz syndrome(two cases) in this article. This is an attempt to highlight its importance in early diagnosing this disease along with the review of literature.

Keywords:gorlin goltz syndrome ,okc, splayed ribs,

1. INTRODUCTION:

Gorlin-Goltz syndrome , which is also known as nevoid basal cell carcinoma syndrome , is an autosomal dominant, rare multisystemic disease with a high degree of penetrance and variable expressivity. It was first reported by Jarisch and White in 1894. Later it was discovered by Robert J. Gorlin and Robert W. Goltz described the distinct syndrome, consisting of the presence of multiple nevoid basal cell epitheliomas, jaw cysts and bifid ribs,hence this syndrome is named after them[1]. Incidence is 1 in 50,000 to 150,000 which could vary by region. It is characterized by ,multiple basal cell carcinoma ,basal cell nevus, odontogenic keratocysts (KCOT), ectopic calcifications of the falx cerebri, and palmar and/or plantar pits,spina bifida occulta. Systemic signs can easily be missed due to the non awareness of this syndrome. The features of the syndrome vary globally. Early diagnosis of the syndrome is very important due to high risk and susceptibility to the neoplasm, and the syndrome can become very destructive as its progresses. Most often, the syndrome will go undiagnosed due to lack of proper investigations and problem targeted treatments. Here, we present a case series of this syndrome.

2. CASE SERIES:

CASE REPORT: 1

A 30yr year old female patient, had came ,with the chief complaint of a painful swelling in the left side of the face for the past 10 days. History reveals that, patient had spontaneously developed swelling on the left side of the face. The swelling was smaller in size initially that gradually increased to attain the present size. Pateints medical history reveals no systemic complications. Patient underwent surgery for cleft lip. On extraoral examination, a solitary diffuse swelling is seen on the left side of the face approximately measuring 3 x 1.5 cms in size and roughly oval in shape,and its extends anteriorly from the base of the mandible and posteriorly upto the angle of the mandible and suprainferiorly it extends from 2cm before the earlobe upto the inferior border of the mandible. The skin over the swelling appears to be normal, smooth and the margins are well defined [figure 1] . On palpation the swelling is firm in consistency, tender, and the skin over the swelling is pinchable and its non compressible and non reducible. The swelling is not mobile. Temperature is afebrile. . Single submandibular lymph node is palpable in both right and left submandibular region which approximately measures about 0.25x0.25 cm in size, oval in shape, firm, non-tender and mobile.

On Intra oral examination, a solitary, diffuse swelling present on the buccal sulcus in relation to 37,38 region approximately measuring 2.5 × 2 cm in size extending anteroposteriorly from the gingiva of 37 region to the retromolar area and superiorly extending from the alveolar ridge and inferiorly obliterating the buccal vestibule. Margins are ill-defined. Surface over the mucosa appears erythematous. Surrounding mucosa appears normal [figure 2]. On palpation Swelling is hard in consistency, margins are ill-defined, tender, and swelling is non compressible and non reducible. Expansion of buccal cortical plate in relation to 37,38 region. , the provisional diagnosis of **benign tumor of the left side of the mandible** was made and further investigations were done.

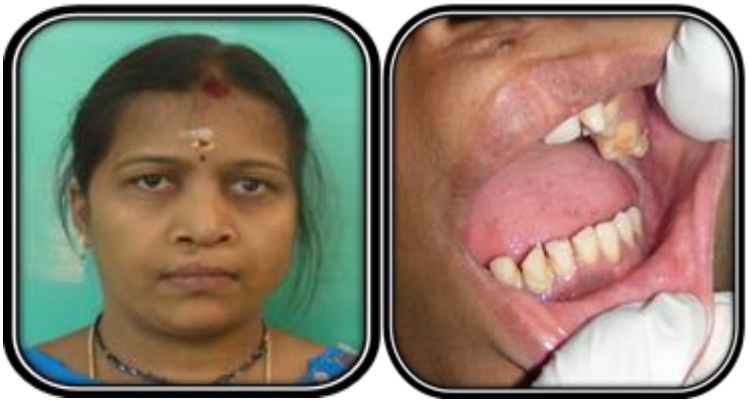


Fig 1-Extra – Oral Examination-gross facial asymmetry noted with the swelling present in the left side of the face and scar evident in the upper lip(pt underwent surgery for cleft lip).

Fig 2-Intra-oral examination- soilitary swelling present in the region of 37 and 38

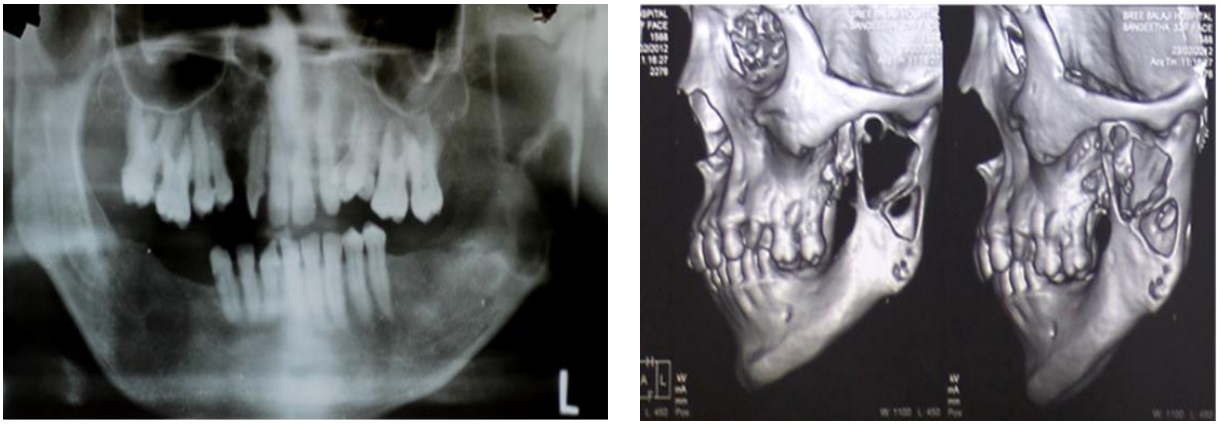
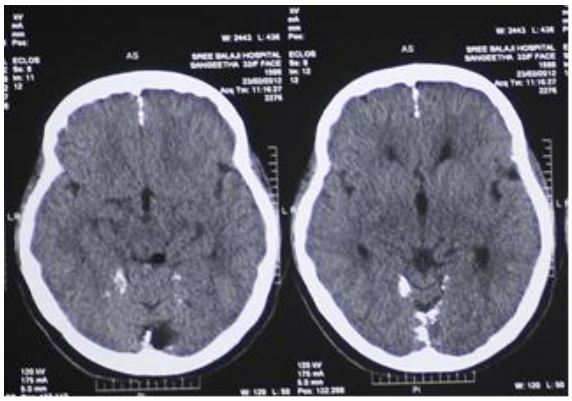


Fig -3--OPG reveals a well defined multilocular radiolucency present on the left side ramus of the mandible approximately measuring 2.5*3 cm in size crossing the angle of the mandible extending upto the coronoid process

Fig 4- 3D CT reveals a large expansile multiple lytic lesion in the left ramus of the mandible.



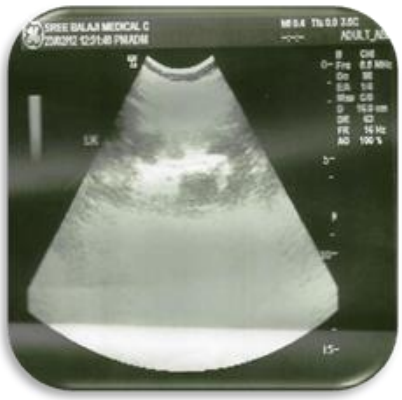


Fig 5-CT axial sections shows the dural calcifications

Fig 6-Ultrasound reveals Para pelvic cyst measuring 2.2x1.9 cm is present in the left inter polar region

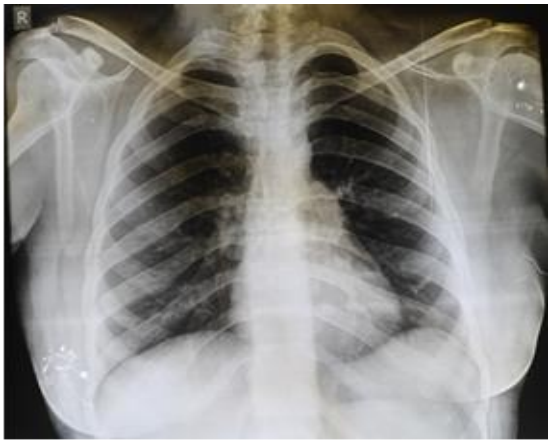


Fig 7- Chest radiograph shows narrow ribs on the right side with increased inter rib distance (i.e) SPLAYED RIBS

Complete cyst enucleation was done and the gross specimen was sent for histopathological examination, and its diagnosed as odontogenic keratocyst. Considering three major criteria- multiple odontogenic keratocyst, dural calcifications, splayed ribs and two minor criteria- cleft lip, pelvic cyst this case was finally diagnosed as ***GORLIN-GOLTZ SYNDROME.*** Patient had uneventful post – operative phase and recovered.

CASE 2:

A 17yr year old female patient, came with a chief complaint of a painless swelling in the right side of the lower jaw for the past 1 month. History reveals that, patient had spontaneously developed swelling on the right side of the lower jaw which was smaller in size initially that gradually increased to attain the present size. Patient was moderetly built with no other medical complications. On extraoral examination, a solitary diffuse swelling is present on the right side of the face approximately measuring 3 x 4 cm in size and roughly oval in shape. The swelling extends anteriorly from the base of the mandible in relation to parasymphysis region and posteriorly upto the angle of the mandible and superioinferiorly it extends from 1cm below the ear lobule upto the lower border of the mandible. The skin over the swelling appears to be normal.On palpation the swelling is hard in consistency, non tender, and the skin over the swelling is pinchable,and the swelling is non compressible, non reducible and not mobile[figure8]. Temperature is afebrile.

On Intra oral examination, there is a solitary, diffuse swelling present on the alveolar mucosa in relation to impacted 47 region approximately measuring 4 × 2 cm in size roughly oval in shape extending anteroposteriorly from the mesial margin of the crown of the impacted 47 to the retromolar area and superiorly extending from the alveolar ridge and inferiorly obliterating the buccal and the lingual vestibule. Margins are ill-defined. Surface over the mucosa appears erythematous. Surrounding mucosa appears normal[figure9]. On palpation, Swelling is firm in consistency, margins are ill-defined, tender, and swelling is non compressible and non reducible. On palpation expansion of buccal and the lingual cortical plates were found in relation to 47 region . Considering the history of painless swelling on the right side of the lower jaw and correlating with the clinical finding of swelling associated with an impacted tooth with bony expansion in the buccal and lingual side of 47 , a provisional diagnosis of **dentigerous cyst in relation to impacted 47** was given and further investigations were done.

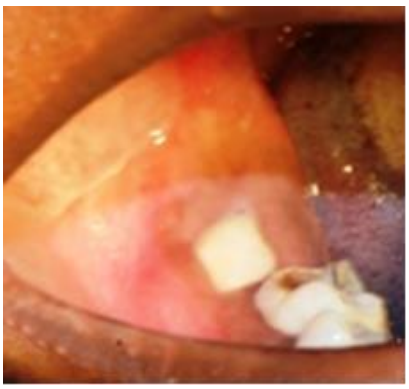
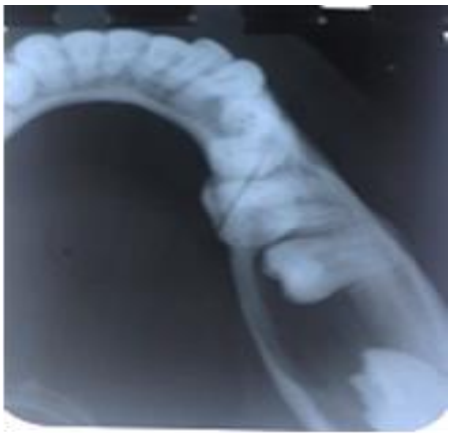


Fig 8-gross facial assymentry is noted

Fig 9-partially imapacted 47 is evident



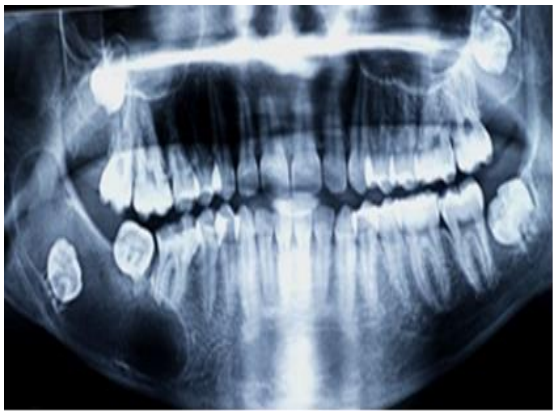


Fig-10 mandibular right lateral oclusal radiograph reveals a a well defined radiolucency approximately measuring 2x3 cm extending from the mesial aspect of impacted 47 to the distal aspect of impacted 48. There is expansion of the buccal and lingual cortical bone

Fig 11-OPG reveals a well defined radiolucency present in relation to impacted 47,48 region approximately measuring 3x6 cm in size extending from the body of the mandible crossing the angle and extends upto the ramus distal to the impacted 48 region.

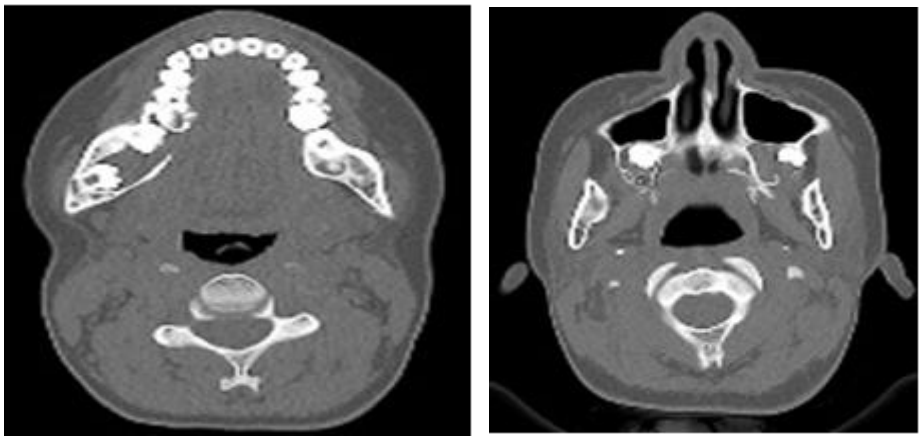


Fig 12, 13- CT axial shows well defined unilocular, expansile, lytic lesion with thin sclerotic rim is seen in the posterior body and angle of right mandible, surrounding the crown of an unerupted molar tooth.Multiple lytic expansile lesions involving all unerupted last molars is seen.

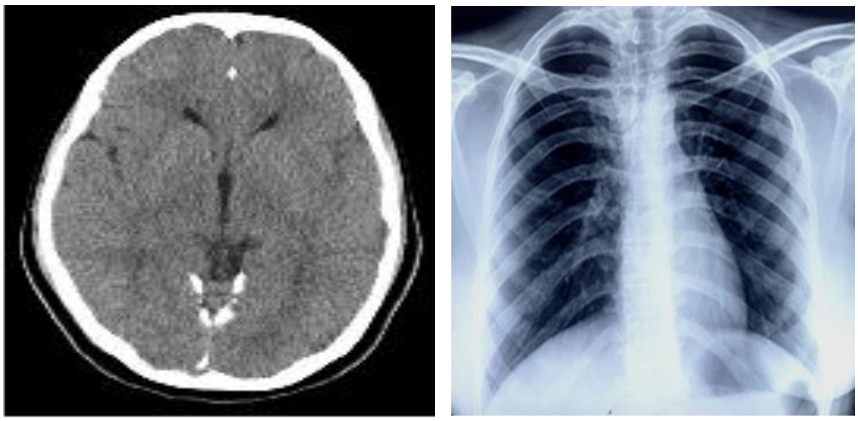


Fig 14- CT axial brain shows dural calcifications

Fig 15- chest x ray shows Anterior margin of right 3rd and left 5th,6th ribs are bifid

Complete cyst enucleation followed by histopathological examination was done .It was diagnosed as odontogenic keratocyst. Considering three major criteria- multiple odontogenic keratocyst, dural calcifications, bifid ribs this case was finally diagnosed as ***GORLIN-GOLTZ SYNDROME.***

3. DISCUSSION:

Gorlin-Goltz Syndrome (GGS) is an infrequent genetic autosomal disease with variable manifestations. Its also called nevoid basal cell carcinoma.The prevalence ranges from 1 in 57,000 to 1 in 2,56,000 in the general population. The GGS is manifested by multiple systemic diseases involving the skin, nervous system, eyes, endocrine system and bones.[2]

Clinical manifestations of the syndrome are

- Cutaneous manifestations: Dermal calcinosis, benign dermal cysts and tumors, palmar pitting, palmar and plantar keratosis and basal cell nevus
- Dental and osseous manifestations : mild mandibular prognathism, frontal and temporoparietal bossing, kyphoscoliosis or other vertebral defects, bifurcated ribs, spina bifida ,multiple okcs,cleft lip.

- Ophthalmic manifestations: Hypertelorism, wide nasal bridge, congenital blindness and internal strabismus.
- Neurological manifestations: Mental retardation, dural calcification, bridging of sella, agenesis of the corpus callosum, congenital hydrocephalus, occurrence of medulloblastoma.
- Sexual anomalies: Hypogonadism, ovarian tumor-like fibrosarcoma[3].

The most common skin sign of Gorlin-Goltz syndrome are basal cell carcinomas. The number of BCCs may vary in mumbers and is more common occurrence between puberty and 35 years of age. Sites mostly affected are thoracic and cervico-facial skin surfaces, periorbital areas, eyelids, nose, malar region, and upper lip[4]. Palmar and plantar pits are another major diagnostic clinical sign of GGS. They are the multiple punctiform brownish black depressions ranging from 2 to 3 mm in diameter and 1 to 3 mm in depth. They are caused by partial or complete absence of stratum corneum[5] . Odontogenic keratocysts are the main oral sign. Mandible have three times higher prediction than the maxilla.[6] The age predilection for this gorlin goltz syndrome is from first to third decade of life, with the onset of cardiac fibroma at 0–1 months, medulloblastoma at 2–3 years, BCC at 3–53 years, KOT at 6–12 years and ovarian fibroma at 16–45 years .[7] The diagnostic criteria was first given by Evans et al in 1993 and later modified by Kimonis et al in 1997 and Bree et al in 2011.[8,,9,10]

Diagnosis of Gorlin goltz syndrome based on- a) 2 major criteria b)1 major and 2 minor criteria c)1 major criteria and molecular confirmation- by bree et al
MAJOR CRETERIA
1.basal cell carcinomas out of proposition with the sun exposure and skin type or <20 yrs of age
2.odontogenic keratocysts of the jaws prior to the age of 20.
3.palmar or plantar pitting
4.lamellar calcifications of falx cerebri
5.medulloblastoma ,typically desmoplastic
MINOR CRETERIA
1.rib anamolies
2.cleft lip/cleft palate
3.other specific skeletal malformation and radiologic changes(vertebral anamolies,kyphoscoliosis,4 th short metacarpal,postaxial polydactyly)
4.macrocephaly
5.ovarian/cardiac fibroma
6.lymphomesentric cysts
7.ocular anamolies(hypertelorism,strabismus,glaucoma,congenital cataract,coloboma)

The treatment of this syndrome requires a multidisciplinary approach. The first-line treatment of basal cell carcinoma is usually surgical excision by standard or micro excisional/Mohs techniques, especially for nodular or aggressive BCCs[11].Low risk basal cell carcinomas are treated with minimally invasive techniques such as cryotheraphy,photodynamic therapy,corbon di oxide laser therapy. Systemic treatment includes oral retinoids like etretinate , isotretinoin, at doses of 0.5–1 mg/kg/day are given to inhibit the further new development of basal cell carcinoma.[12] Chemotherepeutic drugs like fluorouracil also given.
Odontogenic keratocyst is treated by surgical excision in the form of enucleation, curettage, or osteotomy along with usage of carnoys solution to prevent the recurrence,although the recurrence is commonly noted[13].

4. CONCLUSION:

Despite of being a rare disease - Gorlin-Goltz syndrome , is usually a fatal and destructive disease.It is a serious disease with multiple system involvement.As a dentist, knowledge about the orofacial manifestations of this disease helps in early diagnosis and rendering optimal treatment. From a prognostic point of view, early diagnosis with adequate therapy is critical.As early diagnosed as early treated will free the patient from sufferings.Interdisiplinary medical approaches are needed to treat this disease.

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