Gorlin-Goltz Syndrome – A Rare Case Entity in Young Child

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Abstract: Gorlin-Goltz syndrome (GGS) is an infrequent multisystemic disease with an autosomal dominant trait, which depicted presence of numerous basal cell carcinoma in conjunction with multiorgan abnormalities. This syndrome may be diagnosed early by a dentist by routine radiographic exams in the first decade of life, since the keratocystic odontogenic tumour are usually one of the first manifestations of the syndrome. This article includes a case report of the GGS with regard to its history, incidence, etiology, features, investigations, diagnostic criteria, keratocystic odontogenic tumour and treatment modalities.

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Introduction

Gorlin-Goltz syndrome (GGS) is a genetic disorder with autosomal dominant inheritance, high penetrance, and variable expression. The syndrome also termed as nevoid basal cell carcinoma or basal call nevus syndrome. In this syndrome numerous basal cell carcinomas (BCCs), in conjunction with skeletal, ophthalmic, and neurological abnormalities are depicted. In 1987 Gorlin reviewed the syndrome history, tabulated the disease findings and their frequency, and commented on the naming of the syndrome. Historically, the syndrome was documented in two ancient Egyptian skeletons where multiple cysts, bifid ribs, relative shortening of the fourth metacarpal, and other skeletal findings were present.

In 1960 Gorlin and Goltz established the relationship of multiple basal cell epitheliomas, multiple jaw cysts, and bifid ribs, that the term nevoid basal cell carcinoma syndrome was coined (Rafiq et al., 2021). The syndrome also is frequently referred to as Gorlin-Goltz syndrome, Gorlin syndrome, and nevoid basal cell carcinoma syndrome (NBCCS) or the syndrome; dermatologists prefer the term nevoid basal cell carcinoma syndrome. In light of the risk of malignancy it is important to be aware of this syndrome and recognise the need for early referral for multidisciplinary management (Hasan and Akintola, 2018).

Case report

A 13-year-old male patient reported to the Department of Oral and Maxillofacial Surgery with a chief complaint of swelling and pain on right side of the face since

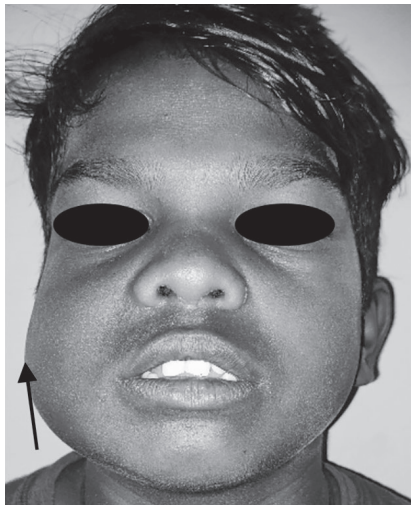

Figure 1 – Extra-oral clinical image shows swelling on right mid face region, hypertelorism.

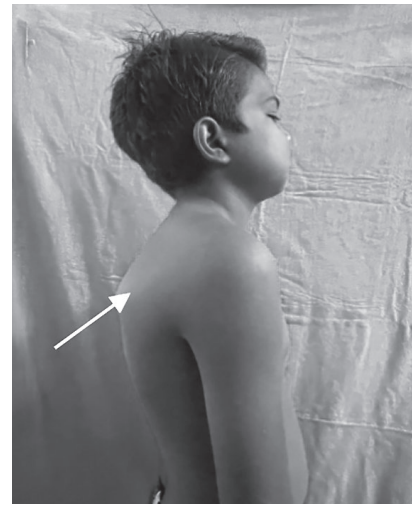

Figure 2 – Kyphosis.

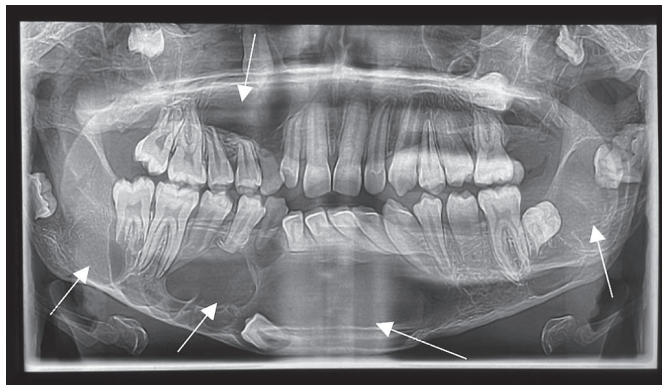

Figure 3 – Multiple radiolucent area.

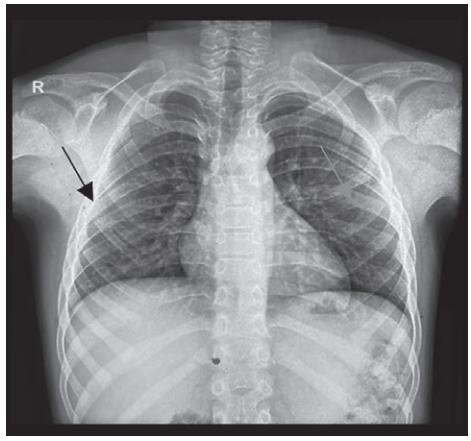

Figure 4 – Bifid rib.

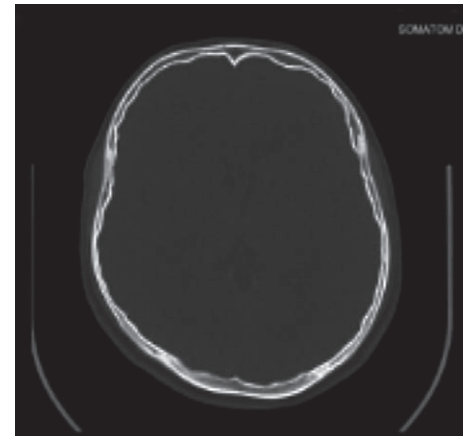

Figure 5 – Computed tomography scan of the skull.

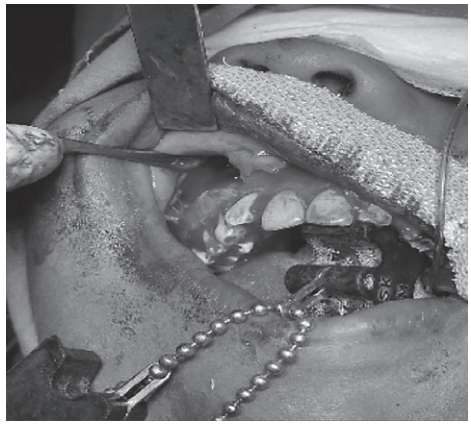

Figure 6 – Enucleated cavity on maxilla.

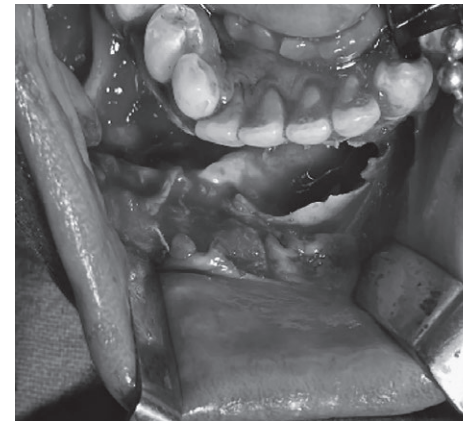

Figure 7 – Enucleated cavity on mandible.

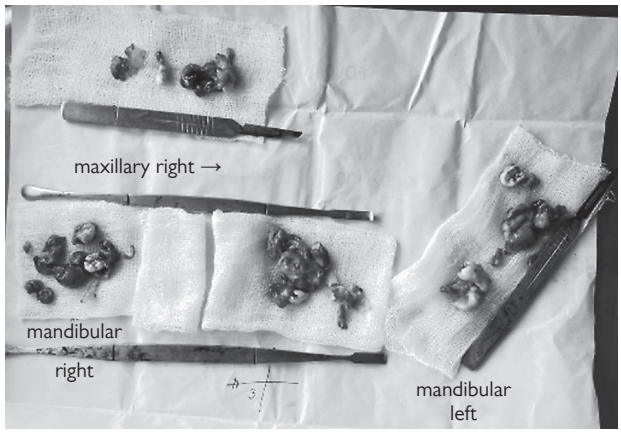

Figure 8 – Enucleated tissues.

last six months. Patient gave history of gradual increased in swelling with pain along with restricted mouth opening. Extraoral swellings were found to be firm and tender (Figure 1). On general physical examination he also had hypertelorism (Figure 1) and kyphosis (Figure 2).

Radiological investigations play a fundamental role in the diagnosis of GGS. An orthopantomograph (Figure 3) revealed multiple radiolucent lesions on both maxilla and mandible along with impacted teeth that are displaced by the cyst. Chest radiograph (Figure 4) showed the presence of a bifid rib on both sides raised suspicion of GGS. Computed tomography scan of the skull showing absence of calcification of the falx cerebri (Figure 5) raised suspicion of GGS.

Routine biochemical and haematological evaluations were carried out and the patient was hospitalized. Under all aseptic precautions, general anaesthesia was administered. Local anesthesia with adrenaline was injected and flap was raised intra orally in all quadrants one after another except maxillary left quadrant. No vital

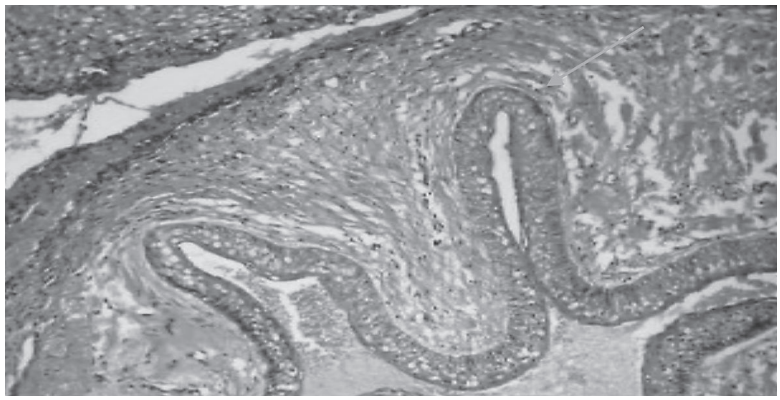

Figure 9 – Para-keratinized stratified squamous epithelium.

structures were seen near the lesions. A surgical curette was used for enucleating the cysts. Curettage was done using a curette and a round bur. The remnants of the cysts were removed using chemical cautery with Carnoy's solution (2.5%) for 3 min without chloroform followed by irrigation with saline (Figures 6 and 7).

The cysts were enucleated from all three quadrants followed by extraction of impacted teeth (Figure 8). The tissues removed were put in separate bottles containing formalin and enucleated tissues were sent for histopathological evaluation. As bone regeneration in children is faster, bone graft was not used.

The histopathology report showed a cystic lumen lined by corrugated, parakeratinized stratified squamous epithelium of 6–8 cell thickness. The epithelium is thrown into folds, with basal palisading nuclei and tomb-stone appearance (Figure 9) (hematoxylin and eosin stain 100×).

Discussion

The name Gorlin syndrome refers to the American oral pathologist and human geneticist Robert J. Gorlin (1923–2006). The American dermatologist Robert W. Goltz (1923–2014) was his co-author, which is the basis for the term "Gorlin-Gotz syndrome" (Al-Jarboua et al., 2019). The prevalence varies from 1/57,000 to 1/256,000 in general population along with regional variations and there is no gender predilection with a male:female ratio of 1:1 (Wadde et al., 2022). The syndrome occurs with equal frequency in both sexes. It has both a sporadic and familial incidence. Although detected in very young children they are commonly expressed between the ages 17 years and 35 years. The pathogenesis of Gorlin-Goltz syndrome is characterized by consequence of abnormalities in the PTCH1 gene. The deprivation of human patched gene, a tumour suppressor gene, forms the molecular basis of the syndrome (Acocella et al., 2009). This gene plays a most important role in embryonic structuring and cellular cycle result in mutation which accelerate further development of the disease including neoplasms.

Features of nevoid basal cell carcinoma syndrome

Clinical manifestations of the syndrome can be grouped into the following nine categories.

Cutaneous anomalies

Basal cell nevus/carcinoma (50–97%), other benign dermal cysts and tumours (21%), palmar/plantar pitting (90%), palmar and plantar keratosis and dermal calcinosis.

Dental anomalies

Multiple odontogenic keratocysts (75–100%), maxillary hypoplasia, mandibular prognathism, high arched palate or prominent palatine ridges (40%), cleft lip/palate (4%), impacted teeth and/or agenesis (3%), ectopic teeth and malocclusion.

Craniofacial anomalies
Calcification of falx (37–79%), tentorium cerebellum calcification (3%), bridged sella turcica (21%), macrocephaly (40%), brachycephaly, frontal bossing (25%), parietal and temporal bossing and coarse face (50%).

Skeletal anomalies
Polydactyly (3%), syndactyly, scoliosis (15%), hemivertebrae or other vertebral defects, flame-shaped lucencies of hand/feet, spina bifida (3%), osteoporosis (3%), cervical/bifurcated/fused/splayed/absent/rudimentary ribs (26%), brachymetacarpalism and shortened fourth metacarpal (12%).

Cardiac
Cardiac fibroma (3%).

Ophthalmic anomalies
Hypertelorism (40%), dystopia canthorum, congenital blindness (15%), internal strabismus (15%), congenital amaurosis, exotropia, glaucoma (3%), ptosis and coloboma (3%).

Neurological anomalies
Mental retardation (6%), dural calcification, bridging of sella, agenesis of corpus callosum, congenital hydrocephalus (3%), medulloblastoma (3–5%), agenesis/disgenesis of corpus callosum, meningioma (1% or less) and schizoid personality.

Table 1 – Diagnostic criteria

Major criteria	More than 2 BCCs, one BCC in patients younger than 30 years of age or more than 10 basal cell nevi
	Any odontogenic keratocyst (proven by histology) or polyostotic bone cyst
	Three or more palmar or plantar pits
	Ectopic calcification in patients younger than 20 years of age (lamellar or early falx cerebri calcification)
	A positive family history of NBCC
Minor criteria	Congenital skeletal anomaly (e.g., bifid, splayed, fused or missing rib, or bifid wedged or fused vertebra)
	Occipital-frontal circumference greater than the ninety-seventh percentile, with frontal bossing
	Cardiac or ovarian fibromas
	Medulloblastoma
	Lymphomesenteric cysts
	Congenital malformations such as cleft lip/palate, polydactylism or eye anomaly (e.g., cataract, coloboma or microphthalmos)

BCCs – basal cell carcinomas; NBCC – nevoid basal cell carcinoma

Table 2 – Modified diagnostic criteria by Kimonis et al. (1997)

Major criteria	More than 2 BCCs or one BCC in patients younger than 20 years of age Odontogenic keratocysts of the jaw (proven by histologic analysis) Three or more palmar or plantar pits Bilamellar calcification of the falx cerebri Bifid, fused or markedly splayed ribs A first degree relative with NBCCs
Minor criteria	Macrocephaly Congenital malformations (e.g., cleft lip or palate, frontal bossing, coarse faces and moderate or severe hypertelorism) Other skeletal abnormalities (e.g., sprengel deformity, marked pectus deformity and marked syndactyly of the digits) Radiological abnormalities (e.g., bridging of the sella turcica, vertebral anomalies, modelling defects of the hands and feet, or flame-shaped lucencies of the hands and the feet)

BCCs – basal cell carcinomas; NBCCs – nevoid basal cell carcinomas

Sexual anomalies

Hypogonadism (3%), uterine and ovarian fibromas (15%), calcified ovarian cysts (3%) and supernumerary nipple.

Laboratory findings

Increased serum uric acid level (3%), increased levels of alkaline phosphate and cyclic adenosine monophosphate.

The diagnostic criteria for nevoid BCC were established by Evans et al. (1993) and modified by Kimonis et al. (1997). According to them diagnosis of Gorlin-Goltz syndrome can be established when two major or one major and two minor are present (Tables 1 and 2).

Keratocystic odontogenic tumour (KCOT) have a greater predilection for the mandible 69% than the maxilla 31% (Maroto et al., 1999). In the mandible, 43% of KCOT occur in the molar-ramus region, followed by 18% in the incisor-canine region and 7% in the premolar region. In the maxilla, 14% occur in the incisor-canine region, followed by 12% in the molar tuberosity region and 3% in the premolar region.

In case of Gorlin-Goltz syndrome, parakeratotic KCOTs are seen. The major differences between OKCs associated with Gorlin-Goltz syndrome and solitary isolated OKCs are listed in Table 3. Our case showed a cystic lining that is thin and has stratified squamous cell lining with pinkish areas of keratinous material. Cystic wall has focal hyperplasia of lining cells and keratinous material with foci of chronic inflammatory cells mainly lymphocytes were seen.

Cone beam computed tomography (CBCT) provides a high-spatial resolution of all anatomic structures and accurate understanding of the relationship with the lesion. Three-dimensional representation of the scan images helps to assess the

Table 3 – Differences between syndromic KCOTs and solitary KCOTs

Feature	Syndromic KCOTs	Solitary KCOTs
Age	young individuals	middle or older aged
Cyst	multiple in layer	single
Site	maxillary posterior region commonly	mandibular posterior region
Recurrence rate	higher (82%)	lower (61%)
Epithelium	less thickness	more thickness
Odontogenic islands	most frequent	less

KCOTs – keratocystic odontogenic tumours

location, size, extent, and expansion of the lesion. CBCT enables us to remove OKC more precisely during surgery, reducing the rate of recurrence (Patel et al., 2022).

Patients should be given special attention and therefore should be monetarized and need multidisciplinary treatments continued in time, even a trivial change of signs and symptoms may be an important indicator of a precipitating event which puts the patient's life under threat. Various surgical procedures for odontogenic lesions that develop in the cortex of the jaw bones are simple enucleation, enucleation along with bone curettage and topical use of cytotoxic chemicals, "En bloc" resection, marsupialization, cryotherapy.

In this simple enucleation procedure, the cyst is completely removed in a single operating session. The bone cavity is spontaneously healed by bone regeneration. Enucleation with Carnoy's solution involves removal of the lesions followed by application Carnoy's solution within the surgical field (Abdoola et al., 2020).

Enucleating with peripheral osteotomy refers to enucleation of the lesion is followed by a peripheral ostectomy. The procedure includes of a rotary instruments for the removal of affected bone, ensuring the elimination of all the residual lining epithelium. Block resection of a jaw bone can be done either as marginal resection procedure or segmental resection procedure. In marginal resection procedure, the lesion is smaller, hence, it is possible to maintain the continuity of the jaw bone by preserving the portion of the uninvolved bone. When the lesion is aggressive it affects the complete or partial portion of the jaw (maxilla and mandible), in these cases the treatment is surgical resection of the affected portion followed by reconstruction of the jaw for rehabilitating the patient functionally and aesthetically. The main disadvantage of a conservative treatment is prolonged therapeutic time.

In marsupialization procedure the cystic sac is converted into pouch by deroofing. After locally anesthetizing the buccal/labial area, an oval/elliptical incision is taken to make a surgical window spanning 1 cm into a cyst; removal of cystic lining is done by creating a window which consist of oral mucosa and thinned out bony cortex and the boundaries of the cystic lining around the surgical opening are sutured to the surrounding oral mucosa.

Cryotherapy technique consist of use of a nitric oxide cryo-probe at a temperature of about –20 °C or lower on the bone walls after enucleation or on the soft tissues. The application is applied for 1 min and is repeated twice with an interval of 5 min. In addition, an increased risk of subsequent spontaneous fracture was also observed.

Hence, a surgeon has a pivot role in treating this type of syndromic cases as he will be the first person to detect such oral findings and predict occurrence of syndrome in future. Comprehensive treatment of this syndrome requires a teamwork with dental and medical opinion as well as genetic counselling.

Conclusion

Gorlin-Goltz syndrome is rare autosomal dominant genetic process. This case illustrates the need for awareness of the syndrome. Proper evaluation and characterization of clinical features are essential for diagnosis and management. In above case, two major criteria (OKC of the jaw and bifid rib) and 2 minor criteria (scoliosis and hypertelorism) were detected, suggesting that the patient had GGS. An appropriate long-term follow-up must be done after surgical treatment, follow-up should involve performing an orthopantomography every 6 months in young patients and a CBCT in case of doubt, or to evaluate contiguity with anatomical structures such as neurovascular bundles, teeth, and maxillary sinuses.

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