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CASE REPORT Open Access

A rare case report of Gorlin-Goltz's syndrome: a multisystemic disorder of otolaryngological domain

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Abstract

Background Gorlin-Goltz's syndrome (GGS) is an extremely rare autosomal dominant disorder showing a high penetrance and variable expressivity. Gorlin-Goltz's syndrome is an infrequent multisystemic disease, which is usually characterized by numerous basal cell carcinomas, odontogenic keratocysts (OKCs), and musculoskeletal malformations along with neurological, ophthalmic, endocrine, and genital manifestations. There are also multiple manifestations in the domain of ENT and patient may primarily present to an ENT clinician with one of the diverse clinical involvements.

Case presentation We report one such infrequent case of a 24-year-old male patient who presented with an oro-antral fistula at our tertiary health care center and was diagnosed to have Gorlin-Goltz's syndrome. The diagnosis was made in our patient by the presence of 4 major and 2 minor criteria.

Conclusion Early diagnosis and management of GGS helps to prevent long-term sequelae including malignancy and oro-maxillofacial deformation. The constellation of symptoms of such rare disorders should be promptly recognized and a high index of suspicion should be maintained. This case report is an appraisal of the diagnosis and management of GGS from an otolaryngological perspective and is being reported here for extreme rarity and clinical interest.

Keywords Gorlin-Goltz's syndrome, Odontogenic keratocysts

Background

Gorlin-Goltz's syndrome (GGS), also known as nevoid basal cell carcinoma syndrome (NBCCS), is a rare chromosomal disorder showing an autosomal dominant pattern. It is characterized by multisystemic developmental abnormalities secondary to mutations in the patched-1 (*PTCH-1*) gene, a tumor suppressor gene found on the long arm of the 9th chromosome. GGS was first reported by Jarisch and White in 1894. It was the detailed work of Robert W. Goltz and Robert J. Gorlin in 1960 who described the distinct syndrome which consists of multiple nevoid basal cell epitheliomas, jaw cysts, and bifid ribs [1]. This syndrome shows a high penetrance and variable expressiveness with an incidence of 1 in 50,000 to 150,000 in the general population, varying by region. It has been reported in all ethnic groups, but most often in whites, males and females being equally affected [2]. It is characterized by numerous basal cell carcinomas (BCCs) (seen in 50–97% of people with the syndrome), maxillary keratocysts (present in about 75% of patients), and musculoskeletal malformations [3]. A spectrum of other neurological, ophthalmic, endocrine, and genital manifestations is also known to be variably associated with this syndrome [4]. The manifestations in the domain of otolaryngology include facial dysmorphism

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and musculoskeletal and oropharyngeal anomalies. Diagnosis is based upon established major and minor clinical and radiological criteria. For this syndrome, an early diagnosis and treatment, as well as genetic counseling, are of utmost importance. We encountered one such case at our tertiary health care center with manifestations in the ENT domain which after detailed investigations was diagnosed as Gorlin-Goltz's syndrome. We report this case for its academic interest as it illustrates a rare addition to our differentials of ENT manifestations.

Case presentation

A 24-year-old male patient reported to the outpatient wing of the Department of ENT with the chief complaint of gradually progressive painless right cheek swelling over a period of 5 months. Examination revealed a large swelling of 4 cm × 3 cm dimension present over the right cheek which was soft, non-tender, fluctuant, and free from the overlying skin. Intraoral examination revealed an oroantral fistula opening above the right first premolar with discharging pus. Incidentally, multiple teeth were found missing. Facial asymmetry was noticed during the clinical examination. Prognathic mandible, flattened nasal bridge, and milia (white spots) over cheek and nose were evident (Fig. 1). Based on suspicion, a detailed set of investigations was carried out. Routine blood investigations were normal. An orthopantomogram was done, which revealed multiple radiolucencies in the mandible and maxilla with impacted third molar and canine on the right side. All radiolucent lesions were multilocular with a well-defined sclerotic border (Fig. 2).

A high index of suspicion was raised regarding Gorlin-Gortz's syndrome and further evaluation was carried out.

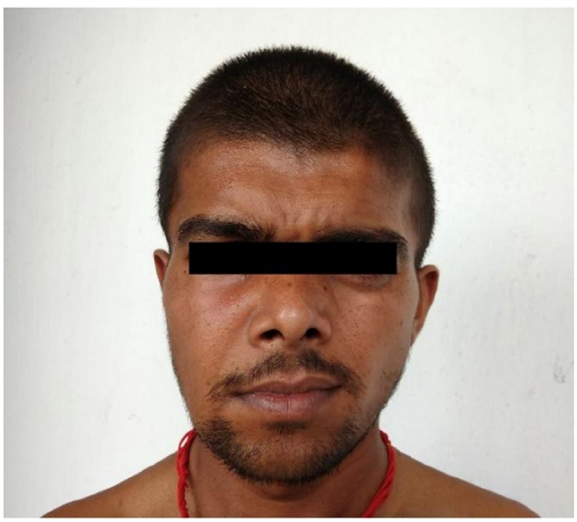

Fig. 1 Facial asymmetry

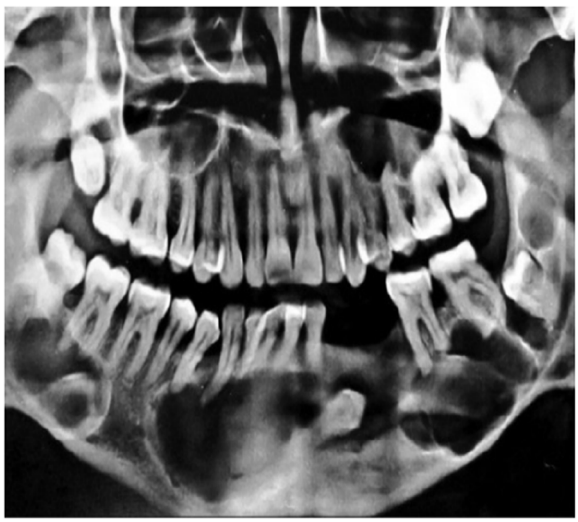

Fig. 2 Orthopantomogram with multiple lesions in the maxilla and mandible

The ophthalmic evaluation showed hypertelorism with ptosis in the right eye and exotropia in the left eye. Milia was present below the right eye. Pectus excavatum was noted on chest examination (Fig. 3). There were multiple palmar pits along with a 1.5 cm by 1.5 cm soft, fluctuant, non-tender cystic swelling over the palm (Fig. 4).

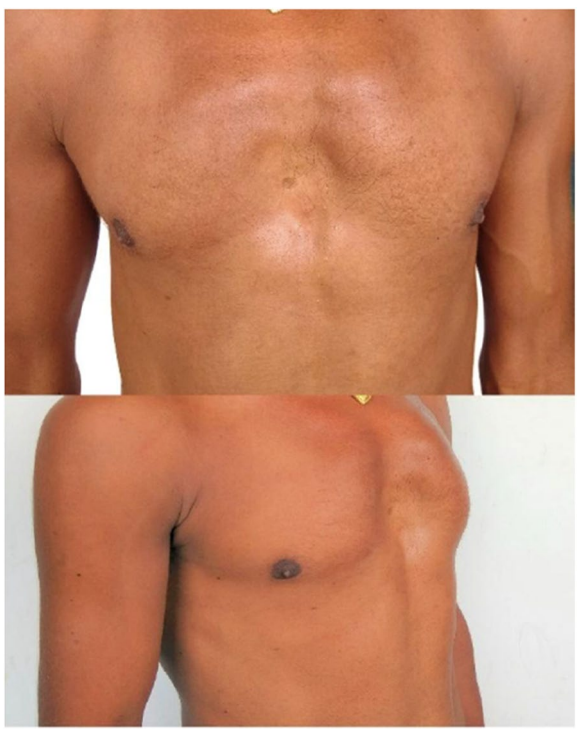

Fig. 3 Pectus excavatum

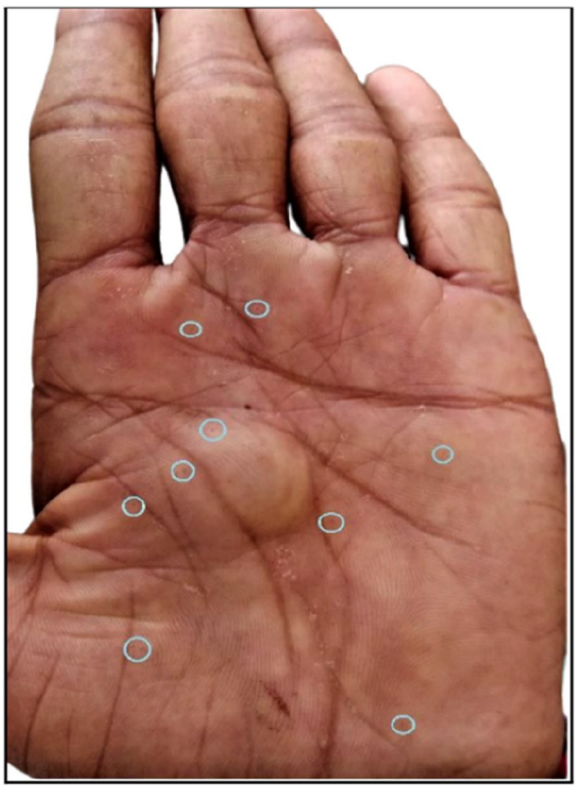

Fig. 4 Palmar pits

Chest X-ray showed bilateral 5th rib splaying (Fig. 5). A computed tomography scan of the face and paranasal sinuses was done for the swelling which showed evidence of ectopic calcification in falx cerebri (Fig. 6). Excisional biopsy was performed for one of the cysts, which on

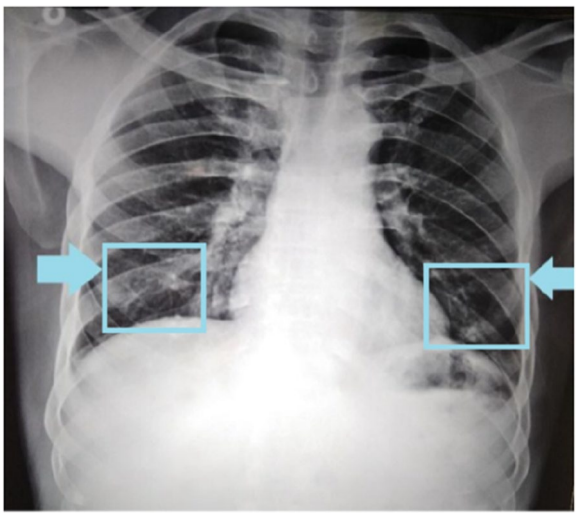

Fig. 5 Bilateral 5th rib splaying

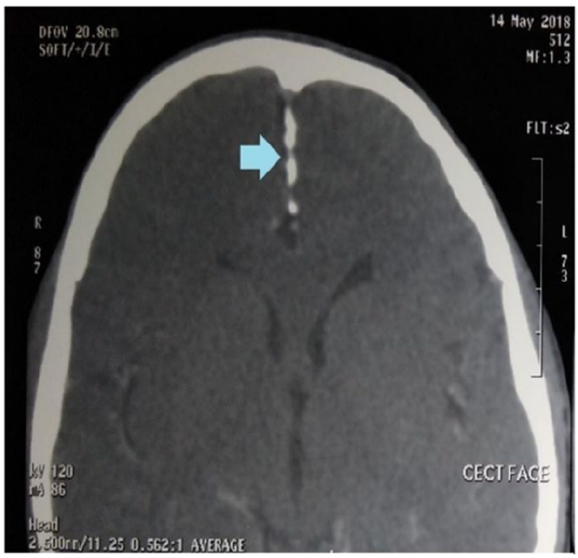

Fig. 6 CT scan showing calcification in flax cerebri

microscopic examination showed a stratified squamous epithelium with basal cells demonstrating a palisading pattern.

Thus, the diagnosis of GGS was established in our patient by the presence of multiple major (odontogenic keratocytes, palmar pits, bifid ribs, and calcifications of falx cerebri) and minor (pectus excavatum and hypertelorism) criteria. A comprehensive and meticulous search for suspected malignant skin lesions was carried out which were conspicuous by their absence. Once the infection was controlled with antibiotics, the fistulous tract was excised and the defect was closed with a buccal advancement flap. The patient is being followed up every 6 months to look for development of new symptoms.

Discussion

Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma syndrome (NBCCS), is an infrequent multisystemic disease. It has had a few different names over time. It was first described by Robert J. Gorlin and Robert W. Goltz in 1960, which led to it being named after them. However, as more research was conducted, other names emerged. Due to the presence of multiple basal cell carcinomas and other skin abnormalities, it was also called "basal cell nevus syndrome." With time, the name "nevoid basal cell carcinoma syndrome" (NBCCS) became more commonly used, as it accurately reflects the characteristic features of the syndrome, such as the development of multiple basal cell carcinomas and the presence of other skin, skeletal, and neurological abnormalities. "Multiple basal epithelioma, jaw cysts and bifid rib syndrome" has also been coined for it, which is the most complex of all

the names given for the syndrome [5]. But it is important to note that while the names for Gorlin-Goltz syndrome have evolved over time, the condition itself and its underlying genetic cause have remained consistent. It is caused by mutations in the patched tumor suppressor gene (PTCH-1), a human homolog of the *Drosophila* gene mapped to chromosome 9q21–23. Genetic studies show that the underlying defect is an abnormality in the signaling pathway mediated by Hedgehog (Hh) gene [1].

Evans et al. [6] first established major and minor criteria for the diagnosis of the syndrome which were later modified by Kimonis et al. [7] in 2004 (Table 1).

The presence of two major and one minor or one major and three minor criteria is necessary to establish the diagnosis [6, 7].

Other diagnostic findings in adults with nevoid basal cell carcinoma reported by Gorlin and his colleagues [8] and their incidence of occurrences are given in Table 2.

Otolaryngological manifestations of GGS include odontogenic keratocysts leading to various oral-maxillofacial deformities and malocclusions, high arched palate, cleft lip and/or palate, and broadened nasal root [4, 8].

The odontogenic keratocysts associated with GGS are known as "keratocystic odontogenic tumor" (KCOT).

Table 1 Major and minor criteria for diagnosis of GGS [6, 7]

Major criteria	Minor criteria
• Multiple basal cell carcinomas or one occurring under the age of 20 years • Multiple OKCs of the jaws • Palmar pits or plantar pits (three or more) • Calcifications in the falx cerebri • Bifid, fuséd, or markedly splayed ribs • First-degree relative with nevoid basal cell carcinoma syndrome	• Macrocéphaly (adjusted for height) • Congenital malformation: cléft lip or cleft palate, frontal bossing, coarse face, moderate or severe hypertelorism • Other skeletal abnormalities: Spréngel deformity, marked pectus deformity, marked syndáctyly of the digits • Radiological abnormalities: bulging of sélla turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of vertebral bodies, modeling defects of the hands and feet, or flame-shaped hands or feet • Ovarian fibroma • Medulloblastoma

Table 2 Other diagnostic findings of GGS reported by Gorlin et al. [8]

A. **Skeletal anomalies** [4, 8]
1. Bifid ribs, splayed/fused ribs, absent/rudimentary ribs (60–75%)
2. Scoliosis — seen in 30–40% of the patients
3. Hemivertebrae
4. Flame-shaped lucencies of hand/feet
5. Polydactyly
6. Syndactyly
7. Shortened 4th metacarpal

B. Craniofacial anomalies [4, 8]
1. Frontal bossing (25%)
2. Brachycephaly
3. Macrocephaly (40%)
4. Coarse face (50%)
5. Calcification of the falxes (37–79%)
6. *Tentorium cerebellum* calcification
7. Bridged sella tursica
8. Heavy fused eyebrows
9. Broadened nasal root

C. Neurological anomalies [4, 8]
1. Agenesis/dysgenesis of corpus callosum
2. Congenital hydrocephalus
3. Mental retardation
4. Medulloblastoma (3–5%) — developing in the first 2 years of life
5. Meningioma
6. Schizoid personality

D. Oropharyngeal anomalies [4, 8]
1. Cleft lip/palate (4%)
2. High arched palate or prominent ridges (40%)
3. Odontogenic keratocysts
4. Malocclusions
5. Dental ectopic position
6. Impacted teeth and/or agenesis

E. Anomalies of the reproductive system [4, 8]
1. Uterine and ovarian fibromas (15%)
2. Calcified ovarian cysts
3. Supernumerary nipple
4. Hypogonadism and cryptorchidism
5. Female distribution of the pubis hair, scarce beard in men, and gynecomastia

F. Ophthalmic anomalies [4, 8]
1. Hypertelorism (40%)
2. Glaucoma
3. Exotropia choroidal and/or optic nerve coloboma
4. Congenital amaurosis, congenital blindness and opaque cornea
5. Cataracts
6. Internal strabismus

G. Skin anomalies [4, 8]
1. Basal cell carcinoma
2. Palmar and/or plantar pits

H. Cardiac anomalies [4, 8]
1. Cardiac fibromas (3%)

These cysts have high mitotic index leading to a higher potential of epithelial lining proliferation which in turn causes cyst expansion. They also show high rate of recurrence and can give rise to ameloblastoma and squamous cell carcinoma [8].

The findings associated with the syndrome vary from person to person and need to be identified with a high index of suspicion in order to draft a treatment plan that addresses multisystem involvement.

In GGS, an early diagnosis is of prime importance in order for prompt detection and management of long-term and potentially fatal complications such as skin and brain malignancies. Early diagnosis also facilitates avoidance of oral-maxillofacial deformities due to the jaw cysts. A meticulous examination of the oral cavity, skin, thorax, cranium, and all potential systems of involvement is called for early detection of this syndrome. Orthopantomography, chest radiograph, and face and head CT scans are routine radiological investigations necessary to detect any osseous defect.

Once the diagnosis has been arrived upon, a multidisciplinary approach is required for apt treatment practice. The management revolves around the removal of cysts and adequate treatment of tumors. Various techniques are available to remove odontogenic keratocysts which range from simple enucleation with curettage to meticulous enucleation with peripheral osteotomy or to osseous resection in block [9], the last being most aggressive with the least chances of recurrence. It is crucial to differentiate a sporadic cyst from a syndromic cyst as the recurrence rate differs significantly; 63% in keratocysts associated with the syndrome, and 37% in the isolated ones [10]. The treatment of skin basal cell carcinoma should follow standard dermatological management protocols. Surgery is indicated when the number of lesions is limited whereas other treatments include laser ablation, photodynamic therapy, and topical chemotherapy [4]. Radiotherapy is not implemented as a treatment modality due to associated high chances of recurrence [4]. Vitamin A analogs may play a preventive role against the development of new BCCs. Exposure to UV light in these patients should be minimized.

Patients identified with GGS should undergo dermatological examination every 3–6 months and a yearly OPG should be advocated to look for new OKCs or recurrence. As children with GGS are more susceptible to developing medulloblastoma, a neurological examination every 6 months is a must for them. Antenatal diagnosis is possible by means of serial ultrasound scans and analysis of DNA extracted from fetal cells (obtained either by amniocentesis or chorionic villus sampling). The patient has up to a 50% chance of transferring the condition to the offspring. So, genetic counseling is of utmost importance.

Conclusion

The importance of recognition of GGS is because of its malignant potential. For early recognition of the disease, a detailed family history and a thorough evaluation of signs and symptoms are the cornerstones for apt management of the syndrome. Owing to the multisystemic involvement and diversity in the clinical picture, a multidisciplinary approach is required once the diagnosis is established for a successful management. Autosomal dominant transmission with good penetrance implies the need for genetic counseling. Regular follow-up is a must due to the high recurrences rates.

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Authors' contributions
RR created the study's manuscript. AA reviewed the earlier research. VK read and approved the final manuscript.

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Availability of data and materials
The data used in the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent for publication of the case report was obtained from the patient.

Competing interests
The authors declare that they have no competing interests.

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