Oral and Maxillofacial Surgeon's Perspective on Gorlin–Goltz Syndrome - A Report of Two Cases

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Abstract

Rationale: Gorlin–Goltz syndrome (GGS) is an autosomal dominant disorder and is associated with multisystem involvement, multiple cysts, neoplasms and other developmental anomalies. The purpose of the study was to highlight the incidental findings of GGS and to lay emphasis on its early diagnosis. **Patient Concerns:** Two patients complaining of pain, swelling and at times pus discharge from the oral cavity were reported with a coincidental finding of odontogenic keratocysts and positive family history. **Diagnosis:** Upon thorough examination, a diagnosis of GGS was made. **Treatment:** The patients were managed by enucleation and chemical cauterisation using Carnoy's solution and were maintained on follow-up semi-annually. **Outcomes:** Both patients showed no signs of recurrence post six months follow-up. **Lessons:** The role of an oral and maxillofacial surgeon is of utmost importance in the early diagnosis of this syndrome to render good quality of life to these patients.

Keywords: Basal cell nevus syndrome, jaw cysts, odontogenic cysts, patched-1 receptor

Introduction

Gorlin–Goltz syndrome (GGS) or nevoid basal cell carcinoma syndrome (NBCCS) or basal cell nevus syndrome is a rare autosomal dominant disorder.[1] It is characterised by multisystem abnormalities, among which odontogenic keratocysts (OKCs) are the most commonly observed and also the first to be noticed in a dental setup.[2]

The prevalence varies from 1/57000 to 1/256000 in general population along with regional variations and there is no gender predilection with a male:female ratio of 1:1.[2,3]

The present case series represents typical features of GGS and its diagnosis based on clinical, radiological and histopathological findings. Furthermore, it emphasises the role of an oral and maxillofacial surgeon in its early detection and treatment.

Case Reports

Case 1

A 26-year-old male patient reported with a chief complaint of pain and pus discharge in the lower front teeth region for the past five days. Medical and family history were non-contributory.

On examination, frontal bossing, confluent eyebrows and palmar and plantar pits were observed [Figure 1], and intraorally, there were two diffuse swellings seen. One of the swellings extended from 32 to 42 region with active pus discharge and laterally displaced mandibular incisors while the other extended from 47 to the retromolar region.

Orthopantomogram revealed a well-defined unilocular radiolucent lesion in the mandibular anterior region with impacted 43 and displacement of mandibular anterior teeth. Another multilocular radiolucent lesion was seen in the right angle and ramus region with an impacted 48. Radiolucent

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lesions were evident bilaterally in the posterior maxilla, involving maxillary sinus [Figure 2a].

CT examination confirmed the findings. Posteroanterior skull view showed calcification of the falx cerebri [Figure 2b]. White cheesy aspirate was seen and OKC was suspected. The patient was planned for enucleation of cysts with peripheral osteotomy and chemical cauterisation with single application of Carnoy's solution under general anaesthesia [Figure 3a]. Histopathological examination revealed a cystic lining of 5–6 layers thick stratified squamous epithelium with corrugated parakeratin surface. The basal cell layer was cuboidal to columnar with well-polarised nuclei. Underlying connective tissue capsule was loose fibrocellular, with supporting vasculature, extravasated blood elements, strands and nests of odontogenic epithelium [Figure 3b]. The patient was given post-operative antibiotics and Ryles tube feeding was given for a week followed by soft diet.

No complications were seen intraoperatively and the patient had an uneventful recovery. OPG was taken post-operatively and no recurrence was seen at six months follow-up [Figure 4].

Case 2

A 19-year-old male patient reported with a chief complaint of swelling and pain in the upper left posterior region of the jaw for seven months.

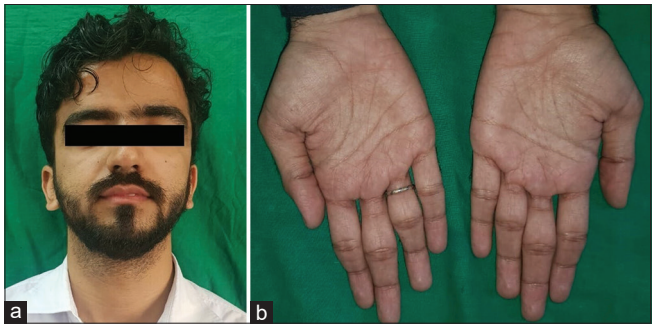

Figure 1: (a) Extraoral photograph of Case 1 exhibiting frontal bossing and confluent eyebrows. (b) Hands showing palmar and plantar pits

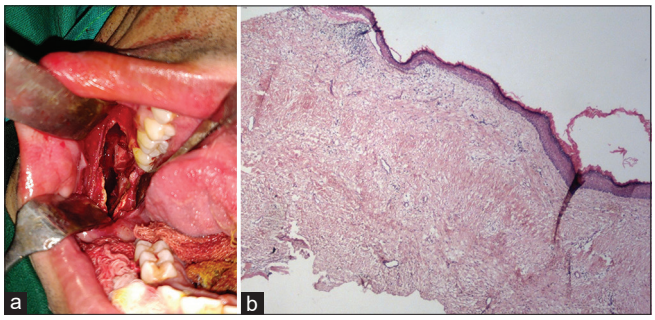

Figure 3: (a) Enucleation followed by peripheral osteotomy and chemical cauterisation with application of Carnoy's solution in right mandibular angle and ramus region of Case 1. (b) Histopathological picture of the excised tissue of Case 1 revealing 5–6 layers thick stratified squamous epithelium with corrugated parakeratin surface and underlying loose fibrocellular connective tissue capsule with nests of odontogenic epithelium

He gave a history of previous surgery in the posterior right mandibular region a few years back and also a positive family history of his parents who had a consanguineous marriage.

General examination of the patient revealed frontal bossing, hypertelorism, confluent eyebrows, palmar-plantar pits, pectus excavatum and polydactyly in the foot [Figure 5].

Radiographically, multiple radiolucencies involving mandibular anterior and maxillary posterior region involving maxillary sinus were seen. An oval well-defined radiolucent lesion was present extending from 34 to 44. Another one was present involving the left maxillary sinus above the apices of 25, 26. Calcification of falx cerebri was noted [Figure 6].

Aspiration of lesion in the mandibular anterior region revealed whitish greasy fluid, while incisional biopsy confirmed the diagnosis of OKC, where the cystic lining showed parakeratinised stratified squamous epithelium [Figure 7b].

Based on these findings, a provisional diagnosis of GGS was considered. The patient was treated in a similar manner as the aforementioned case [Figure 7a] and was kept under six months follow-up where he showed no signs of recurrence [Figure 8].

Discussion

The first case of this syndrome was reported in 1894 by Jarisch and White. In 1960, Gorlin–Goltz established this disorder as

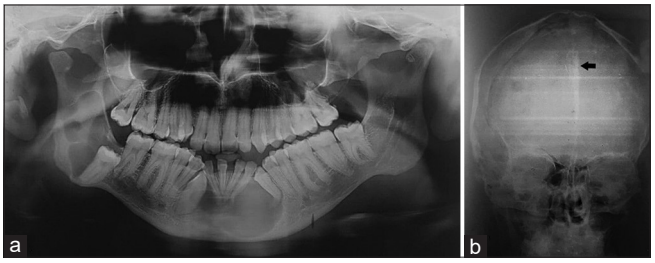

Figure 2: (a) Pre-operative orthopantomogram of Case 1 revealing well-defined radiolucent lesions in mandibular anterior region, right angle and ramus region and in the posterior maxilla involving maxillary sinus. (b) PA skull view of Case 1 showing calcification of falx cerebri. (PA: Posteroanterior)

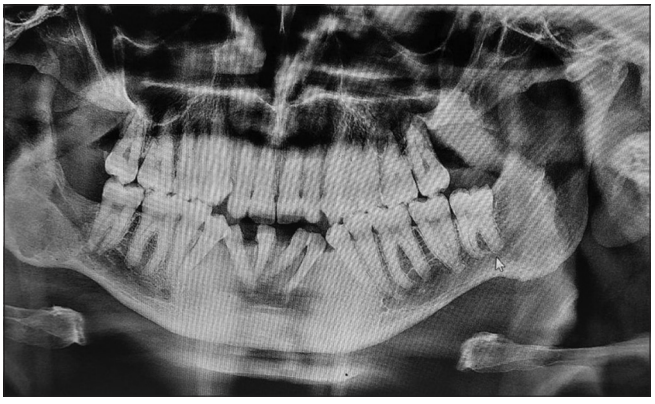

Figure 4: Post-operative radiograph of Case 1 post six months follow up

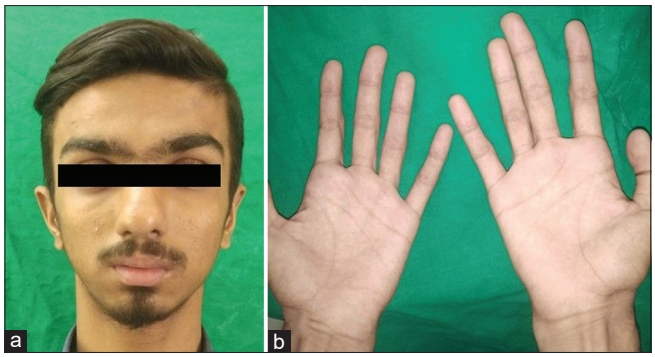

Figure 5: (a) Extraoral photograph of Case 2 showing frontal bossing, hypertelorism and confluent eyebrows. (b) Hands showing palmar and plantar pits

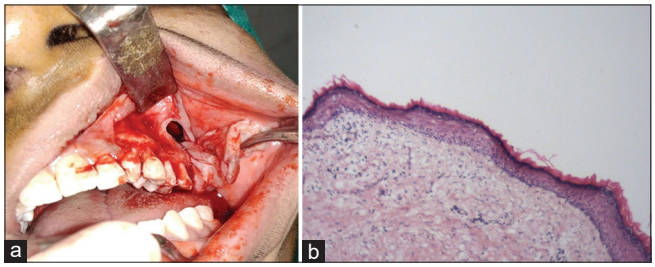

Figure 7: (a) Enucleation followed by peripheral osteotomy and chemical cauterisation with application of Carnoy's solution in left maxillary posterior region of Case 2. (b) Histopathological picture of the excised tissue of Case 2 revealing OKC where the cystic lining showed para keratinised stratified squamous epithelium of 5–6 layers thick. (OKC: Odontogenic keratocyst)

a separate entity thus giving its name, GGS. They discovered that patients suffering from this syndrome had a classical triad of basal cell carcinoma (BCC) (50%–97%), OKCs (75%) and bifid ribs (40%).[4]

The diagnosis of the syndrome is based on presence of few features classified as major and minor criteria. The original triad of features were modified by Rayner *et al* by including calcification of falx cerebri (37%–79%) and/or palmar and plantar pits (60%–90%) as additional features.[2]

Recently, an international colloquium was organised to define the physical findings associated with this syndrome and diagnose it based on the findings of less stringent criteria of (1) one major criterion and molecular confirmation, (2) two major criteria or (3) one major and two minor criteria [Table 1]. After evaluation of both cases, we found three major and two minor criteria based on clinical, radiographic and histopathological findings.[5]

OKC is the most common, hallmark finding and usually the first manifesting sign of this syndrome.[6] A high recurrence rate of up to 60% is attributed to the thin and friable lining, presence of high mitotic activity in basal epithelium, daughter cysts, microcysts and satellite cysts. Thus, it is important to do serial sectioning of histopathological tissue to arrive at correct diagnosis. Serial sectioning is defined as obtaining a

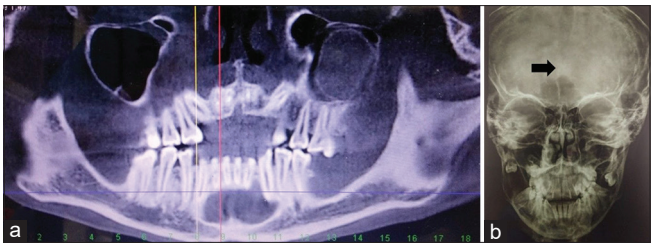

Figure 6: (a) Pre-operative Orthopantomogram of Case 2 revealing multiple radiolucencies involving mandibular anterior, and maxillary posterior region. (b) PA skull view of Case 2 showing calcification of falx cerebri. (PA: Posteroanterior)

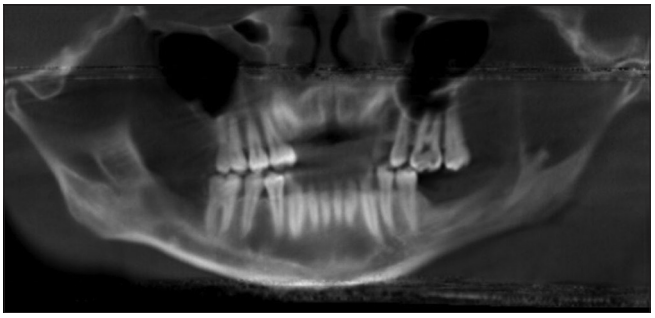

Figure 8: Post-operative radiograph of Case 2 post six months follow up

Table 1: Diagnostic criteria for Basal Cell Nevus Syndrome

Criteria	Associated features
Major criteria	BCC prior to 20 years old
	OKC of the jaw prior to 20 years old
	Palmar and plantar pitting
	Lamellar calcification of the falx cerebri
	Medulloblastoma, typically desmoplastic
	First degree relative with basal cell nevus syndrome
Minor criteria	Rib anomalies
	Other specific skeletal malformations and radiologic changes (i.e., vertebral anomalies, kyphoscoliosis, short fourth metacarpals, postaxial polydactyly)
	Macrocephaly
	Cleft lip/palate
	Ovarian/cardiac fibroma
	Lymphomesenteric cysts
	Ocular abnormalities (i.e., strabismus, hypertelorism, congenital cataracts, glaucoma, coloboma)

BCC=Basal cell carcinoma; OKC=Odontogenic keratocyst

continuous ribbon of sections from a paraffin block and placing all the sections on multiple slides. Cystic lesions like OKC will have thin tissue that will be curled during the processing and the sections may not show the complete epithelial lining, and therefore, deeper sections are mandatory.[7]

It has been reported that along with cyst enucleation, adjunctive modalities like Carnoy's solution (3 ml of chloroform, 6 ml of absolute ethanol, 1 ml of glacial acetic acid and 1 g of ferric chloride) application for three min after enucleation results in the recurrence rate of 9% to 17.4% in OKCs not associated to

NBCCS. Hence, we treated the cases with cyst enucleation, peripheral osteotomy followed by chemical cauterisation with Carnoy's solution.[8]

None of our patients had BCCS which was in concordance with Ahn *et al*., suggesting the incidence of BCC low in Asia.[9]

Our patients showed dyskeratotic palmar-plantar pitting, early calcification of the falx cerebri, frontal bossing, hypertelorism and unibrow, which fulfilled the major and minor criteria important for diagnosis of the syndrome.

GGS is caused by genetic mutation of the patched homolog 1 (PTCH1) gene present on the long arm of chromosome 9. Further research will help provide new treatment strategy for specific drug treatment of disease in future to suppress tumour growth.[10] There are a few limitations in this case series, the first one being limited follow-up and the other is that the patients involved were not checked for any PTCH1 gene mutation. In the present series, out of two patients, only one had family history.

This case series emphasises the importance of prompt diagnosis in young patients with GGS who do not exhibit skin lesions, which were successfully managed conservatively without recurrence post three years follow-up**.**

Conclusion

The role of the oral and maxillofacial surgeon in the management of GGS starts from the time the patient enters the outpatient department. As most cases are detected due to incidental findings of multiple jaw cysts, a surgeon should always be vigilant. Owing to its cancerous predisposition, conservative management of such disorders is as important as their early diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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