

# Gorlin syndrome: A rare case report

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## Abstract

Gorlin syndrome is an autosomal dominant inherited condition that exhibits high penetrance and variable expressivity. The syndrome is caused by mutations in PTCH, a tumor suppressor gene that has been mapped to chromosome 9q22.3-q31. It is observed that most aggressive forms of keratocystic odontogenic tumor are the first signs of this syndrome which show a high recurrence rate due to its varied histopathological features. The other components are multiple basal cell carcinomas of the skin, intracranial calcifications and rib and vertebral anomalies. In addition, >100 minor criteria have been described with two major and one minor criteria or one major and three minor criteria necessary for confirmatory diagnosis. It is a rare syndrome having an estimated incidence of 1 in 50,000–150,000 in the general population with a 3:1 male/female gender predilection. Here, we report the case of a 14-year-old female patient diagnosed with Gorlin syndrome.

**Keywords:** Gorlin syndrome, keratocystic odontogenic tumor, nevoid basal cell carcinoma

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## INTRODUCTION

Gorlin syndrome was first described by Binkley and Johnson in 1951 and has been thoroughly reviewed by Gorlin *et al.*<sup>[1]</sup> Gorlin syndrome is an autosomal dominant inherited condition that exhibits high penetrance and variable expressivity. The syndrome is caused by mutations in patched Drosophila segment polarity gene Patched (PTCH), a tumor suppressor gene that has been mapped to chromosome 9q22.3-q31.<sup>[2]</sup> It is characterized by basal cell carcinomas, keratocystic odontogenic tumor (KCOI), palmar and/or plantar pits and ectopic calcifications of the falx cerebri. More than 100 minor criteria have been described. The presence of two major and one minor criteria or one major and three minor criteria is necessary

to establish a diagnosis. Early diagnosis and treatment of Gorlin–Goltz syndrome, as well as family screening and genetic counseling, are essential as it may be associated in 10% of the patients with aggressive basal cell carcinomas and malignant neoplasia.<sup>[3]</sup>

## CASE REPORT

A 14-year-old female patient reported to the outpatient department with the chief complaint of pain and swelling in the lower left anterior region of the jaw for 2 months. There was no significant contributing family history. The patient gave a history of surgery in the same region 4 years back. The patient gave a history of slowly enlarging swelling which gradually increased to the present size of 2

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cm × 3 cm and was associated with mild pain for the past 10 days. Extraorally, the swelling extended superoinferiorly from the corner of the mouth to the lower border of the mandible and anterioposteriorly from the parasymphseal region to the lower border of the mandible. Other extraoral findings included mild ocular hypertelorism, flattened nasal bridge, frontal bossing and mandibular prognathism [Figure 1]. Intraorally, the swelling extended from 36 to 41 with Grade II mobility of 31, 32 and 34. On palpation, the swelling was tender and soft in consistency with areas of decortication [Figure 2].

Diagnostic orthopantomograph showed well-defined radiolucency with scalloped margin extending from distal root of 36 to the root of 43 with missing 33 and resorption of root with 31, 32 and 41 [Figure 3]. Chest X-ray posteroanterior view showed crowding of the upper ribs, spina bifida involving the lower cervical and upper dorsal vertebrae, kyphoscoliosis and bifid fifth rib [Figure 4].

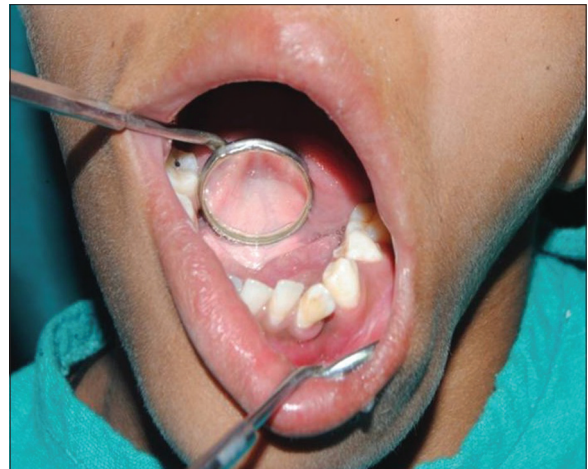
Informed written consent was obtained from the patient, and surgical enucleation was done under sedation. The specimen was sent for the histopathological examination. After processing and staining, the H and E section revealed the presence of parakeratinized stratified squamous epithelium of 6–8 layer thickness with surface corrugation and basal palisaded hyperchromatic cells [Figure 5]. Few foci showed the dense inflammatory cell infiltrate with loss of epithelium. Based on histological findings, the diagnosis of odontogenic keratocyst with secondary infection was made and the final diagnosis based on the clinicopathological correlation was given as Gorlin syndrome. The patient was kept under follow 1½ years without any recurrence.

## DISCUSSION

The nevoid basal cell carcinoma syndrome (NBCCS) is an autosomal dominant inheritable condition due to mutations in the patched (PTCH) gene found on chromosome 9q22.3-q31, which affects the skin, jaws and other bones,



**Figure 1:** Picture showing hypertelorism, flattened nasal bridge and extraoral swelling



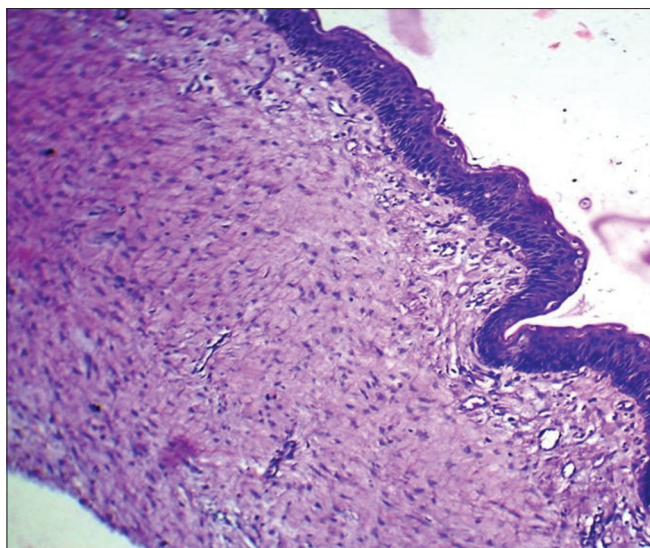
**Figure 2:** Intraoral swelling extending from 36 regions to 41



**Figure 3:** Orthopantomograph showing radiolucency with scalloped margins



**Figure 4:** Chest radiograph showing rib and vertebral anomalies



**Figure 5:** Parakeratinized stratified squamous epithelium with surface corrugation and palisaded basal hyperchromatic cells (under  $\times 20$  magnification)

nervous system, eyes and endocrine system, with high penetrance and variable expressivity. Skin lesions appear in childhood or adolescence. Multiple nevoid basal cell carcinomas over the nose, eyelids, cheeks and elsewhere are often an early sign. There may also be pitting of the palms or soles, and basal cell carcinomas can originate in these areas. Multiple jaw odontogenic keratocysts (OKCs) are seen in 75%–90% of the patients with NBCCS (these are the most prevalent abnormality), and anomalies of the vertebrae and ribs and many other bone abnormalities may be associated. Calcification of the falx cerebri is pathognomonic. There are frontal and temporoparietal bossing, a broad nasal root, prominent supraorbital ridges and a degree of mandibular prognathism. Short fourth metacarpals are common.<sup>[4]</sup>

Diagnosis of the syndrome is made using major and minor criteria which include the following; Major criteria: multiple basal cell carcinoma or one occurring under the age of 20 years, histologically proven OKCs of the jaws, palmar or plantar pits (three or more), bilamellar calcification of the falx cerebri, bifid or fused or markedly splayed ribs and first-degree relative with NBCCS. Minor criteria: macrocephaly (adjusted for height), congenital malformation (cleft lip or palate), frontal bossing, coarse face and moderate or severe hypertelorism. Other skeletal abnormalities include Sprengel's deformity, marked pectus deformity and marked syndactyly of the digits. Radiological abnormalities include bridging of the sella turcica, vertebral anomalies (hemivertebrae, fusion or elongation of the vertebral bodies), modeling defects of the hands

and feet or flame-shaped hands or feet, ovarian fibroma and medulloblastoma.<sup>[5]</sup>

More than 100 minor criteria have been described. The presence of two major and one minor criteria or one major and three minor criteria is necessary to establish a diagnosis. In our patient, diagnosis of Gorlin syndrome was established by the presence of two major criteria (histologically proven KCOT and rib and vertebral anomalies) and four minor criteria (hypertelorism, frontal bossing, flattened nasal bridge and mandibular prognathism).

The peak incidence is seen in the 2<sup>nd</sup>–3<sup>rd</sup> decade, but occurrence in children is not uncommon. The male-to-female ratio for those who are not having nevoid basal cell carcinomas are 1:0.62, but it varies to 1:1.22 among patients with nevoid basal cell carcinoma, but an equal distribution among people is accepted by everyone. Keratocyst involvement is more predominantly seen in the mandible, in which the ramus part of the mandible (43%) is affected more commonly followed by the anterior region (18%) and the premolar region (7%).<sup>[6]</sup> In the maxilla, anterior regions are more involved (14%) than the posterior (12%) and the premolar region (3%).<sup>[7]</sup>

In 2013, Luana *et al.* reported 14 patients with Gorlin syndrome, out of which 8 presented a single OKC, 4 showed synchronous tumors, 1 had 3 metachronous lesions and another patient had 2 synchronous lesions at initial evaluation and then developed other 3 metachronous lesions. Besides the 31 primary OKCs, 18 lesions were located in the mandible and 13 in the maxilla. Most tumors presented unilocular pattern and association with a tooth.<sup>[8]</sup>

In 2007, Rai and Gauba reported the case of an 11-year-old male patient with multiple OKCs and rib anomalies.<sup>[9]</sup> In 2012, Agrawal *et al.* reported the case of a 25-year-old female patient with bifid rib and multiple OKCs in the maxilla and mandible.<sup>[6]</sup>

The treatment of this syndrome is multidisciplinary depending on the system involved. In case of OKCs, there are different treatment techniques to eliminate and avoid the high recurrence rate which can reach up to 62% of the cases.<sup>[10]</sup> In order to decide which technique must be employed, the following factors have to be taken into account: lesion size, lesion extension, location, possible cortical and soft parts damage, the age and whether it is a primary or recurrent lesion. The therapeutic technique may vary from simple enucleation to curettage, to the enucleation with peripheral osteotomy or to osseous resection.<sup>[11]</sup>

A new treatment strategy, based on the understanding of the hedgehog signaling pathway and with the understanding that the tumors arise due to its over activity, it is proposed that inhibition of this pathway with specific pharmacological treatment might suppress tumor growth.<sup>[12]</sup>

### Complications

Aggressive basal cell carcinomas have caused death of the patients as a result of tumor invasion to the brain or other vital structures. Medulloblastoma associated with the syndrome causes death during infancy. Because of the recurrence of OKCs, varying degrees of jaw deformity may result from operations for multiple cysts.<sup>[13]</sup>

### CONCLUSION

Patients suffering from Gorlin syndrome have to undergo checkups at least once a year, especially the ones having odontogenic keratocyst. Thus, attention is required from oral clinicians to recognize the condition at an early stage so as to render effective treatment.

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### Conflicts of interest

There are no conflicts of interest.

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