Management of Syndromic Odontogenic Keratocysts: A Report of Two Cases

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Abstract:
Gorlin-Goltz syndrome is an autosomal dominant condition with prevalence varying from 1/60000 to 1/256000, and a male to female predilection of 1:1. We report two previously undiagnosed cases of Gorlin-Goltz syndrome, which originally presented with multiple odontogenic keratocysts (OKC). We report the management protocol followed for these two cases of bimaxillary OKC. Both patients were treated at the Department of Oral and Maxillofacial Surgery, Nasser Institute Hospital in Cairo, Egypt. Lesions smaller than 2 cm in diameter were enucleated with peripheral ostectomy while lesions larger than 2 cm were marsupialized and enucleated at a second stage. Clinically, both patients were followed up for 18 months with no reported complications. Radiographically, both patients exhibited satisfactory resolution and bony ingrowth of the previously radiolucent cystic cavities.

Key Words: Basal cell nevi, Gorlin-Goltz syndrome, odontogenic keratocyst

Introduction
We present two cases of Gorlin-Goltz syndrome, treated at the Department of Oral and Maxillofacial Surgery (OMFS) at Nasser Institute Hospital, Cairo, Egypt. Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma Syndrome, is an autosomal dominant condition with prevalence varying from 1/60000 to 1/256000, with a male to female predilection of 1:1. It was first described by Jarisch and White in 1894, and later ascertained and studied by Dr. Robert Gorlin and Dr. Robert Goltz in 1960.1,2

The syndrome has both major and minor manifestations. Major manifestations include multiple basal cell nevi, OKC of the jaw, palmar or plantar pitting, calcification of the falx cerebri, desmoplastic medulloblastoma, and a first degree relative with Gorlin-Goltz syndrome. Minor manifestations include rib anomalies, skeletal malformations, macrocephaly and frontal bossing, cleft lip and/or palate, lymphomesenteric cysts, and ovarian or cardiac fibromas.3,4

A diagnosis of Gorlin-Goltz syndrome can be made in the presence of 2 major manifestations, 1 major manifestation and molecular confirmation or 1 major and 2 minor manifestations.3

The anomaly is thought to arise from a mutation in the PTCH1 gene on chromosome 9. PTCH1 encodes the protein patched homolog 1 in the hedgehog signaling pathway, which is important for development of normal tissues during embryogenesis and cell signaling in adults.5

Odontogenic keratocysts (OKC) are aggressive odontogenic cysts, most commonly occurring in the posterior mandible. They may also arise in the anterior maxilla or any other bimaxillary region, with a peak incidence during the second and third decades of life. They originate from either the remnants of the dental lamina (60%) or the reduced enamel epithelium (40%). Accordingly, Marx classified OKCs as being of either primordial origin or dentigerous origin, respectively. Stoelinga et al. argued that the offshoots of the basal layer of epithelium of the oral mucosa also played a role in the etiology of OKC.6,7

On a microscopic level, Crowley et al. found two variants of the cyst lining exist: parakeratinized epithelial lining and orthokeratinized epithelial lining, with a frequency of approximately 86.2% and 12.2%, respectively. 1.6% of lesions examined had features of both parakeratinized and orthokeratinized epithelial lining.8

Among the unique characteristics of OKC are their mitotic activity, daughter cysts arising from the original cyst and tendency for the epithelial lining of the cyst to separate from the underlying connective tissue. All of this contributes to both the relatively rapid enlargement and high recurrence rate of the lesion.7,8

Both patients presented at OMFS Department at Nasser Institute Hospital without being previously diagnosed with Gorlin-Goltz syndrome. The triad of multiple OKC, basal cell nevi, and bifid ribs arose our suspicion at first. Further examination revealed calcified falx cerebri, frontal bossing, and palmar pits.

Case Report
Patient 1, a 22-year-old female (Figure 1), was referred to OMFS outpatient clinic when her Dentist incidentally...
discovered multiple radiolucencies associated with several impacted teeth in both jaws on a routine orthopantomogram (OPG).

She gave a history of mild to moderate pain related to both jaws in the preceding 2 years. Panoramic radiograph (Figure 2) showed impacted right mandibular canine, bilateral mandibular third molars, bilateral maxillary second molars, maxillary right first premolar and third molar, and congenitally missing maxillary left third molar. All impacted teeth were associated with radiolucencies that extended to both mandibular rami, subsequently causing displacement of the roots of left mandibular second molar and left maxillary lateral incisor. Aspiration resulted in the turbid yellowish fluid. An incisional biopsy on the mandibular right lesion proved to be an OKC histopathologically.

Clinically, the patient presented with multiple basal cell nevi across her face, neck, and back. A routine pre-operative plain chest radiograph revealed bifid left sixth rib (Figure 3). A skull and facial bone computed tomography (CT) was requested as a further investigation, revealing a calcified falx cerebri.10

Her surgical treatment plan involved marsupialization of mandibular lesions except the one associated with the right canine, which was enucleated and enucleation of all maxillary lesions.

Following the first surgery, all marsupialized lesions were irrigated twice daily with a normal saline (0.9% NaCl) solution. 5 months after the first surgery, enucleation of the mandibular lesions was done with the extraction of any impacted teeth. The patient had an uneventful recovery following that.

Patient 2, a 30-year-old male (Figure 1), presented with OPG exhibiting multiple radiolucent lesions. This included a well-
defined multi-locular radiolucency extending from the left mandibular angle and ramus to the contralateral side of the mandible, crossing the midline (Figure 2). This lesion was associated with an impacted lower left third molar adjacent to the left angle of the mandible.

Other lesions included a round, well-defined, unilocular radiolucency measuring 2 cm in diameter on the right angle of the mandible. This lesion was involved with the root of an erupted lower right third molar. Two separate lesions, involved with bilateral impacted maxillary canines were also present, these round, well-defined, unilocular lesions measured roughly 1.5 cm in diameter. Pre-operative CT scan also revealed a calcified falx cerebri (Figure 4).

Patient 2 was first admitted for biopsy, and a histopathological diagnosis of an OKC was confirmed (Figure 5). He was subsequently admitted for a second surgery, where a small lesion in the upper left quadrant was enucleated, along with the associated upper left lateral incisor and upper left canine. Larger lesions in the upper right, lower right, and lower left quadrants underwent marsupialization, with a partially impacted lower right third molar also removed. Drainage from the open cystic cavities was initially achieved via tubes secured in the upper right and lower left quadrants, and the extraction socket of the lower right third molar.

Post-operatively, the patient was instructed to irrigate the marsupialized cavities daily with saline and povidone iodine solutions. Acrylic plugs were fabricated for the marsupialized lesions. The patient was followed up for 18 months and exhibited an uneventful recovery.

**Discussion**

The common treatment modalities for OKC (now termed keratocystic odontogenic tumors [KCOT] by the WHO) include enucleation, marsupialization, and resection in more extensive lesions. The use of Carnoy’s solution as an adjunct to peripheral ostectomy is also common, and the use of cryotherapy has also been advocated by some clinicians.

The main issue with OKC is their tendency to recur. Crowley et al. found a recurrence rate of 42% in parakeratinized variants, compared to 2.2% recurrence rate in orthokeratinized OKC.

Given this recurrence rate, enucleation remains the treatment of choice. However, marsupialization may be indicated in lesions adjacent to vital structures or in lesions of dentigerous origin where an associated unerupted tooth is in a favorable position to erupt. Resection is indicated in recurrent lesions where enucleation has failed, or in large lesions where enucleation would lead to a continuity loss, such as cases with cortical perforation.

The guidelines we followed for the management of the OKC depended on the size of the individual lesions; with lesions smaller than 2 cm in diameter being enucleated with peripheral ostectomy performed. Lesions >2 cm in diameter underwent marsupialization. These lesions were then followed up clinically and radiographically until they shrunk in size and were subsequently indicated for enucleation and ostectomy.

Patients were routinely followed up post-surgically, with meticulous oral hygiene measures enforced. Patients performed daily irrigation of the marsupialized cavities at home with normal saline. The patients exhibited an uneventful follow-up at the outpatient clinic over the course of the 1st year.
post-operatively. Post-operative radiographs revealed a satisfactory degree of resolution and bony infill of the multiple bimaxillary radiolucencies (Figure 6).

**Conclusion**
Although relatively uncommon, we were able to detect two cases of Gorlin-Goltz syndrome at our department over the course of a few months. This highlights the importance of looking for tell-tale signs of the syndrome when faced with multiple bimaxillary radiolucencies; subsequently increasing the clinician’s index of suspicion. This becomes even more important when considering the malignant potential of basal cell nevi.

**References**