

Case Report

Gorlin Goltz Syndrome – 5 Cases in Two Related Families: A Single Center Experience

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Abstract: Multiple KCOT's (Keratocystic odontogenic tumors) of maxilla and mandible are rare and most of the times they are associated with a syndrome. Gorlin Goltz or Nevoid Basal Cell Carcinoma Syndrome (NBCCS) is an autosomal dominant systemic disease associated with multiple KCOTs of jaws along with cutaneous, ophthalmologic, skeletal, neurologic and genital abnormalities. KCOTs associated with Gorlin Goltz Syndrome reportedly have high recurrence rates of up to 82% and are the presenting complaint in many cases of this syndrome. Hence maxillofacial surgeons play a crucial role in early identification of the disease. Although life expectancy is not significantly altered, early diagnosis may prevent morbidity due to existing complications improving the quality of life. Our aim is to report experience with 5 cases of Gorlin Goltz Syndrome in two related families.

Keywords: Gorlin Goltz syndrome, Nevoid Basal Cell Carcinoma Syndrome, multiple odontogenic keratocysts, Keratocystic odontogenic tumors, multiple OKC

INTRODUCTION

The roots of Gorlin Goltz syndrome dates back to the Dynastic Egyptian times (3000 years ago) as revealed by the skeletal findings in mummies that belonged to the ancient population of Pompeii in an anthropological study conducted by Giovanni Ponti *et al* [6]. They studied the skeletal remains from the Museum of Anthropology and Ethnography of Turin, University of Modena and Reggio Emilia and hypothesized that some individuals of the Pompeii population were affected by Nevoid Basal Cell Carcinoma Syndrome. Cystic cavities in maxilla and mandible are one of their constant findings (thought to be keratocyst of jaws) along with frontoparietal bossing, asymmetric skull base, bifid ribs and short 4th metacarpal. It was recognized as a distinct syndrome in 1963.

This syndrome is caused due to a genetic defect or mutations in the human analog of patched gene (PTCH) located on the long arm of chromosome 9q 22.1-3-1. It is a tumor suppressor gene responsible for growth and development of normal tissue explaining the occurrence of multiple neoplasms of skin, brain and ovarian tissue. It is autosomal dominant with almost complete penetrance and variable expression. Early

diagnosis, family screening and genetic counselling are essential as 10% are associated with aggressive neoplasms. We treated 5 patients for multiple KCOTs of mandible and maxilla, from two related families with GGS. All the five patients presented, with a chief complaint of swelling irt jaws or toothache. The details of two patients are discussed in detail.

CASE REPORT 1

An 18 year old female presented with swelling and pain irt lower right back teeth region since 6 months. Extraorally face appeared asymmetric due to diffuse swelling over right side of mandible. No signs of inflammation or secondary changes were noticed over the skin. Obliteration of lower labial vestibule, multiple missing teeth, and tenderness on percussion of the right lower anterior teeth with grade 1 mobility are the positive findings intraorally. Bicortical expansion in the anterior mandible is appreciated.

Other relevant findings are microphthalmia (congenitally rudimentary left eyeball) Fig 1, mild mandibular prognathism Fig 2, dermoid cyst irt right ring finger Fig 3, palmar pits < 0.5mm in diameter Fig 4.



Fig-1: Left microphthalmia



Fig-2: Mild mandibular prognathism



Fig-3: Dermoid cyst, right ring finger

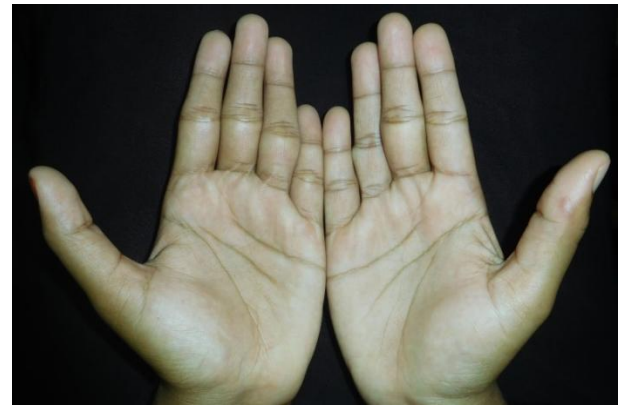


Fig-4: Left palmar pits



Fig-5: Multiple cystic radiolucencies with well-defined borders in mandible and maxilla. Right lower third molar displaced and inverted

On examination of Orthopantomogram (OPG) Fig: 5, multiple well defined cystic radiolucencies are noticed in the maxilla and mandible. Right lower third molar is inverted and displaced due to the cystic expansion. Left upper third molar is impacted. Displacement of teeth is evident at the sites of cysts. No other skeletal abnormalities were noticed.

Cyst enucleation and chemical cauterization with Carnoy's solution was performed under general anesthesia. Impacted and involved teeth were extracted. Intraoperatively there was pathological fracture of right mandibular angle which was successfully plated using titanium miniplates and screws Fig: 6. Histopathology confirmed the lesions were odontogenic keratocysts Fig: 7.



Fig-6: 9 months postoperative OPG showing satisfactory bone formation at the enucleated sites and two miniplates with screws, healed fracture site

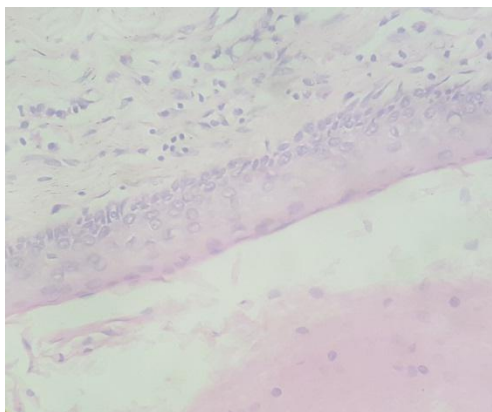


Fig-7: 40 x magnification of the specimen showing picket fence appearance of the cyst lining, keratin material in the lumen classic features of Odontogenic Keratocyst



Fig-9: Mild Scoliosis

CASE REPORT 2

Family history is highly contributory. The patient is middle among three female siblings. Non consanguineous marriage of parents. Father and all the three daughters, had similar complaints (swelling of jaws). Each one diagnosed and operated for multiple cystic lesions of jaws at their early ages respectively. Father's brother's son was also diagnosed with the same condition during his childhood and was operated. Histopathologically all the lesions are KCOTs. Upon careful systemic examination they are diagnosed with Gorlin Goltz Syndrome. Father has coarse facial features, frontal bossing, Fig: 8 multiple nevi in the mid face region, multiple keratocysts of jaws and mild scoliosis Fig: 9.

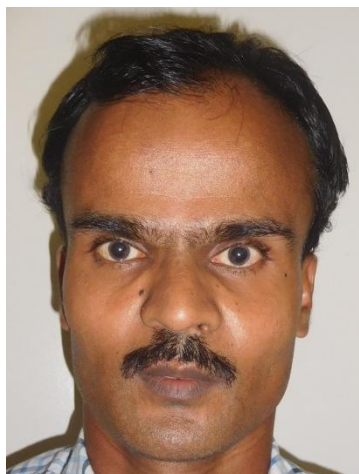


Fig-8: Frontal bossing, multiple nevi in the midface region

DISCUSSION

Nevoid basal cell carcinoma syndrome, Gorlin syndrome, Basal cell nevus syndrome, Multiple basilooma syndrome, Hereditary cutaneomandibular polyoncosis, Jaw cyst basal cell nevus bifid rib syndrome are several names for Gorlin Goltz syndrome [3]. In 1894 Jarisch & White first described the patients with this syndrome emphasizing on multiple basocellular carcinomas. In 1939 Straith described similar case with cysts. 1953 Gross added synostosis of the first left rib and bilateral bifurcation of the sixth ribs to literature. Bettley & Ward related the presence of palmar and plantar pits [3]. Calnan in 1953 described palmo-plantar pits as a peculiar dyskeratosis of palms and soles caused by partial or complete absence of stratum corneum with diameter from 1-3mm. In 1960 Gorlin and Goltz described the classical triad. In 1965 Gorlin put forth the clinical criteria for diagnosis of NBCCs. Kimonis *et al.* in 1997 revised the clinical criteria given by Evans *et al.*, and stated that two major or one major and 2 minor criteria should be present for diagnosis of NBCC [6].

Major criteria

1. Multiple BCC or one occurring under the age of 20 years.
2. Histologically proven OKCs of the jaws.
3. Palmar or plantar pits (three or more).
4. Bilamellar calcification of the falx cerebri.
5. Bifid, fused or markedly splayed ribs.
6. First degree relative with NBCCS.

Minor criteria

1. Macrocephaly (adjusted for height).
2. Congenital malformation: Cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism.
3. Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
4. Radiological abnormalities: Bridging of the sella turcica, vertebral anomalies such as hemi vertebrae, fusion or elongation of the vertebral

bodies, modelling defects of the hands and feet or flame shaped hands or feet.

5. Ovarian fibroma.
6. Medulloblastoma.

In case 1, diagnosis was made by three major criteria - histologically proven multiple OKCs of jaws, 1st degree relative with GGC and palmar pits. Microphthalmia, mandibular prognathism and dermoid cyst are additional findings.

In case 2 (father) multiple OKC, 1st degree relative with GGS is the major and frontal bossing and scoliosis are the minor criteria.

The autosomal dominant inheritance pattern of this syndrome with almost complete penetrance and high variability makes it strongly familial, though sporadic cases of upto 60% are reported [2, 4, 9]. Our cases represent the strong familial tendency of this syndrome with high female predilection for syndrome associated OKCs in accordance with the study by Kannan KS *et al* [7].

Involvement of OKCs associated with GGS is more common in mandible 69% compared to maxilla 31%. 43% OKCs occurs in the molar ramus region followed by incisor-canine area 18%. In maxilla, 14% OKCs were found to occur in the incisor-canine area, followed by molar tuberosity with 12%, 7% in the mandibular premolar region and 3% in the maxillary premolar region [8]. Our case in accordance with the above results had 2 lesions in bilateral ramus area, 1 in the lower incisor canine area and 1 in the right maxillary posterior area.

The recurrence rate of KCOTs associated with GGS is high 82% [10]. This may be attributed to high number of satellite cysts than non-syndromic cases as studied by Wooglar *et al* [11]. Intense heparanase expression in GGS associated KCOTs suggests their accentuated neoplastic nature.

The treatment modality for KCOT in the literature ranges from marsupialization to resection. Main aim is to reduce the recurrence rate and preserve the vital structures. [1]. While surgical enucleation and chemical cauterization with Carnoy's solution is a widely accepted modality for elder population, some studies suggest a two stage treatment in young patients - initial marsupialization followed by enucleation and peripheral ostectomy at a later date. For all the five patients enucleation and chemical cauterization was performed with no recurrence till date.

CONCLUSION

Gorlin Goltz syndrome is rare with estimated prevalence of 1 in 57,000 to 2,56,000 among different studies. 76% of the cases are associated with OKCs and are the only presenting complaint in most of the cases.

Hence a maxillofacial surgeon plays a crucial role in early identification of the underlying syndrome which in turn helps to prevent morbidity due to the disease. Younger patients can be treated with marsupialization initially followed by enucleation and chemical cauterization or peripheral ostectomy at a later date to prevent morbidity. Proper genetic counselling should be encouraged.

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