Gorlin-Goltz syndrome with situs oppositus

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ABSTRACT

Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma syndrome, is caused due to a genetic alteration produced by a mutation in the “Patched” tumor suppressor gene, and it is inherited in a dominant autosomal way, though sporadic cases have been found. This syndrome shows a high penetrance and variable expressiveness. It is a multisystemic process that is characterized by the presence of multiple pigmented basocellular carcinomas, keratocysts in the jaws, palmar and/or plantar pits and calcification of the falx cerebri. Together with these major features, a great number of processes considered as minor features have also been described. The latter include numerous skeletal, dermatology related and neurological anomalies, among others. In some occasions, the presence of very aggressive basocellular carcinomas has been described as well as other malignant neoplasia. Due to the importance of oral maxillofacial manifestations of this syndrome, it is fundamental to know its characteristics in order to make a diagnosis, to provide an early preventive treatment and to establish right genetic advice. We report a rare association of Gorlin–Goltz syndrome with situs oppositus.

Key words: Basocellular carcinoma, Gorlin-Goltz syndrome, odontogenic keratocyst, situs oppositus

INTRODUCTION

Gorlin–Goltz syndrome, also known as basal cell nevus syndrome, is an uncommon, autosomal dominant inherited disorder, which 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. Robert J. Gorlin and Robert W. Goltz described the distinct syndrome, consisting of the presence of multiple nevoid basal cell epitheliomas, jaw cysts, and bifid ribs. The incidence of this disorder is estimated to be 1 in 50,000 to 150,000 in the general population, varying by region. It appears in all ethnic groups, but most often in Whites; males and females are equally affected. Along with multiple BCCs, jaw cysts and musculoskeletal anomalies are lesser known manifestations of this disorder involving the skin, central nervous system, ophthalmic, endocrine, urogenital system, and so on. This syndrome has received several names throughout the times such as “basal cell nevus syndrome”, “neviod basal cell carcinoma syndrome” or the most complex name, i.e., “multiple basal epithelioma, jaw cysts and bifid rib syndrome”. We present a case of Gorlin–Goltz syndrome with situs oppositus. Oppositus a rare association (also called situs transversus or situs inversus); it is a congenital condition in which the major visceral organs are reversed or mirrored from their normal positions.

CASE REPORT

A 15-year-old male patient referred to the Department of Oral and Maxillofacial surgery, presented with a chief complaint of swelling on right lower one-third of the jaw since 2 months, with a history of slowly progressing swelling. The approximately 5 × 4 cm facial swelling extended superiorly from right corner of mouth to 1 cm inferiorly beyond the lower border of the mandible, medially from left para-symphysis region to distally half of the body of the mandible [Figure 1].

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Intraoral examination revealed missing right and left mandibular canines, while in the maxilla the right canine and left maxillary second molar were missing with the left maxillary canine in erupting phase, and with rotated left maxillary premolars. Intraoral swelling was present in relation to mandibular anterior teeth [Figure 2]. Based on the history and clinical findings, a provisional diagnosis of dentigerous cyst in relation to right mandibular canine was made. The patient was subjected to the following radiographic examination.

Orthopantomograph revealed multiple unilocular well-defined radiolucencies with sclerotic border in maxilla and mandible [Figure 3]. Mandibular occlusal radiograph [Figure 4] revealed a well-defined radiolucent lesion with a sclerotic border extending from periapical region of lower anteriors extending to the lower border of the mandible in relation to 33 and 43.

The presence of multiple cysts in the jaws, in association with unerupted teeth, raised a suspicion of Gorlin–Goltz’s syndrome. The patient was further evaluated for this. Lateral skull view revealed bridging of the sella turcica [Figure 5]. Computed tomographic (CT) images showed multiple cystic lesions in maxilla [Figure 6] and mandible [Figure 7]. Postero-anterior [Figure 8] chest radiograph revealed a bifid third rib in the right side and an unusual finding of dextrocardia. CT images of the brain showed areas of hyperdensities, suggestive of falx cerebri [Figure 9] and tentorial cerebelli [Figure 10] calcification. CT images of spine revealed bifid spine in relation to C6 C7 T1 [Figure 11]. Ultrasonographic images showed the presence of spleen in the right hypochondrium [Figure 12] and liver in the left hypochondrium [Figure 13] with transposition on great vessels [Figure 14]. The dorsum of the patient revealed the presence of sprengei deformity. There were multiple palmer pits [Figure 15] measuring 0.2–0.3 mm in diameter, which were brownish black in color, and were present on the palms of both his hands. Excisional biopsy was done for one of the cysts and was taken for microscopic examination, which revealed a stratified squamous parakeratinized epithelium with palisading pattern of basal cells [Figure 16], suggestive of odontogenic keratocyst. Enucleation was done under local anesthesia followed
by chemical cauterization with carnoy’s solution since odontogenic keratocyst has high recurrence rate due to the presence of daughter or satellite cysts and highly adherent epithelial layer. The patient was asked to have a regular follow up.

Since the patient fulfilled the three major criteria for multiple odontogenic keratocysts (palmer pits, falx cerebri and tentorial cerebelli calcification) with three minor criteria of bifid rib, spina bifida and sprengel deformity, the final diagnosis was made as Gorlin–Goltz syndrome with situs oppositus (also called situs transversus or situs inversus), which is a congenital condition in which the major visceral organs are reversed or mirrored from their normal positions.
**Discussion**

Gorlin–Goltz syndrome is autosomal dominant with a high penetrance and variable expressivity. It is caused by mutations in the patched tumor suppressor gene (PTCH), a human homolog of the *Drosophila* gene mapped to chromosome 9q21–23.[1,4] The diagnostic criteria for nevoid BCC were established by Evans et al, and modified by Kimonis et al, in 1997.[3] According to them, diagnosis of Gorlin–Goltz syndrome can be established when two major or one major and two minor criteria are present as described below.[2,3]

**Major criteria**

More than two BCCs or one BCC at younger than 30
years of age or more than 10 basal cell nevi.
Any odontogenic keratocyst (proven on histology) or polyostotic bone cyst.
Three or more palmar or plantar pits (present in about 65% of patients).
Ectopic calcification: Lamellar or early at younger than 20 years of age.
Falx cerebri calcification.
Positive family history of nevoid BCC.

Minor criteria
Congenital skeletal anomalies; fused, splayed, missing, or bifid ribs, wedged or fused vertebrae.
Occipital–frontal circumference more than 97%.
Cardiac or ovarian fibroma.
Medulloblastoma.
Lymphomesenteric cysts.
Congenital malformations such as cleft lip or palate, polydactylism or eye anomalies (cataract, coloboma, microphthalmus).

Other diagnostic findings in adults with Gorlin-Goltz syndrome are:
Skeletal anomalies: Hemivertebrae, scoliosis, syndactyly, polydactyly, shortened fourth metacarpal.
Craniofacial anomalies.
Neurological anomalies: Agenesis/dysgenesis of corpus callosum, congenital hydrocephalus, meningioma; mental retardation, schizoid personality.
  • Oropharyngeal anomalies: Cleft lip/palate, high arched palate or prominent ridges.
  • Anomalies of the reproductive system
  • Cardiac anomalies.

Diagnosis and therapy of this syndrome require a multidisciplinary approach (dentists, maxillofacial surgeons, dermatologists, and neurologists). Therapy consists of removal of tumors (surgical excision, topical chemotherapies, and laser ablation) and adequate treatment of jaw cysts. In the case of odontogenic keratocysts, there are different treatment techniques to eliminate them and avoid the high rate of recurrence, which can reach up to a 62% of the cases.[5,6] The therapeutic techniques for the keratocysts vary from simple enucleation with curettage, to enucleation with peripheral osteotomy or to osseous resection in block.[7] This last technique is the most aggressive and it logically follows that the recurrence rate decreases.[8] There are also more conservative options such as enucleation for small cysts and chemical cauterization with carnovy’s solution, with cryotherapy or marsupialization of the cysts, or decompression followed by a secondary enucleation.[9,10] Nevertheless, these methods are not efficient in the long term and their use is considered to be controversial.[9,10] In order to decide on the technique to 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.[10] It is also important to detect if it is an isolated keratocyst or if it is associated with the syndrome. However, further research is needed to confirm the association between situs oppositus and Gorlin–Goltz Syndrome.

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