Case Report:
Radiological features of Gorlin-Goltz syndrome
Dr. Ganesh Vikhe*, Dr. Y. P. Sachdev, Dr. R. D. Kawade, Dr. Neha Garg, Dr. Chetana Borkar

Department of Radiodiagnosis, Rural Medical College of Pravara Institute of Medical Sciences, Loni, Maharashtra, India
Corresponding author*

Abstract:
Gorlin-Goltz syndrome is an uncommon autosomal dominant syndrome with complete penetrance and variable expressivity, which is principally characterized by multiple odontokeratogenic cysts, skeletal, dental anomalies, basal cell carcinoma, neurological abnormalities, intracranial calcifications of the falx cerebri. The basic pathology is attributed to the mutation in PTH tumour suppressor gene and abnormalities in the long arm of chromosome no. 9. Diagnosis is made upon established major and minor clinical and radiological criteria. We report a case of a 40-year-old male presenting with three major and two minor criteria of Gorlin-Goltz Syndrome. Radiological features of the syndrome are easily identifiable on CT-scan, chest x-ray and aid in early identification of the disease, to prevent recurrence and better survival rates.

Key words: Odontokeratogenic cysts; calcifications of the falx cerebri, fused ribs, spina bifida

Background:
Gorlin-Goltz syndrome is also known as nevoid basal cell carcinoma syndrome, and basal cell nevus syndrome. Robert J. Gorlin and Robert W. Goltz described a distinct syndrome consisting of multiple nevoid BCCs, cysts in jaw and bifid ribs. Gorlin-Goltz syndrome is an autosomal dominant inherited condition that exhibits high penetrance and variable expressivity, however this disorder can arise spontaneously. Almost 60% of the patients with Gorlin-Goltz syndrome have no known affected family members. The Gorlin-Goltz syndrome gene has been mapped to chromosome 9q22.3-q31. The prevalence of Gorlin-Goltz syndrome has been estimated about 1 per 60,000. Males and females are equally affected. The main clinical features of Gorlin-Goltz syndrome includes multiple keratocystic odontogenic tumor, basal cell nevi, and skeletal anomalies. Diagnosis is based upon established major and minor clinical and radiological criteria. A case of Gorlin-Goltz syndrome is presented in which the above mentioned findings are evident. The syndrome manifests with some major and minor criteria like odontokeratogenic cysts, BCCs, palmar/plantar pits and ectopic calcifications of the falx cerebri. To establish the diagnosis of Gorlin-Goltz syndrome two major and one minor criteria or one major and two minor criteria are necessary. (6,7)

Case Report
A 40-year-old male patient was referred to our department of radiodiagnosis for CT-Scan mandible with the complaints of pus discharge from multiple cystic lesions of the jaw since 3 months. The findings on CT-Scan of mandible were presence of a well defined, multilocular, expansile cystic lesion in the maxilla in midline and paramedian region, multiple well defined fluid filled cystic lesions seen involving body of mandible on both sides (Fig. A). Above findings raised the possibility of Gorlin-Goltz syndrome and further investigations were carried out. Calcification of falx cerebri was also observed (Fig. B). Spina bifida in cervical spine (Fig. C), Chest radiograph revealed the bifid fourth and eighth rib on the right side (Fig. D). Clinical photograph shows Hypertelorism (Fig. E)
FIG. A - CT SCAN - MULTILOCULAR, EXPANSILE CYSTIC LESIONS

FIG. B - CALCIFICATION OF FALXCEREBRI
FIG. C- CT CERVICAL SPINE SCREENING SHOWS SPINA BIFIDA

FIG. D- CHEST RADIOGRAPH REVEALED THE BIFID FOURTH AND EIGHTH RIB ON THE RIGHT SIDE
In our patient, the diagnosis of Gorlin-Goltz syndrome was established by the presence of three major criteria (i.e. multiple OKC, falx cerebri calcifications and bifid ribs) and two minor criteria (i.e. spina bifida and hypertelorism)

**Discussion**

In order to establish a diagnosis of the syndrome, some diagnostic criteria have to be taken into consideration. The most important criteria to make diagnosis are presence of pigmented BCCs, odontokeratogenic cysts, palmar/plantar pits and ectopic falx cerebri calcifications. (8-11).

There are more than 100 minor criteria have been described. (4,8,12,13)

Evens et al. (6) first established major and minor criteria for the diagnosis of the syndrome which were latter modified by Kimonis et al. (7) in 2004. The presence of two major and one minor or one major and three minor criteria are necessary for the establishment of diagnosis. (6,7)

**Major criteria**

- Multiple basal cell carcinomas or one occurring under the age of 20 years.
- Histologically proven OKCs of the jaws.
- Palmar or plantar pits (three or more).
- Bilamellar calcifications of the falx cerebri.
- Bifid, fused, or markedly splayed ribs.
First degree relative with nevoid basal cell carcinoma syndrome.

Minor criteria

- Macrocephaly (adjusted for height).
- Congenital malformation: Cleft lip or cleft palate, frontal bossing, coarse face moderate or severe hypertelorism.
- Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits.
- Radiological abnormalities: Bulging of sella turcica, vertebral anomalies such as hemi vertebrae, fusion or elongation of vertebral bodies, modeling defects of the hands and feet, or flame-shaped hands or feet.
- Ovarian fibroma.
- Medulloblastoma.

Gorlin-Goltz syndrome is an autosomal dominant disorder with a high penetrance and variable expressivity. It is caused by mutations in the patched tumor suppressor gene (PTCH), a human homologue of the Drosophila gene mapped to chromosome 9q21-23. Chromosomal mapping and genetic studies suggest that the underlying basis for this disease is an abnormality in the Hedgehog (Hh) signaling pathway. The role of this pathway in embryogenesis is well known. The PTCH gene product is part of a receptor for the protein called Sonic Hedgehog, which is involved in embryonic development. More recent investigations reveal the role of the Hh pathway in cell cycle regulation in adults. In the Drosophila model, the primary receptor for the Hh signaling pathway has two transmembrane protein components: Patched (Ptc) and Smoothened (Smo). In the absence of Hh protein, the Ptc protein inhibits the Smo. Under normal conditions, Hh, when present, binds Ptc, releasing Smo to affect downstream events such as cell growth and differentiation. Based on this model, inactivation of Ptc or constitutive activity of Smo or Hh could lead to overactivity of Smo, resulting in neoplasm formation.[5]

Woolgar et al. in 1987 concluded that mean age group for syndromic cases is 10 to 30 years and females are more affected than males. In syndromic cases, more commonly maxillary molar area is affected. Recurrence rate is higher in syndromic cases (63%).[14] Woolgar et al. have also noted significant differences histologically. OKC associated with Basal Cell Nevus Syndrome showed more number of satellite cyst, solid islands of epithelial proliferation and odontogenic rests within the capsule, and increased mitotic figures in the epithelium lining the main cavity.[14]

OKC’s falling in the category of Keratocystic Odontogenic Tumor (KCOT) may be associated with Gorlin-Goltz Syndrome in the form of multiple cystic lesions.[3,11] Katase et al. analyzed the neoplastic nature and biological potential of sporadic and nevoid basal cell carcinoma syndrome (NBCCS)-associated KCOT.[15] Heparanase is an endo-d-glucuronidase enzyme that specifically cleaves heparan sulfate and the increase of its level in tumors promotes invasion, angiogenesis, and metastasis. In his study, all odontogenic cysts have shown positive immunoreactions for the heparanase for the heparin protein in various intensities. Intense gene and protein expressions have been observed in KCOT associated with NBCCS, as compared with sporadic ones and dentigerous cyst. So, heparanase expression may be correlated with the neoplastic properties of KCOT, particularly in NBCCS-associated cases.[3,11]

Apart from surgical enucleation for cystic lesions, adjunctive therapies like chemical cauterization is useful to prevent recurrence by fixing the daughter cyst or remnants of epithelial lining that are not removed during the enucleation procedure. Carnoy’s solution is a phenolic compound with tissue fixative properties.[13] Voorsmit et al. have demonstrated that Carnoy’s
solution penetrates the bone to the depth 1.54 mm following a 5 minutes application without any damage to the inferior alveolar nerve.[16]

CONCLUSION
Gorlin-Goltz syndrome is a well-known Autosomal Dominant disorder. The incidence reported worldwide ranges from 1 in 50,000 to 1 in 150,000. Not many cases have been reported in India, and hence we report here a rare case and importance of multidisciplinary approach in management of the syndrome. Thorough extraoral and intraoral examinations along with OPG, skull and chest radiographs help in proper diagnosis of the condition. This investigation prompts an early verification of the disease, which is very important to prevent recurrence and better survival rates from the existent diseases.

REFERENCES


