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Gorlin goltz syndrome: A case report and literature review

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Abstract
A rare multisystemic disease, Gorlin-Goltz syndrome (GGS) is an autosomal dominant hereditary disorder characterised by multiple basal cell nevi carcinomas, multiple keratocystic odontogenic tumours (KCOT) in the jaws, and abnormalities in the skeletal structure. Gorlin-Goltz syndrome should be diagnosed as early as possible because it can develop into aggressive basal cell carcinomas and neoplasias. Seldom have cases of Gorlin-Goltz syndrome been documented in eastern Indian subcontinent. This article offers a thorough literature analysis on the illness and details the case of a 15-year-old girl patient with Gorlin-Goltz syndrome.

Keywords: Gorlin-goltz, odontogenic keratocysts, pits

Introduction
Gorlin Goltz Syndrome (GGS) is an autosomal dominant condition with high penetrance and variable expression. It is a rare disease with a propensity for cysts, tumours, and other aberrant developmental conditions as well as multisystem involvement [1]. The essential characteristics of this disease were first identified by Jarisch and White in 1894, who named it 'Nevoid Basal Cell Carcinoma Syndrome'. In 1960, Robert Gorlin and Robert Goltz described various clinical traits of GGS in their publication on "multiple naevoid basal cell epithelioma, jaw cysts, and bifid rib syndrome [2]." In order to prevent maxillofacial abnormalities associated with jaw cysts and to lessen the severity of associated comorbidities, such as brain tumors and basal cell carcinomas, early detection of GGS is crucial. A 15year old girl patient with GGS is the subject of this research. A review of the GGS literature is also included.

Case Presentation
A 15year old girl came with her father to the outpatient department of DR. R. Ahmed Dental College, Kolkata with chief complaint of swelling on right lower jaw region for ten months. She had a positive family history; her brother also had similar type of swelling in lower jaw 5 years ago which was operated back then. On extra-oral examination, ocular hypertelorism found. (Figure1) Examination of skin on palmar and planter surface of both hands and feet showed punctiform brownish mild depression suggestive of palmar and planter pits. (Figure 2, 3) A diffuse, nontender swelling was present on the right cheek region which was hard in consistency. (Figure 4) On intraoral examination the swelling was extending mesiodistally from right deciduous lower second molar to mesial aspect of right permanent first molar region.

Investigations
An orthopantomogram (OPG) showed multiple radiolucent lesions with well-defined margin associated with impacted mandibular second premolar in right side and impacted lateral incisor, canine, first premolar and second premolar on left side. (Figure 5)
Postero-anterior view of chest X-ray showed bifid rib on both right and left side. (Figure 6)
Histopathology of the excised tissue revealed cystic cavity lined by parakeratinized stratified columnar epithelium with corrugated pattern confirmed the diagnosis of odontogenic keratocyst. (Figure 7)

Discussion
Gorlin-Goltz syndrome is a rare hereditary condition with an extremely variable symptom. The prevalence of the disease ranges from 1 in 57,000 to 1 in 2,56,000 [3]. This syndrome is caused due to mutation in PTCH1, a tumor suppressor gene located on chromosome 9q22.32 [4, 5, 6]. The PTCH gene encodes a transmembrane receptor protein that recognizes the Hedgehog (Hh) protein. This signal transduction pathway is called Hedgehog signalling pathway.
This signalling pathway controls various functions, including embryogenesis, maintenance of homeostasis in aged tissues, tissue repair under persistent chronic inflammation, and carcinogenesis. Mammals have three Hedgehog homologues: Desert Hedgehog (DHH), Indian Hedgehog (IHH), and the most studied Sonic Hedgehog (SHH). This internal signalling route is named after a polypeptide ligand, the Hh protein, which is found in Drosophila fruit flies [9]. The transmembrane receptor protein that the PTCH gene encodes is capable of identifying Hedgehog (Hh) protein, which is encoded by SHH, the gene located on chromosome 7q36.3. SHH attaches to the patched1 receptor (PTCH1) after it reaches its target cell. A downstream protein in the pathway called Smoothened (SMO) is inhibited by PTCH1 when there isn't a suitable ligand present. PTCH controls the intracellular location of the protein that regulates SMO. During inactive signalling, the membrane-bound protein PTCH1 keeps smoothened (SMO) in an inactive/unphosphorylated state, making it susceptible to endocytosis and destruction. Consequently, it is unable to activate the GLI proteins, transcription factors necessary for the activation (or repression) of genes dependent on pathways. Furthermore, the corepressor complex's protein suppressor of fused

(SUFU, encoded by the SUFU gene), which adds additional negative control through direct binding, aids in the GLI factors' negative regulation. After hedgehog ligands like sonic hedgehog [SHH], bind to PTCH1, SMO is hyperphosphorylated, and GLI returns to the nucleus. During almost every stage of development, this results in transcriptional changes and a range of downstream effects. Constitutive activation of the hedgehog signalling pathway under pathogenic conditions, caused by variations in critical regulatory proteins, leads to the proliferation of tumour cells.

Diagnostic criteria for nevoid basal cell carcinoma syndrome

Major criteria

1. Basal cell carcinoma before 20 years of age
2. KCOT before 20 years of age
3. Palmar or plantar pitting
4. Lamellar calcification of falx cerebri
5. Medulloblastoma, typically desmoplastic
6. First degree relative with nevoid basal cell carcinoma syndrome

Minor criteria

1. Rib abnormalities
2. Other specific skeletal malformations and radiologic changes (i.e., vertebral anomalies, kyphoscoliosis, short fourth metacarpals,
3. postaxial polydactyly)
4. Macrocephaly
5. Cleft lip or palate
6. Ovarian or cardiac fibroma
7. Lymphomesenteric cysts
8. Ocular abnormalities (i.e., strabismus, hypertelorism, congenital cataracts, glaucoma, coloboma)

Evans *et al*. initially suggested the diagnostic criteria for nevoid basal cell carcinoma syndrome in 1993. Kimonis *et al*. refined them in 1997, and Bree *et al*. updated them in 2011. The diagnosis of can be established based on one of the following criteria, according to the most current publication: (i) one major criterion with genetic confirmation; (ii) two major criteria; or (iii) one major criterion plus two minor criteria

In this present case three major criteria and two minor criteria are present

Major Criteria

1. OKC prior to age 20 years
2. Palmar or plantar pitting
3. First degree relative with Basal Cell Nevoid Syndrome.

Minor Criteria

1. Rib anomalies
2. Ocular abnormality(hypertelorism)

Treatment options for KCOT include conservative measures as well as aggressive ones. When caring for young patients, conservative treatment approaches should always be taken into account because vigorous therapy may negatively affect the development of the affected jaw, the teeth, and the eruption process. To confirm the diagnosis, a histopathological examination of the removed tissue is required. In this instance, Patient received conservative treatment.

Conclusion

The autosomal dominant genetic condition known GGS has multiple diagnostic criteria. While treating this illness requires a multidisciplinary team, the provided case study lends credence to the idea that dentists are crucial to the early diagnosis.

Fig 1

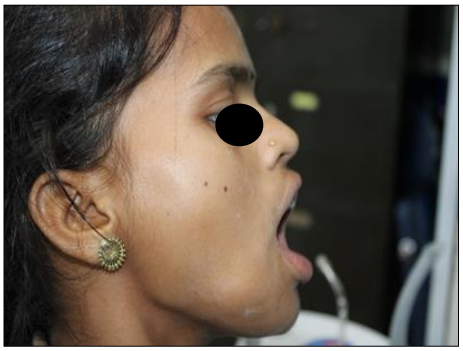

Fig 2

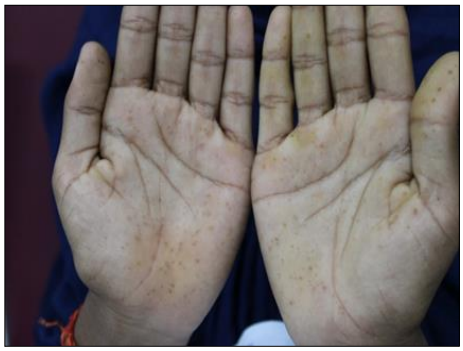

Fig 3

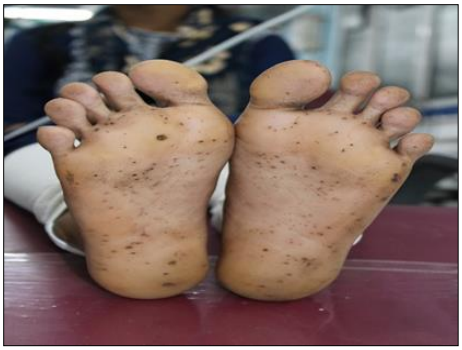

Fig 4

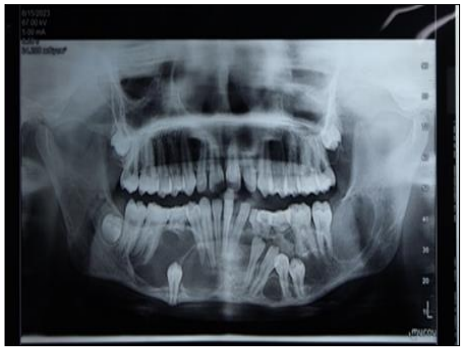

Fig 5

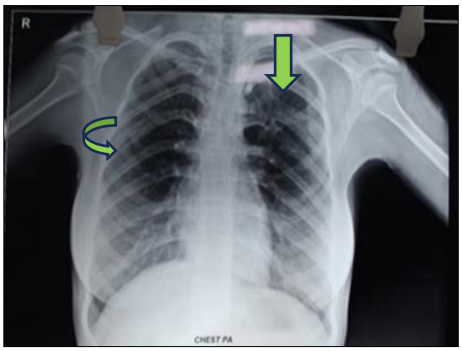

Fig 6

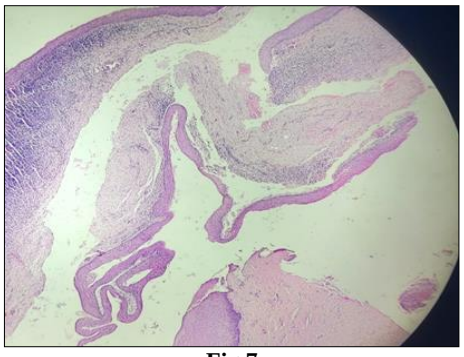

Fig 7

First degree relative showing similar hypertelorism, palmer & planter pits

*All Photographs Are Given After Taking Consent from Patient & Her Family.

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