Nevoid basal cell carcinoma – A case report with familial manifestation

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Abstract
Nevoid basal cell carcinoma syndrome is a rare genetic disorder characterised by multi-organ abnormities such as odontogenic keratocysts in the jaw, skeletal abnormities and multiple basal cell carcinoma etc. Herein, we report a case of nevoid basal cell carcinoma in a 10 year old boy with multiple odontogenic keratocyts of jaw, syndactyly on the left hand, palmar and plantar pits, frontal bossing and whose mother and younger brother also have clinical manifestations of the syndrome. No evidence of basal cell carcinoma seen.

Keywords: Nevoid basal cell carcinoma, Gorlin-Goltz syndrome, Odontogenic keratocyst, KCOT, Multiple OKC.

Introduction
Nevoid basal cell carcinoma syndrome (NBSCC) or Gorlin-Goltz Syndrome is an autosomal dominant inherited disease which is linked to mutations in PTCH, a tumor suppressor gene that was mapped to chromosome 9q22.1−22.33.[1] The existence of this syndrome dates back to dynastic Egyptian times[2] but was compiled as a distinct syndrome by Gorlin and Goltz in 1960 who described the syndrome as the simultaneous occurrence of multiple nevoid basal cell epithelioma, multiple jaw cysts, bifid ribs, and other skeletal anomalies.[3] The estimated prevalence varies from 1 in 57,000 to 1 in 256,000, with a male-to-female ratio of 1:1.[4] In the following report, we discuss about the case of a patient with NBSCC whose mother and younger brother also have the similar condition.

Case Report
A 10 year old boy reported to our institution referred by a private practitioner for the management of bilateral cysts in relation to his lower posterior jaw region, which was noticed in a routine radiograph. The patient was clinically asymptomatic pertaining to the cause of referral. He had no relevant medical history. From the family history, his mother was a diagnosed case of NBSCC fulfilling 2 major diagnostic criteria of 1. Being opertated for multiple odontogenic keratocysts (OKC) in the year 2015 and 2. Presence of palmar and plantar pits (Fig. 1). His younger brother was also evaluated for the same who was fulfilling 3 major criteria of having palmar and plantar pits, bifid ribs and first degree relative with NBCCS; and one minor criteria of having frontal bossing (Fig. 2). He was also operated for a cyst in relation to impacted 23 in July 2019 which was histopathologically diagnosed as Odontogenic Keratocyst. Their parents had a non-consanguineous marriage. On general examination, the patient was moderately built and nourished weighing 20 kgs with the height of 115 cm. No abnormality was detected in his gait and posture. On extraoral examination, macrocephaly was noticed with fronto-occipital head circumference as 55cm; distance between the inner and outer canthus of the eye was 3.5cm and 13cm respectively; frontal bossing was present; nose, eyes, lips and ears were normal and no obvious facial asymmetry was evident. Palmar and plantar pits were present with diffuse distribution. Complete syndactyly of left side middle and ring finger was noted. The overlying skin appears normal. (Fig. 3)

Intra oral examination revealed a mixed dentition with all normal teeth compliments present. No abnormalities were detected in the soft tissues like labial mucosa, buccal nucosa, floor of the mouth, gingival and tongue. No cleft lip or palate present. Fair oral hygiene with mild plaque accumulation. No hypoplasia or microdontia seen in relation to any of the teeth and the dental occlusion was normal.

On radiographic investigation, Orthopantamogram reveals developing permanent teeth at various developmental stage with a well-defined, relatively homogenous unilocular radiolucency in relation to the cemento-enamel junction of unerupted 47 and 37, extending to the entire right and left ramus of the mandible. The developing 48 and 38 are displaced superiorly along the ramus (Fig. 4). PA skull view does not reveal the calcification of falx cerebri. There is no evidence of bridging of sella tursica or fusion of anterior and posterior clenoid process in the true lateral skull view. Hand-wrist radiograph suggests only complete simple sndactyly with soft tissue fusion. PA chest radiograph does not reveal bifid, fused or splayed ribs.

Based on the fulfilment of the diagnostic criteria of NBCCS, clinically inevident but radiographically expanding lesion, the provisional diagnosis was given as Odontogenic Keratocyst. Subsequently the cyst enucleation was done bilaterally along with extraction of 36, 75, 37, 46, 47, 48, under general anaesthesia and chemical cauterisation was done with Carnoy solution.

For histopathological diagnosis the right and left specimens were processed separately. The right side section exhibited odontogenic cystic lining having uniform thickening with features of keratinisation and corrugation towards the luminal side. The basal cells were prominent and with parallel arrangement. The underlying fibrous capsule showed wavy bundles of collagen fibres. The left side section consisted of uniformly lined corrugated and

keratinised lining epithelium with parallel arrangement of basal cells. Some areas exhibited discontinuous epithelium wherein it showed inflammatory features. The capsule was fibrous in nature. Both the right and left specimen were histopathologically diagnosed as Odontogenic Keratocyst (Fig. 5).

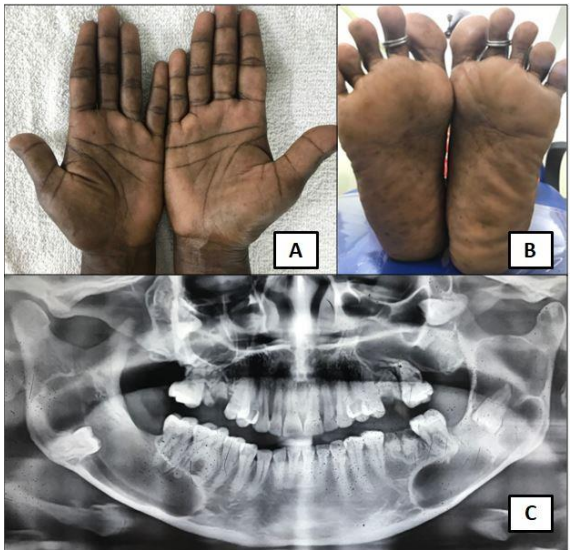

Fig. 1: Syndromic presentations of the mother with **(A):** Palmar pits **(B):** Plantar pits **(C):** Preoperative OPG revealing bilateral Cyst present on the posterior mandible which were histopathologically diagnosed as OKCs. (Operated in 2015)

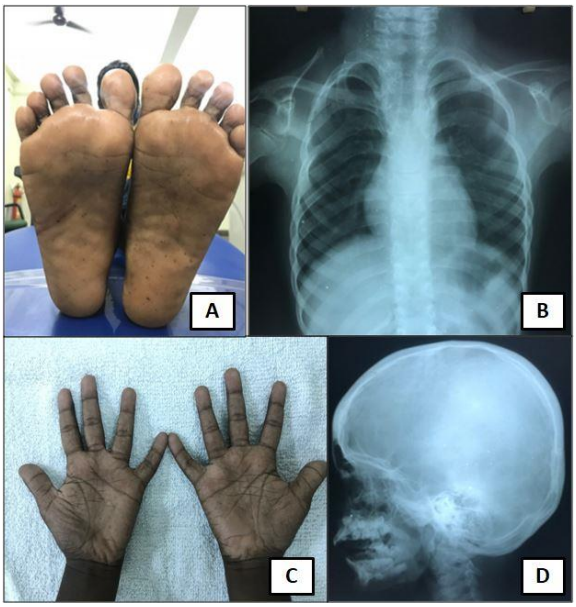

Fig. 2: Syndromic presentations of the sibling with **(A):** Plantar **(B):** Bifid ribs **(C)**: Palmar pits **(D):** Frontal bossing

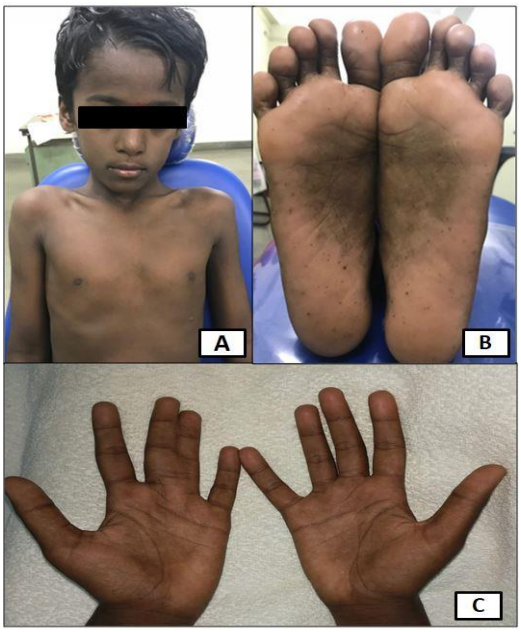

Fig. 3: Clinical presentation of the patient with **(A)**: Profile view exhibiting macrocephaly **(B)**: Plantar pits **(C)**: Syndactyly of left side middle and ring finger

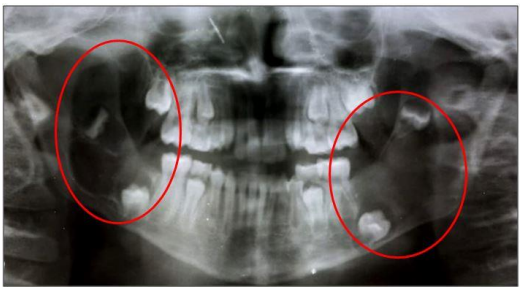

Fig. 4: OPG revealing bilateral unilocular radiolucency involving the entire right and left ramus of the mandible

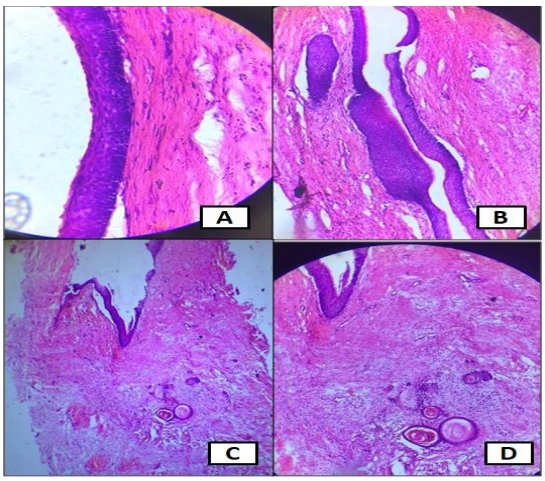

Fig. 5: Histopathology picture showing **(A):** uniform lining epithelium showing keratinisation with hyperchromatic pallisaded basal layer **(B)**: Lining epithelium showing basilar hyperplasia **(C)**: Satellite cysts within the fibrous wall **(D)**: Satellite cysts under 40x

Table 1: Diagnostic criteria for Gorlin-Goltz syndrome (major and minor)

	Diagnostic Criteria	Present Case
Major criteria	Multiple basal cell carcinomas or single, which occur in patients under 20 years of age.	-
	OKCs of the jaws (histologically confirmed).	+
	Plantar or palmar pits (≥three).	+
	Bilamellar calcification of the falx cerebri.	-
	Bifid, fused or markedly splayed ribs	-
	First-degree relative with Gorlin-Goltz syndrome.	+
Minor criteria	Macrocephaly (adjusted for height).	-
	Congenital abnormalities: frontal bossing, cleft lip or palate, moderate or severe hypertelorism, coarse face.	+
	Other skeletal abnormalities: marked pectus deformity, marked syndactyly of the digits, Sprengel deformity.	+
	Radiographical abnormalities: modeling defects of the hands and feet or flame-shaped hands or feet, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, bridging of the sella turcica.	-
	Ovarian fibroma.	-
	Medulloblastoma.	-

Discussion

Nevoid basal cell carcinoma syndrome is also called as Gorlin syndrome, Gorlin-Goltz syndrome, Basal cell nevus syndrome, Fifth phacomatosis, Hereditary cutaneomandibular polyoncosis, Epitheliomatose multiple generalisee, Jaw cysts-basal cell tumors-skeletal anomalies syndrome.[5] The chief manifestations are multiple basal cell carcinomas of the skin, OKCs, intracranial calcification, rib and vertebral anomalies, and intracranial neoplastic change.[1] The syndrome occurs due to the mutation of tumor suppressor PTCH gene. Knudson's suggested a two hit mechanism of the gene where first hit is a germline mutation in PTCH1 gene which results in the characteristic developmental abnormalities associated with Gorlin syndrome and it is followed by a second hit which is somatic inactivating mutation or deletion causing BCC as a result of loss of heterozygosity from the second hit.[6]

Evans et al. in 1993 established the major and minor criteria for the diagnosis of the syndrome, which was further modified by Kimonis et al. in 1997.[7] (Table 1) In the present case, the diasnosis of NBCCS was made on the basis of presence of odontogenic keratocysts of the jaws which were histologically confirmed, palmar and plantar pits and first degree relative with NBCCS (Mother). The minor criteria noted were the presence of frontal bossing and complete syndactyly of left hand middle and fourth finger. Syndrome keratocysts were different from solitary OKCs such that the former were found to have a markedly increased number of satellite cysts, solid islands of epithelial proliferation, odontogenic rests within the capsule, and mitotic figures in the epithelial lining of the main cavity.[8]

The management of NBCCS requires a multi-disciplinary approach. For OKCs of jaw in a young patient, conservative treatment is preferred than the aggressive mode on taking the development of the involved jaw, development of teeth and eruption process into consideration.[9] To decrease the secondary morbidities, careful and periodic observation is required through radiographic imaging, especially during the first year.[10]

Conclusion

The propensity of the patients with NBCCS to develop multiple neoplasms makes it imperative to diagnosis the condition at early stage. Diagnosis at an early stage is important for counseling the patients about the increased risk of developing basal cell carcinoma from the harmful exposure to UV and ionizing radiation and also to prevent further complications by regular multi-disciplinary follow-up. Therefore optimum knowledge is required for the diagnosis and management of the condition by the dental surgeon which would pave way for the better sustenance of the patient.

Source of funding

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Conflict of interest

None.

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