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Case Report

Gorlin-Goltz syndrome: an uncommon case

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ABSTRACT

Nevoid basal cell carcinoma syndrome, or basal cell nevus syndrome (Gorlin-Goltz syndrome), is a rare autosomal dominant inherited disorder which is characterized by multiple basal cell carcinomas from a young age. Other distinguishing clinical features that are seen in a majority of patients, includes keratocystic odontogenic tumors (formerly odontogenic keratocysts) and dyskeratotic palmar and plantar pitting. Estimated prevalence is 1 in 57,000 to 1 in 164,000. We report a case of this syndrome seen in a 43-year-old female patient with multiple black pigmented papules and plaques on face and trunk that first appeared when she was teenager. Her clinical features of were fitting within the criteria for the diagnosis of BCNS. Early diagnosis and treatment of this syndrome is important to reduce severity of complications including cutaneous and cerebral malignancy and oromaxillofacial deformation and destruction due to jaw cysts.

Keywords: Gorlin syndrome, Palmoplantar pits, Nevoid basal cell carcinoma syndrome

INTRODUCTION

Basal cell nevus syndrome (BCNS) is rare disorder which is inherited as autosomal dominant manner. It is characterized by development of early-onset basal cell carcinomas.[1,2] Gorlin and Goltz 1st defined this condition, comprising principal triad of basal cell carcinoma, bifid ribs, and jaw cysts.[3,4] It has been reported that loss of function mutation of human patched gene (PTCH1 gene), which is tumor suppressor gene, located on long arm of chromosome 9 (q22.3-q31) could be molecular origin of syndrome.[5]

Human patched gene (PTCH1 gene) is significant for embryonic structuring and cellular cycle and thus its mutation comprises key event for development of this syndrome.[5] In this case report, gave our experience with patient who presented with multiple basal cell carcinomas and palmoplantar pits and was diagnosed as Gorlin syndrome.

CASE REPORT

A 43-year-old lady presented to the outpatient department with complaints of multiple hyperpigmented lesions over face and trunk for 20 years. These lesions were progressively increasing in size and number. One of them subsequently ulcerated 5 months back (Figure 1 A and B) On examination there multiple hyperpigmented papules and plaques with smooth surface ranging in size from 1×1 to 5×5 cm over face and trunk. There was no family history of similar lesions. Patient also had multiple palmo-plantar pits since last 15 years (Figure 2). No swelling was seen over jaw and in intramural examination. No acrocephaly, hypertelorism, frontal bossing, marfanoid habitus, vertebral and rib abnormality was present. Patient underwent thorough evaluation. The largest pigmented plaque of size 5×5 cm present on the back was excised and sent for histopathological examination which showed large basaloid lobules with cleft formation in between lobules. The stroma is fibromyxoid, (Figure 3 A: 10× H and E stain). The lobules of basaloid cells having retraction artefacts

(Figure 3 B: 40× H and E stain) The CT scan head, USG pelvis came out to be normal. Based on the above findings' diagnosis of Gorlin-Goltz was made as the patient fulfilled 2 major criteria using the Kimonis et al criteria for diagnosis.

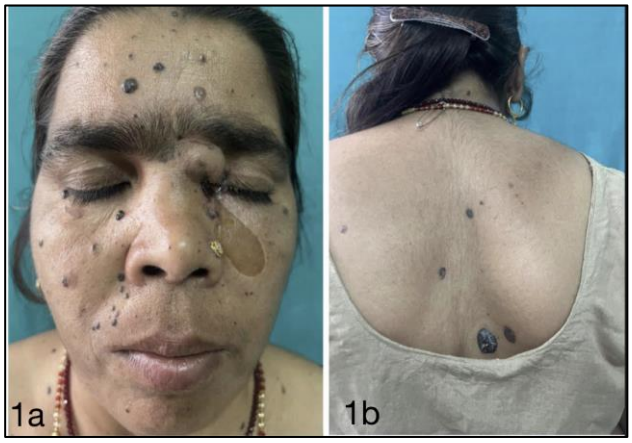

Figure 1 (A and B): Multiple hyperpigmented papules and plaques with a smooth surface ranging from size 1×1 cm to as large as 5×5 cm present over face, trunk and back.

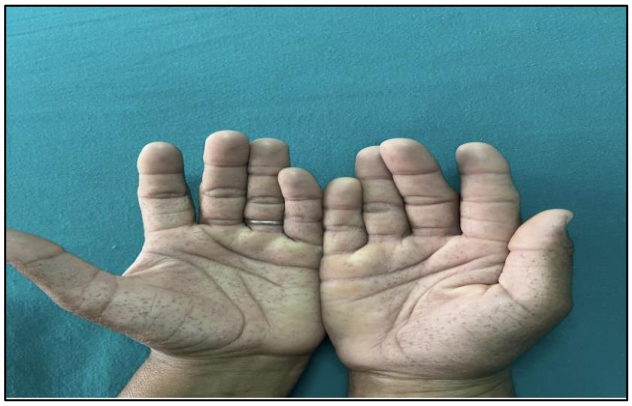

Figure 2: Multiple coarse Palmo-plantar pits.

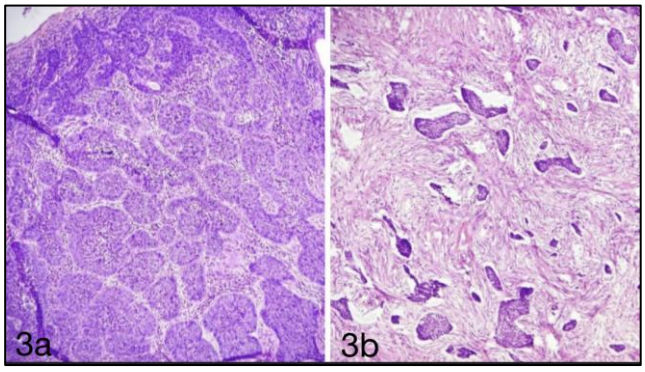

Figure 3 (A and B) (H and E 10X): Histopathological examination showed large basaloid lobules with cleft formation in between lobules. Stroma is fibromyxoid, (H and E 40X) the lobules of basaloid cells having retraction artefacts.

DISCUSSION

NBCCS is a rare autosomal dominantly inherited genodermatosis with variable penetrance characterized by development of cutaneous BCCs from an early age typically puberty, in some cases occurring earlier in childhood.[6] Its development was mainly associated with variations in the PTCH1 gene. PTCH1 regulates the growth of normal tissues and produces a tumor suppression factor.[7] The estimated prevalence is 1 in 57,000 to 1 in 164,000 and no sex predilection.[8] BCCs in an affected individual may be up to 500 in number in a lifetime and are often clinically aggressive, occurring more frequently in lighter pigmented individuals and in populations with higher ultraviolet (UV) light exposure.[8,9] BCCs most commonly occurs on the face, but also appear on the trunk and limbs. [8]

Other well-recognized clinical features, occurring in 70-80% of patients, include keratocystic odontogenic tumour, dyskeratotic palmar and plantar pitting, early calcification of the falx cerebri, rib and spin. Characteristic facial features including frontal bossing, macrocephaly, hypertelorism,, cleft lip and/or palate are also present in a significant number of patients.[8] Although less common, patients are also susceptible to desmoplastic medulloblastoma during childhood, and numerous other neoplasms including rhabdomyosarcomas, ovarian and cardiac fibromas, mesenteric keratocysts, and meningiomas.[8,10] Agenesis of the corpus callosum has also been reported.[6] Although the disease is characterized by high penetrance, individuals display varying levels of expressivity even within families, sometimes making diagnosis challenging.[5]

A diagnostic criterion was put forward by Kimonis et al.[12]

Major criteria

>2 BCCs or 1 BCC in those <20 years, bilamellar calciScation of the falx cerebri, keratocystic odontogenic tumour of the jaw (diagnosed by histopathology), palmar or plantar pits (three or more in number), first-degree relative with NBCCS, Bifold, fused, or markedly splayed ribs were major criteria.

Minor criteria

Macrocephaly, other skeletal abnormalities-Sprengel deformity, marked pectus deformity, and syndactyly of the digits, radiologic abnormalities such as bridging of the sella turcica, hemivertebrae, fusion or elongation of the vertebral bodies, modelling defects, and same-shaped lucencies of the hands and the feet minor criteria.

Congenital malformations such as cleft lip or palate, frontal bossing, coarse facies, and moderate or severe hypertelorism, medulloblastoma and ovarian Sbroma.

To make a diagnosis of NBCCS, the patient should satisfy at least two major or one major and two minor criteria.

Table 1: Differential diagnosis for multiple basal cell carcinomas occurring at an early age.

Disorder	Additional clinical features
Bazex-Dupré-Christol syndrome	Hypotrichosis, follicular atrophoderma primarily occurring on the dorsum of the hands (no skeletal or extracutaneous developmental abnormalities)
Rombo syndrome	Follicular atrophoderma occurring on the elbows and cheeks, generalized cyanotic erythema
Excess UV exposure	Skin neoplasia only without features of a heritable syndrome
Xeroderma pigmentosum	Freckle-like hyperpigmentation, squamous cell carcinoma, melanoma, malignancies of internal organs, neurologic abnormalities

Histopathology

BCCs developing in NBCCS are histologically indistinguishable from sporadically occurring lesions. A histologic clue that is suggestive of, but probably not specific for NBCCS is the presence of multiple incidental minute buds of early superficial BCC in otherwise unremarkable skin of an excision for BCC. BCCs in NBCCS exhibit a range of histologic patterns, including nodular, superficial, and infiltrative types.

The treatment of BCNS requires a multidisciplinary approach due to its various clinical manifestations. Various treatments for BCNS have been suggested, no ideal treatment exists. Previous studies have focused on surgical excision using the standard or Mohs technique.[13]

Topical treatment options include 5 FU and imiquimod.

Vismodegib, that binds to and directly inhibits SMO was recently FDA approved for recurrent, locally advanced, or metastatic basal cell carcinoma.[14]

CONCLUSION

In summary, NBCCS is a rare disease that is difficult to diagnose and treat early. If suspected, various tests and evaluation should be done at an early age, along with annual follow ups. In addition, family members of patients diagnosed with NBCCS should undergo genetic testing.

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