case report

Skin tags as a presenting sign of basal cell nevus syndrome in three sisters of the same family

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Basal cell nevus syndrome (BCNS), which is also known as nevoid basal cell carcinoma, Gorlin's syndrome, and MIM 109400 (Mendelian Inheritance in Man), is an autosomal dominant genodermatosis characterized mainly by the presence of multiple basal cell carcinomas (BCCs), jaw cysts, and palmoplantar pits.[1] It was first described by Jarish and White in 1894,[1] but its syndromic nature was not defined until 1960 by Gorlin and Goltz.[2] The PTCH 1 gene, the human homologue of the Drosophila patched polarity gene, has been shown to be involved in the development of BCNS[3-5] with some cases appearing as spontaneous mutations of the same gene.[6] In this article we describe three sisters of different ages with an almost exactly identical presentation. Their main complaint was multiple skin tag-like papules on the skin.

Case 1

A 10-year-old girl presented to the dermatology clinic with a complaint of an increasing number of skin tags since the age of 4 (Figure 1, 2). Many dermatologists had seen her and the condition was misdiagnosed as skin tags, warts, and nevi. No skin biopsy had been done before from the skin tags. The medical history revealed hydrocephalus since birth for which she had undergone a shunt operation. She had borderline mental retardation with learning disability; she was still in the first grade. Physical examination showed multiple skin-colored to brownish soft papules; some were pedunculated, located on the face, neck, trunk, axillae and extremities. She had multiple small 0.5-1 mm palmoplantar pits. She also had characteristic phenotypic abnormalities: macrocephaly, bossing of the skull, a broad nasal root, ocular hypertelorism, scleral melanocytosis, high arched palate, uplifting of the nose, and narrow sloping shoulders. Other aspects of the physical examination were unremarkable. Radiological examination of the skull revealed hydrocephalus, calcification of the falx cerebri in addition to the ventriculoperitoneal shunt tube. X-ray of the hands revealed shortening of the fourth metacarpal bone. Other aspects of the radiographic survey were unremarkable. Panoramic x-ray of the mandible revealed no jaw cysts. A skin biopsy found follicular basal cell carcinoma (BCC) (Figure 3).

The patient was treated by snipping off those pedunculated lesions followed by cryotherapy to the base to

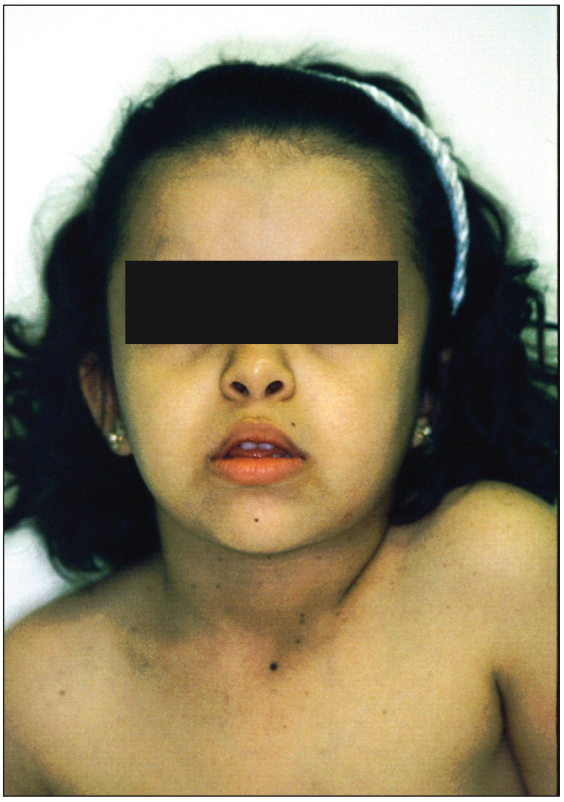

Figure 1. Case 1 showing characteristic phenotype with bossing of the skull, hypertelorism, broad nasal root, up-lifting of the nose, and a few dark brown skin tag-like lesions on the face and neck.

minimize scarring. In addition, the patient was provided with photoprotection and genetic counseling.

Cases 2 and 3

An 8-year-old sister of the patient described in case 1 presented in exactly the same way with skin tags, hydrocephalus, a shunt operation, characteristic facies and palmoplantar pits. She was dropped from school because of poor performance. A 6-year-old sister of the previous 2 patients, presented with only multiple skin tags and palmoplantar pits. There was no hydrocephalus yet she had a characteristic facies as well. Cases 2 and 3 did not come back for further investigation. The parents were first-degree relatives, but there were no similar problems in them or in their families.

DISCUSSION

BCNS is a genodermatosis transmitted as an autosomal dominant trait exhibiting high penetrance and variable expressivity, mapped to chromosome 9q22.3-31.[7,8] Inherited or spontaneous mutations in the human homologue of the Drosophila patched gene underlie the disorder.[7] The diagnosis of BCNS relies mostly on the clinical features. Table 1 summarizes both major and minor features of this syndrome.[9] For diagnosis we need at least two major features, or one major feature and an affected first-degree relative or two minor features and an affected first-degree relative, or multiple BCCs in childhood.[6,10,11]

The main complaint of the patients was the presence of multiple skin tag-like papules that were increasing in number. Skin tags are benign fibroepithelial polyps and are distinctly uncommon in this age group. Our cases developed many of the features of this syndrome early in life, with hydrocephalus, characteristic facie, palmo-

Table 1. Diagnostic criteria of basal cell nevus syndrome.[6,9-11]

Major features
Multiple basal cell carcinomas
Basal cell carcinoma before age 20
Odontokeratogenic cysts confirmed by histology
Palmar or plantar pits (>3)
Bilamellar clarification of falx cerebri
Positive family history
Minor features
Congenital skeletal anomaly
Macrocephaly
Cardiac or ovarian fibroma
Medulloblastoma
Lymphomesenteric cysts
Congenital malformations

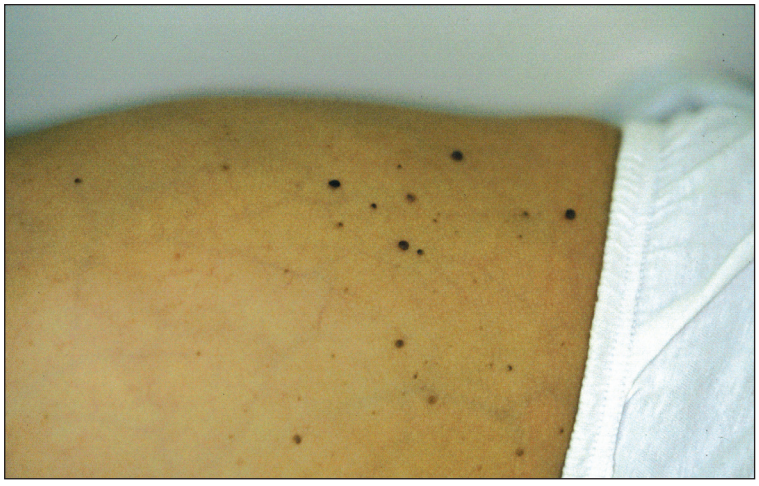

Figure 2. Same case with multiple dark brown skin tag-like papules on the back.

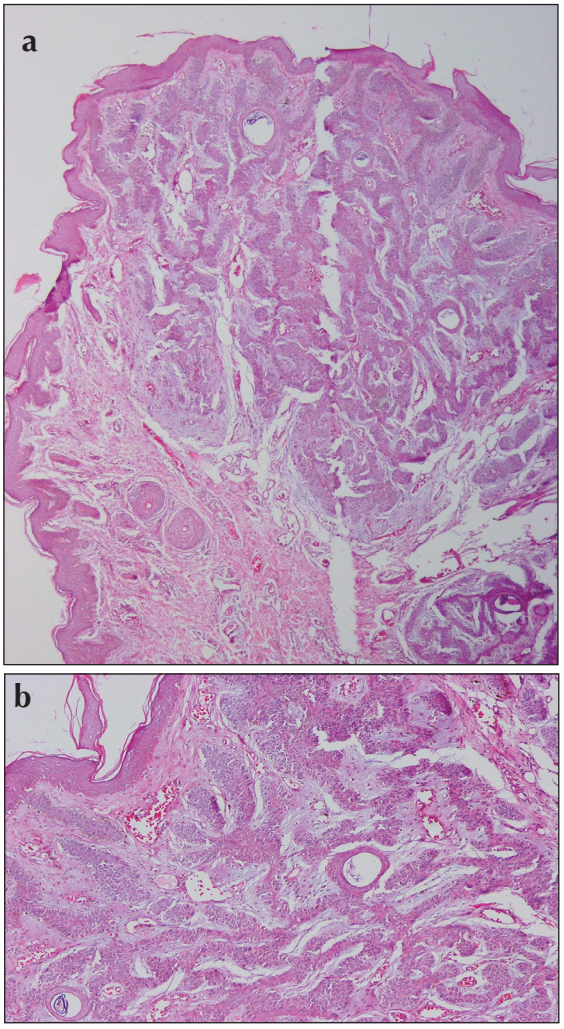

Figure 3. (a,b) Basal cell carcinoma, follicular type from Case 1. (Hematoxylin-eosin stain)

plantar pits, and skin tag-like lesions being among the early manifestations. Despite the fact that they were not twins, they developed almost exactly the same features. Nomland described skin tags in association with this syndrome and used the term "nevus of basal cell".[12] Elvira Chiritescu et al described 7 children with the same presentation. Multiple skin tags in this age group could represent an early sign for BCNS.[11] The first case also had scleral melanocytosis, which had not been reported before with BCNS; whether it is part of the syndrome or just an isolated finding is not known.

BCCs develop much more in sun-exposed areas,[13,14] especially the head and neck. Thus, a high index of suspicion and early detection of this syndrome could help in the proper management of those cases. Early use of sunscreen could decrease the number of BCCs and/or prevent aggressive growth.

Patients with BCNS should be followed closely and therapy must be directed at the individual lesions as they arise, most importantly tumors. BCCs could be treated with different modalities, cryotherapy being the least scarring. Delta-aminolevulinic acid and blue light photodynamic therapy and 5-aminolevulinic acid photodynamic therapy were reported to be successful in the treatment of multiple BCCs in BCNS with an excellent cosmetic outcome.[15,16] Other modalities of treatment include electrocautery, excisions, topical imiquimod,[17] and CO_2 laser resurfacing.[18] Genetic counseling is important as the disease is autosomal dominant and any child of an affected family is at 50% risk of carrying the affected gene and developing the disease.[19-22] In conclusion, we need to have a high index of suspension to diagnose these rare syndromes as early diagnosis and genetic counseling could prevent major consequences.

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