Infantile-onset palmo-plantar basal cell carcinomas and pits in Gorlin syndrome

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INTRODUCTION

Gorlin syndrome (also known as nevoid basal cell carcinoma syndrome [NBCCS]) is caused by an autosomal-dominant mutation in patched tumor suppressor genes 1 and 2 (PTCH1, PTCH2), or suppressor of fused homolog (SUFU) genes, involved in the hedgehog pathway. It carries a variable expressivity¹ and manifests with a typical facies (macrocephaly, frontal bossing, coarse features, hypertelorism), palmo-plantar pits, multiple basal cell carcinomas (especially of the face, back, and chest¹), and a propensity for other tumors (medulloblastomas, cardiac, and ovarian fibromas), among other features.

Few cases are described of basal cell carcinomas (BCCs) developing in a palmo-plantar distribution in patients with Gorlin syndrome.² Moreover, to date, only 2 patients with the syndrome have been reported as having early-onset acral BCCs.³ The following case aims to enrich the current literature of this rare manifestation of Gorlin syndrome and suggests contiguity between palmo-plantar pits and BCCs of the same distribution.

CASE

A 14-month-old girl, with no personal medical history or pertinent familial medical history of this condition, presented with asymptomatic palmo-plantar papules, many of which were congenital. Examination found dozens of erythematous, 2- to 3-mm, sometimes edematous papules located on the palms, lateral fingers, and soles. Some were slightly crusted, hyperkeratotic, or eroded (Figs 1 and 2). On dermoscopy, arborizing microtelangectasias were observed in some. Subtle palmo-plantar pits were also noted. The rest of the physical examination found subtle hypertelorism, frontal bossing, and bilateral third toe underlapping.

Through follow-up, every 4 to 6 months, it was noted that some papules had either spontaneously regressed or diminished in size, often adopting the appearance of palmo-plantar pits. Accordingly, over a 1-year period, about one-third of the initial lesions had changed aspect. It was also noted that new papules had developed at other sites on the palmo-plantar surfaces (Fig 3).

Two papules on the fingers, clinically compatible with BCC, were treated surgically, whereas the others were observed clinically. Biopsy found a dermal tumor composed of basaloid cells consistent with a basal cell carcinoma (Fig 4). Genetic testing found a mutation in the PTCH1 gene of the c.3404T>C variant.

DISCUSSION

To date, only 2 cases of Gorlin syndrome with early-onset acral BCCs have been reported. These 2 young patients did not have the same mutation, revealing no genotype-phenotype correlation.³ The

Abbreviations used:
BCC: basal cell carcinoma
PTCH: patched tumor suppressor
SUFU: suppressor of fused homolog
specific mutation in the present case did not correspond to the previous variants either. Thus, early-onset acral BCCs (appearing at birth or infancy) should be considered an initial manifestation of Gorlin syndrome.3 This case supports this hypothesis. Furthermore, this case suggests that palmo-plantar pits, traditionally known to appear in the second decade of life,4 may also be considered an initial manifestation of NBCCS.

Earlier literature proposed that palmar pits were an attenuated form of BCC, a *forme fruste*.1 Many reports described a second hit, such as radiation therapy to the palms, before development of carcinoma.1 It has since been suggested that basaloid cell nests, histologically similar to BCCs, reside within palmo-plantar pits5 but remain a different clinical entity.6 Palmo-plantar pits were previously reported as being quiescent, nonevolutive.7 In this case, however, the fact that nodular BCCs were limited to the palms and soles (atypical locations) of an infant (without a possible second hit), along with the presence of palmo-plantar pits, strongly suggests that pits may indeed represent early BCC. In complement to this premise, considering its striking evolution, this case suggests a pathologic continuum between pits and BCCs. One could hypothesise that palmo-plantar pits may become inflamed and resemble BCCs, and as inflammation regresses, the residual clinical image may be one of a pit or may give change for regression of the entire lesion. The key factors determining whether a lesion presents as a pit or a papule and explaining the evolution from one form to another and the implications for tumor surveillance of these findings remain to be elucidated.

Fig 1. Right hand, photographed at 14 months of age, shows multiple small erythematous papules and discrete palmar pits.

Fig 2. Right foot, photographed at 14 months of age.

Fig 3. Right foot, photographed at 23 months of age, shows variation in the number of papules and pits.

Fig 4. Histopathology from a shave biopsy of a papule of the fourth finger of the right hand shows BCC.
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