

# 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 expressivity<sup>1</sup> 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 chest<sup>1</sup>), 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.<sup>2</sup> Moreover, to date, only 2 patients with the syndrome have been reported as having early-onset acral BCCs.<sup>3</sup> 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

### Abbreviations used:

BCC:	basal cell carcinoma
PTCH:	patched tumor suppressor
SUFU:	suppressor of fused homolog

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.<sup>3</sup> The

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



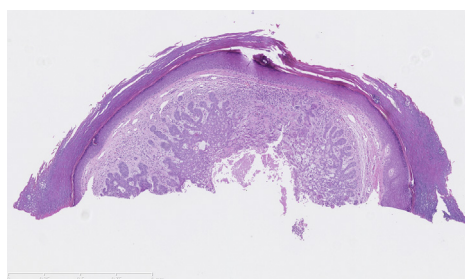
**Fig 2.** Right foot, photographed at 14 months of age.

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.<sup>3</sup> This case supports this hypothesis. Furthermore, this case suggests that palmo-plantar pits, traditionally known to appear in the second decade of life,<sup>4</sup> may also be considered an initial manifestation of NBCCS.

Earlier literature proposed that palmar pits were an attenuated form of BCC, a *forme fruste*.<sup>1</sup> Many reports described a second hit, such as radiation therapy to the palms, before development of carcinoma.<sup>1</sup> It has since been suggested that basaloid cell nests, histologically similar to BCCs, reside within palmo-plantar



**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.

pits<sup>5</sup> but remain a different clinical entity.<sup>6</sup> Palmo-plantar pits were previously reported as being quiescent, nonevolutive.<sup>7</sup> 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 hypothesize 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.

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