Management of pedal fibrovascular papillomas in Goltz-Gorlin syndrome

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INTRODUCTION

Focal dermal hypoplasia, also known as *Goltz-Gorlin syndrome* (GGS) or *Goltz syndrome*, arises from a rare genetic abnormality in the WNT/β-catenin signaling pathway first described by Goltz et al in 1962.[1] Molecularly, Goltz syndrome is caused by a mutation or deletion in *PORCN* that occurs sporadically or through X-linked dominant inheritance. We report on a 17-year-old patient who presented to our clinic with extensive papillomas on her right foot and focal dermal hypoplasia. The papillomas were a source of significant pain and prevented our patient from wearing adequate footwear. She was referred to plastic surgery for excision and skin grafting because of persistent symptoms that were not adequately controlled by topical therapy. We report this case because of paucity in the literature for this cutaneous finding and lack of reports for management.

CASE REPORT

A 17-year-old white girl with a history of GGS and a 10-year history of papillomatous growths on the right foot was referred to the Department of Dermatology at the University of Texas Medical Branch. On clinical examination, erythematous verrucous papillomas were present on the right foot on the medial, lateral, and plantar surface of the third toe and on the medial surface of the fourth toe (Fig 1, *A*). Examination of the head found low-set ears, strabismus affecting the left eye, and malocclusion with dystrophic and absent teeth. Ophthalmic examination found colobomas of the iris and retina on the left side. The patient's left hand had 5 digits, and the right hand had 4 digits with bilateral pollicization* surgeries and syndactyly releases. Skin examination found diffuse linear atrophic streaks present on the thighs bilaterally, diffuse 1-cm patches of atrophic dermis present on both legs, and onychodystrophy (Fig 2, *A* and *B*). Histologic examination of the papillomas present on the distal and proximal plantar surface of the right third toe showed an inflamed squamous papilloma without evidence of malignancy.

Abbreviation used:

GGS: Goltz-Gorlin syndrome

The patient opted for surgical management comprising near full-thickness excision of the papillomas with subsequent 2- × 4-cm split-thickness skin graft transferred from the right thigh (Fig 1, *B*). At 6-month follow-up, our patient had no recurrence of the lesions and was pain free.

DISCUSSION

The molecular pathology resulting in GGS was elucidated in 2007 when deletions of *PORCN (Xp11.23)* were detected in 2 females.[2] The gene product is a putative membrane-bound O-acetyltransferase found to be involved in the processing and secretion of Wnt proteins, important signaling molecules in embryogenesis and carcinogenesis.[3] Although the implicated gene has been identified, there has yet to be a definitive link between genotype and phenotype. In their 2011 mutation update, Lombardi et al[4] published their *PORCN* variation database, which currently contains 119

*Hand surgery technique to form a thumb from an existing digit, typically the index finger.

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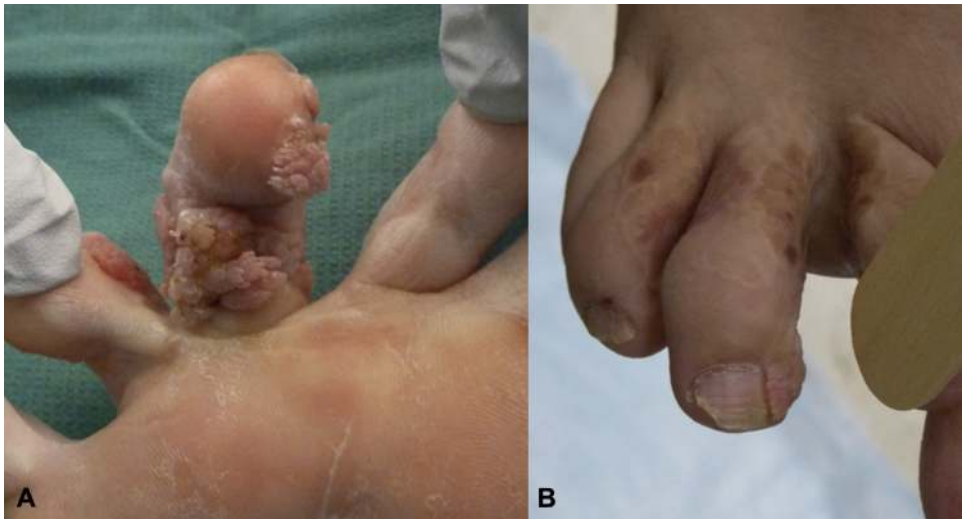

Fig 1. Goltz-Gorlin syndrome. **A**, Multiple macerated fibrovascular papillomas on the right third and fourth toes. **B**, Postoperative follow-up after split-thickness skin grafting.

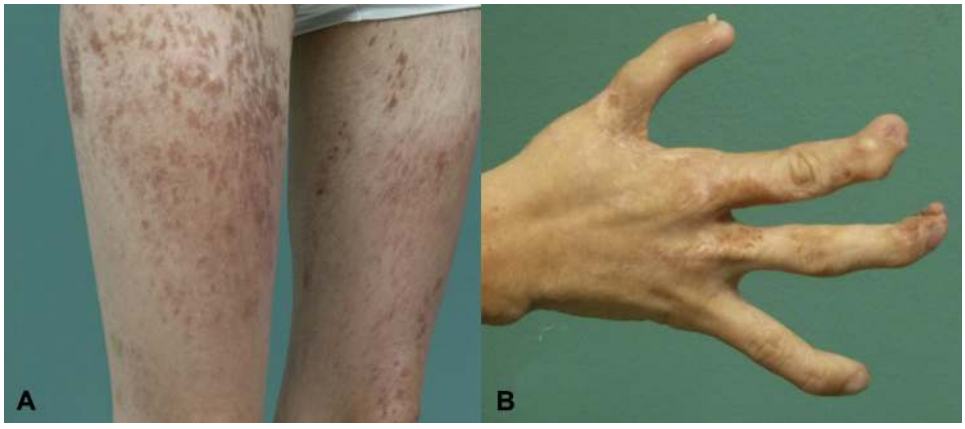

Fig 2. Goltz-Gorlin syndrome. **A**, Bilateral linear hyperpigmented atrophic patches on the legs following a Blaschkoid distribution. **B**, Right hand shows ectrodactyly.

PORCN anomalies comprising 105 mutations and 14 gene rearrangements.

The wide range of physical manifestations echoes the variability of genetic lesions resulting in GGS. Although the amount of functional *PORCN* required for embryonic viability has yet to be studied, it is thought that the physical variability is related to lyonization in females; however, physical variability in males has been attributed to tissue mosaicism, as nonmosaic males show true embryonic lethality.[5]

Clinical diagnosis of focal dermal hypoplasia is possible based on previously described cutaneous and systemic abnormalities, but diagnostic gene sequencing of *PORCN* may confirm the presence of this condition.[6] Typical findings in GGS are asymmetric atrophic hypo-/hyperpigmented linear streaks along the lines of Blaschko on the trunk or extremities, mucocutaneous papillomas, skeletal abnormalities (ectrodactyly, syndactyly, polydactyly, oligodactyly), and eye abnormalities (strabismus, coloboma, microphthalmia).[7] Less common features seen in GGS are intellectual impairment (15%); auditory defects; microcephaly; cleft lip/palate; hypoplastic kidneys; umbilical, inguinal, epigastric, or diaphragmatic hernias; and congenital heart diseases such as truncus arteriosus.[8]

Our patient had multiple fibrovascular papillomas on the right foot. Previous reports of GGS showed recurrent periorofacial, perineal, vulvar, and perianal distributions of papillomas as well as esophageal papillomatosis.[9] Extremity papillomas in the setting of focal dermal hypoplasia sparsely populate the literature, and their management has not been established. One case report described treatment of recurrent cutaneous papillomas with cryotherapy; however, the papillomas continued to recur.[10] The

papillomas found on our patient are of similar morphology to the papillomas discussed in the literature; however, in this case their pedal distribution created a nidus for infection and necessitated further management. Currently, it is unclear if surgical excision is superior to cyrotherapy in preventing papilloma recurrence, although our patient did not show recurrence at 6 months.

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