Pachyonychia Congenita: A Case Report

Nita Kohli, MD, MPH

A 21-year-old man presented with hypertrophic nail dystrophy and subungual debris of all 20 nails, hyperkeratotic plaques on the heels of both feet, and oral leukokeratosis. He had an extensive family history of similar clinical findings. The patient's clinical presentation and history were consistent with pachyonychia congenita (PC), an autosomal dominant genodermatosis caused by mutations in the genes for keratin 6, K6a *and* K6b; *keratin 16,* K16; *and keratin 17,* K17.

Cutis. 2009;84:269-271.

Case Report

A 21-year-old man was referred from primary care to the dermatology clinic for bilateral nail thickening of the hands and feet that was present since birth. The patient was given a trial of terbinafine hydrochloride tablets by his primary care physician for presumed onychomycosis, but the treatment failed. He had a family history of the same disorder in his mother, grandfather, aunt, and 3 cousins. The patient also reported blistering easily and some hyperhidrosis. He was otherwise healthy, had no surgical history or allergies, and did not smoke or drink.

On physical examination, the patient had poor dentition and a geographic tongue with a small 3-mm white plaque on the right lateral tongue (Figure 1). He had hypertrophy of all nails on the hands and feet (Figures 2 and 3). Yellow, thick, hyperkeratotic plaques were present on the heels and pressure points of both feet with some blistering on the posterior heels (Figure 4). Follicular hyperkeratosis of the cheeks and shoulders also was present. A diagnosis of pachyonychia congenita (PC) was made, and the patient was educated on the disease.

Dr. Kohli was from Kinser Medical Branch Clinic, Okinawa, Japan, and currently is at the Department of Family Medicine, Division of Occupational and Environmental Medicine, University of California, Los Angeles.

The author reports no conflict of interest.

Correspondence: Nita Kohli, MD, MPH (nkohli@mednet.ucla.edu).

After he was satisfied with the information provided, he was then referred to the PC Project Web site (www.pachyonychia.org) for both support and more information.

Comment

Pachyonychia congenita is an autosomal dominant genodermatosis linked to mutations in the genes encoding keratin 6, *K6a* and *K6b;* keratin 16, *K16;* and keratin 17, *K17*.[1] The condition is a rare form of palmoplantar keratoderma and fewer than 300 cases have been reported worldwide.[2] It can affect all races and equally affects both sexes. The lesions are not life threatening but can be disfiguring. Affected nails usually are present at birth.

There are 2 types of PC (Table). The classic type 1 (Jadassohn-Lewandowski syndrome) is the most common variant and is due to mutations of the *K6a* and *K16* genes that disrupt assembly of the keratin filament.[2] Nail dystrophy is the most salient feature; all fingernails and occasionally toenails are thickened with a brownish gray nail plate projecting upward at the free edges over a mass of subungual keratotic debris.[3] Paronychial inflammation may result in shedding of the nails. Other features include palmoplantar keratoderma, which may be associated with blisters and hyperhidrosis in the hyperkeratotic areas; follicular hyperkeratosis on the face, elbows, and knees; and oral leukokeratosis, which consists of patchy whitish areas on the posterior tongue, buccal mucosa, and gingiva.[2,3]

Pachyonychia congenita type 2 (Jackson-Lawler type) is associated with mutations in the *K6b* and *K17* genes. Symptoms are similar to PC type 1; however, there is increased evidence of cyst formation (steatocystoma multiplex) and natal teeth in PC type 2.[4] Hair anomalies, such as unruly, coarse, or twisted hair, also have been described.[2,4] Other findings in patients with PC types 1 and 2 include hoarseness or laryngeal involvement, corneal opacities, and cataracts; the latter two are rare.

Laboratory and Histologic Findings—DNA analysis reveals deletion, substitution, and other mutations of *K6a, K6b, K16,* and *K17* genes.

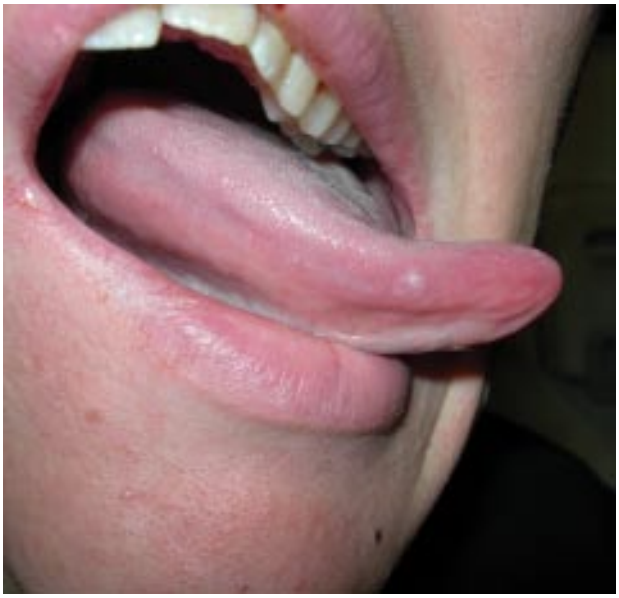

Figure 1. Leukokeratosis plaque on the tongue.

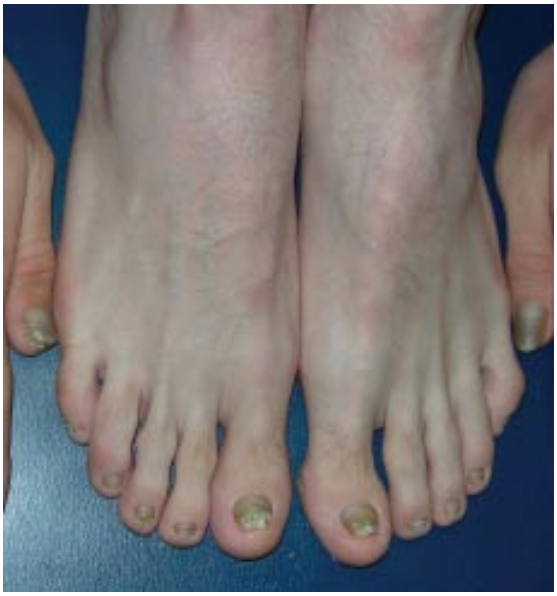

Figure 2. Hypertrophic nail dystrophy.

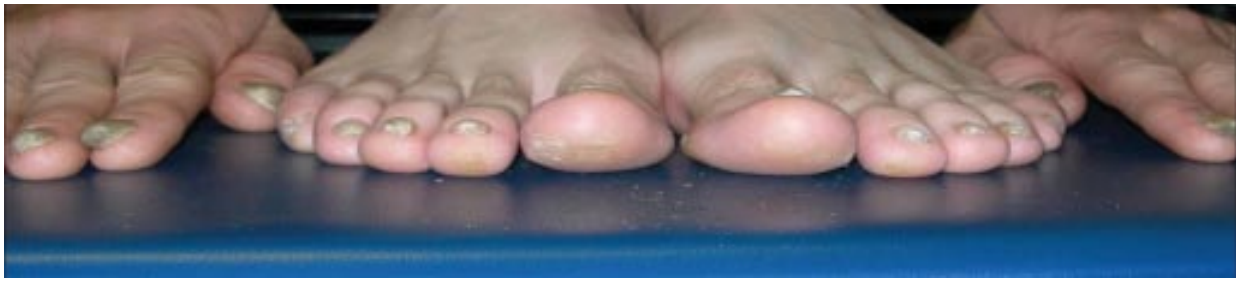

Figure 3. Nail thickening with subungual debris.

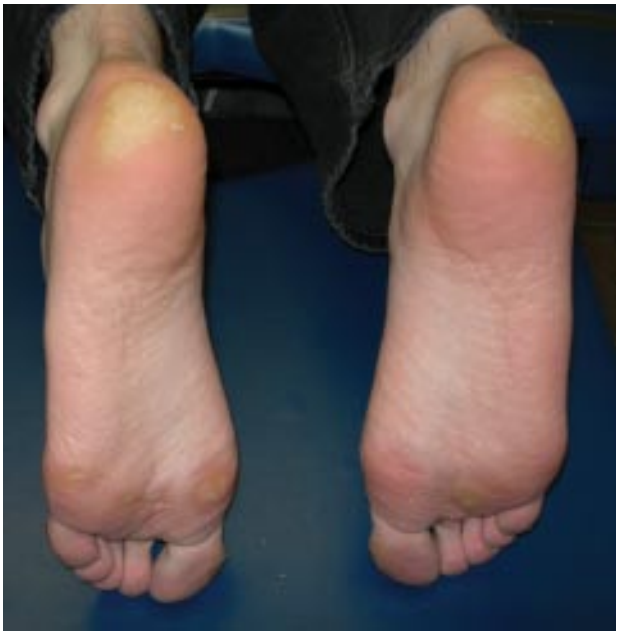

Figure 4. Plantar keratoderma.

Histology shows acanthosis, hyperkeratosis, and parakeratosis. Electron microscopy performed on palmar or plantar skin samples illustrates thickened, clumped, intermediate filaments and enlarged keratohyalin granules.[2]

Treatment—There are no ideal therapies for PC. Available therapeutic options are directed at specific manifestations of the disease. The goals of treatment are to address the major manifestations of the disease, including excess accumulation of keratin in the nail unit, skin, or mucous membranes; blisters and pain associated with them in hyperkeratotic areas; and keratin cysts in the dermis.[5]

Thickened nail plates can be softened with salicylic acid 20% or urea 20% and salicylic acid 10% in hydrophilic ointment with occlusion at weekly intervals, which promotes removal of excess keratin in hyperkeratosis.[2] After softening, the nail plate can be scraped by the patient using a variety of tools, such as pumice stones, emery boards, paring knives, clippers, curettes, or razor blades.[5] A formulation

Classification of Pachyonychia Congenita

	PC Type 1 (Jadassohn-Lewandowski Syndrome)	PC Type 2 (Jackson-Lawler Type)
Gene mutation	*K6a, K16*	*K6b, K17*
Clinical findings	Nail dystrophy, PPK, follicular hyperkeratosis, oral leukokeratosis	Similar to PC type 1 but increase in steatocystoma multiplex, natal teeth, hair anomalies

Abbreviations: PC, pachyonychia congenita; K, keratin; PPK, palmoplantar keratoderma.

of fluorouracil 5% applied twice daily after scraping can help inhibit cell proliferation of the nail matrix. Systemic treatment with retinoids in a dosage of 1 mg/kg daily is somewhat effective in that the nail plate becomes thinner and smoother, and retinoids have been shown to improve hyperkeratotic skin lesions.[2,6]

Surgical approaches include removing the affected nails; however, unless the nail bed is ablated, the nails regrow with the abnormality. Electrofulguration, deep curettage, and excision followed by an autograft from an unaffected site have been more successful in nails than on the palms or soles.[5]

Hyperhidrosis has been treated with aluminum chloride, which also reduces blistering.[7] A glutaraldehyde 2% topical solution also can be used for plantar hyperhidrosis as well as hyperkeratotic plantar lesions.[8] One study found that plantar injections of botulinum toxin reduced pain and hyperkeratosis in 3 patients.[5] The ideal solution would be a gene therapy procedure to replace the defective PC gene. A recent clinical trial showed clinical response with intralesional injections of a mutation-specific small interfering RNA (siRNA), TD101; however, due to the intolerable pain from these injections, further research is needed in developing technologies to deliver nucleic acids to the skin.[9] Another study using oral sirolimus in 3 patients with PC showed therapeutic response in callus quality and reduction in painful cutaneous thromboses; however, the study ended due to side effects of the medication.[10]

Because the manifestations of PC can be disabling or disfiguring, attention also must be given to pain and depression as part of the overall treatment plan. A psychiatry consultation may be necessary. In addition, the patient should be told that because PC is an autosomal dominant condition, it can affect one-half of his/her offspring.

REFERENCES

1. Strober BE. Pachyonychia congenita, type II. *Dermatol Online J*. 2003;9:12.
2. Kansky A. Pachyonychia congenita. *Emedicine* [serial online]. http://emedicine.medscape.com/article/1106169-overview. Updated March 23, 2007. Accessed October 24, 2009.
3. Behrman RE, Kliegman RM, Jenson HB. *Nelson Textbook of Pediatrics*. 17th ed. Philadelphia, PA: Saunders Co; 2004.
4. Leachman SA, Kaspar RL, Fleckman P, et al. Clinical and pathological features of pachyonychia congenita. *J Investig Dermatol Symp Proc*. 2005;10:3-17.
5. Milstone LM, Fleckman P, Leachman SA, et al. Treatment of pachyonychia congenita. *J Investig Dermatol Symp Proc*. 2005;10:18-20.
6. Lim TW, Paik JH, Kim NI. A case of pachyonychia congenita with oral leukoplakia and steatocystoma multiplex. *J Dermatol*. 1999;26:677-681.
7. Tidman MJ, Wells RS. Control of plantar blisters in pachyonychia congenita with topical aluminum chloride. *Br J Dermatol*. 1988;118:451-452.
8. Cardinali C, Torchia D, Caproni M, et al. Case study: pachyonychia congenita: a mixed type II–type IV presentation. *Skinmed*. 2004;3:233-235.
9. Kaspar RL, McLean WH, Schwartz ME. Achieving successful delivery of nucleic acids to skin: 6th Annual Meeting of the International Pachyonychia Congenita Consortium. *J Invest Dermatol*. 2009;129:2085-2087.
10. Hickerson RP, Leake D, Pho LN, et al. Rapamycin selectively inhibits expression of an inducible keratin (K6a) in human keratinocytes and improves symptoms in pachyonychia congenita patients. *J Dermatol Sci*. 2009;56:82-88.