Nail removal in pachyonychia congenita: Patient-reported survey outcomes

To the Editor: Pachyonychia congenita (PC), a genodermatosis characterized by onychodystrophy and painful palmoplantar keratoderma, is caused by mutations in several keratin genes (*KRT6A, KRT6B, KRT6C, KRT16, KRT17*). The nail dystrophy may cause pain, infection, and functional and psychosocial impairment.[1] Prior studies on nail removal are limited.[2,3]

To assess the value of nail removal in PC, we performed a retrospective survey of patients enrolled in the International Pachyonychia Congenita Research Registry (IPCRR). The study was approved by the Western Institutional Review Board.

Of 538 patients in the IPCRR, 25 had nails removed; key results from the 18 who responded to a questionnaire are described in Table I. Six individuals had both fingernails and toenails removed, 3 only fingernails, and 9 only toenails. A variety of chemical and surgical techniques were used to prevent nail regrowth. Prevention of nail regrowth was more complete for toenails than fingernails. Of the 91 toenails removed, 35 never grew back, 28 partially regrew, 18 grew back completely, and 10 had unknown regrowth status. Of 18 individuals, 13 indicated they would recommend nail removal to others with PC and most commonly cited reduction of pain or tenderness as the reason. Absence of nail regrowth seemed to influence that opinion: 8 of 9 patients who had at least 1 nail showing no evidence of regrowth would recommend removal to others.

Regarding toenails, the majority of patients indicated that pain and risk of injury were better after the procedure than before. With regard to infection, function, care, and appearance, the majority of patients reported results being the same or better than before the procedure. Fig 1 illustrates postprocedure clinical findings and degree of patient satisfaction.

Table I. Nail removal in pachyonychia congenita

Patient	Gene	Mutation	Sex	Age when nails removed, y	Age when questioned, y	Procedure to prevent regrowth	Fingernail regrowth (no. of nails)	Toenail regrowth (no. of nails)	Would like more nails removed	Would recommend nail removal to others
1	*KRT6A*	*A463P*	F	12	26	Unknown	T (4)		Yes	Yes
2	*KRT6A*	*E472K*	M	11	25	Surgery	N (4), P (6)	P (1), T (1)	Yes	Yes
3	*KRT6A*	*F174S*	F	1	23	Surgery	T (10)		No	No
4	*KRT6A*	*N172del*	F	3	53	Surgery		N (10)	No	Yes
5	*KRT6A*	*N172del*	M	3	32	Surgery		N (2)	No	Yes
6	*KRT6A*	*N172del*	F	8	18	Surgery	N (1), P (1)	N (5)	No	Yes
7	*KRT6B*	*E472K*	M	10	49	Unknown		P (2)	No	No
8	*KRT6B*	*E472K*	M	30	50	Phenol		P (1), T (5)	No	Yes
9	*KRT6B*	*N172del*	F	31	50	Unknown	T (1)		No	No
10	*KRT16*	*L132P*	F	10	40	Phenol	T (1)	N (8), P (2)	Yes	Yes
11	*KRT16*	*L132P*	F	8	32	Fungal creams	T (6)	T (10)	No	No
12	*KRT16*	*R127C*	F	18, 30	54	Phenol		N (4)	No	Yes
13	*KRT16*	*R127C*	F	24	45	Cautery		N (1)	No	No
14	*KRT17*	*L388P*	F	50	63	Laser	P (1), T (3)	N (3), P (5)	No	Yes
15	*KRT17*	*L388P*	F	48	59	Silver nitrate		P (9)	Yes	Yes
16	*KRT17*	*L99P*	M	6, 8, 10, 12	25	Surgery	P (8), T (2)	P (8), T (2)	No	Yes
17	*KRT17*	*N92S*	M	10	47	Unknown		All removed; no comment on regrowth	No	Yes
18	*KRT17*	*N92S*	M	28	48	Unidentified chemical application		N (2)	Yes	Yes

F, Female; *M*, male; *N*, no regrowth; *P*, partial regrowth; *T*, total regrowth.

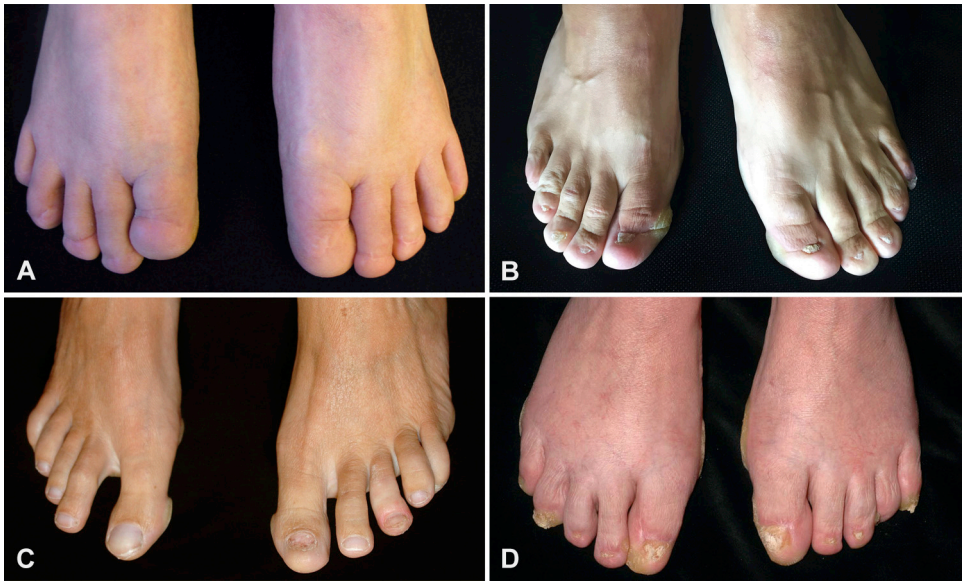

Fig 1. Illustrative examples of nail removal outcomes in patients with pachyonychia congenita. **A**, Patient 4. *KRT6A* mutation. Surgery. No regrowth. Pleased with outcome and would recommend removal to others. **B**, Patient 16. *KRT17* mutation. Several surgeries, partial regrowth of all nails. Improved quality of life and would recommend removal to others. **C**, Patient 13. *KRT16* mutation. Nail removed followed by cautery. No nail plate regrowth. Increased sensitivity in nailbed and would not recommend procedure to others. **D**, Patient 10. *KRT16* mutation. Nail removal followed by phenol. Varying degrees of regrowth. Reduced pain and need for care. Desires more treatments herself and would recommend treatment to others.

The PC keratins have different expression patterns in the nail unit that could explain why some patients respond better to nail removal and matrix ablation than others.[4] Keratin 17 is expressed throughout the entire nail bed epithelium and in the nail matrix. Keratins 6 and 16 are expressed in the proximal nailfold and in the nail bed epithelium but not in the matrix[5]; they are induced in nonnail epidermis after injury. For example, abnormal nail bed epithelium (*KRT16* mutation) may result in increased sensitivity after nail removal (Fig 1, *C*). However, in our study, genotype alone does not appear to determine outcomes.

Although this study is limited by its retrospective nature, patient reporting, small numbers, and incomplete reporting, the majority of patients who had nails removed would recommend nail removal to others and reported an overall positive outcome. Nail removal in patients with PC may not be universally beneficial, but we do not know whether the reason for lack of satisfaction relates to issues intrinsic to the individual patient, genotype, or type of procedure attempted. Our limited data suggest that procedures that completely prevent nail regrowth result in the best patient satisfaction. These findings suggest that nail removal is beneficial for a subset of patients with PC and may be underused. Additional studies are needed to establish which patients with PC and which nails may benefit most from nail removal, and which procedure or procedures can reliably achieve the best outcome.

We are grateful to Pachyonychia Congenita Project and the International Pachyonychia Congenita Research Registry (IPCRR) for performing the surveys and giving us access to the results. Complete data sets may be obtained from IPCRR upon request. We are indebted to Frances Smith, PhD, Chief Scientific Officer of the Pachyonychia Congenita Project, for reviewing the article and for her continued support of the Pachyonychia Congenita Project. Thanks also to Holly Evans of Pachyonychia Congenita Project for all her help with data preparation.

Cynthia Marie Carver DeKlotz, MD,[a] Mary E. Schwartz, AA, Hon LLD,[b] and Leonard M. Milstone, MD[c]

MedStar Washington Hospital Center/Georgetown University Hospital, Georgetown University School of Medicine, Washington, DC[a]; Pachyonychia Congenita Project, Salt Lake City, Utah[b]; and Yale Medical School, New Haven, Connecticut[c]

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: Cynthia Marie Carver DeKlotz, MD, MedStar Washington Hospital Center, Department of Dermatology, 5530 Wisconsin Ave NW, Suite 730, Chevy Chase, MD 20815

E-mail: Cynthia.M.DeKlotz@medstar.net

REFERENCES

1. Eliason MJ, Leachman SA, Feng BJ, et al. A review of the clinical phenotype of 254 patients with genetically confirmed pachyonychia congenita. *J Am Acad Dermatol*. 2012;67:680-686.
2. Cosman B, Symonds FC, Crickelair GF. Plastic surgery in pachyonychia congenita and other dyskeratoses. *Plast Reconstruct Surg*. 1964;33:226-236.
3. Thomsen RJ, Zuehlke RL, Beckman BI. Pachyonychia congenita: surgical management of the nail changes. *J Dermatol Surg Oncol*. 1982;8:24-28.
4. Milstone LM, Fleckman P, Leachman SA, et al. Treatment of pachyonychia congenita. *J Investig Dermatol Symp Proc*. 2005;10:18-20.
5. McGowan KM, Coulombe PA. Keratin 17 expression in the hard epithelial context of the hair and nail, and its relevance for the pachyonychia congenita phenotype. *J Invest Dermatol*. 2000;114:1101-1107.

http://dx.doi.org/10.1016/j.jaad.2016.08.060

Comparing the sensitivity of auramine-rhodamine fluorescence to polymerase chain reaction in the detection of *Mycobacterium leprae* in Fite-negative tissue sections

To the Editor: Twenty-three skin biopsy specimens from 18 patients with leprosy that were Fite-negative but positive by polymerase chain reaction studies were stained with auramine-rhodamine (AR) and examined under a fluorescent microscope. The clinical features and details of armadillo exposure have been described in a separate report. The current study focused on the utility of AR staining in these patients.

Only 1 completely intact large rod was detected in the patient specimens, but AR-positive fragments could be identified within granulomas in 7 of 18 patients (Fig 1). These fragments were ovoid or elongated and clearly distinct from fluorescent lipofuscin pigment, which can be noted in various tissues but is most prominent in the eccrine coil (Fig 2). No fluorescent material was noted in specimens from the remaining 11 patients. Strong fluorescence was present in a control specimen of lepromatous leprosy run in parallel with the study slides.

AR has been used to detect atypical mycobacteria in tissue sections, but is rarely used for the evaluation of leprosy in the United States. The idea is not entirely new—fluorescent vital dyes including auramine and auramine O and ethidium bromide have been used in the setting of leprosy to examine skin smear and histologic sections.[1-6] In the setting of Fite-negative leprosy, Bhatia et al[3] described "coccoid organisms" with auramine staining, which may be similar to the fluorescent fragments we identified with AR.

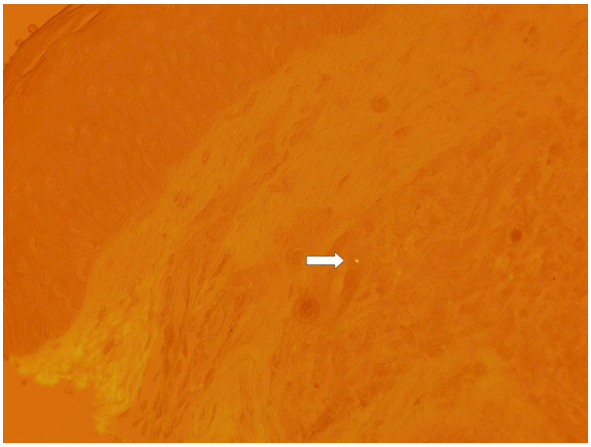

Fig 1. Leprosy. Fluorescent fragment within a horizontally oriented granuloma surrounding a neurovascular bundle. (Auramine-rhodamine stain; original magnification: ×200.)

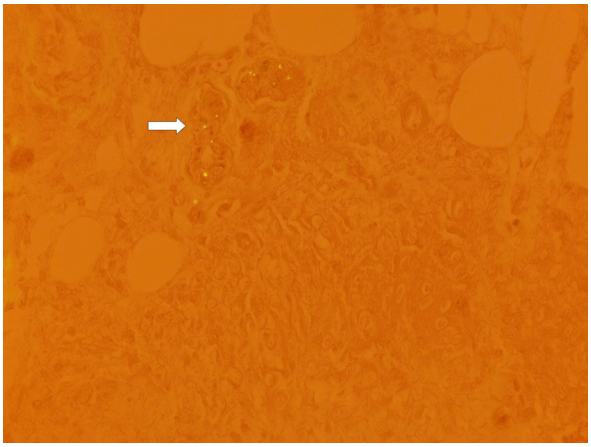

Fig 2. Leprosy. Fluorescent lipofuscin within eccrine coils. This is a normal finding in skin. (Auramine-rhodamine stain; original magnification: ×100.)

AR is more readily available than polymerase chain reaction studies, and our findings suggest it may be of value in patients with clinical and histologic features suggestive of leprosy but with no visible organisms in Fite-stained sections. Fluorescent fragments are more likely to be observed than intact rods. They can be distinguished from artefacts, such as lipofuscin and elastin, by the bright fluorescence and location within perineural granulomas.