Published in final edited form as:

J Am Acad Dermatol. 2010 August ; 63(2): 244–251. doi:10.1016/j.jaad.2009.08.042.

Acral Lesions in Tuberous Sclerosis Complex: Insights into Pathogenesis

Shelley Aldrich, MD^a, Chien-Hui Hong, MD, MS^{a,b,*}, Leslie Groves^a, Cara Olsen, DrPH^c, Joel Moss, MD, PhD^d, and Thomas N. Darling, MD, PhD^a

^a Department of Dermatology, Uniformed Services University of the Health Sciences, Bethesda, MD

^b Department of Dermatology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

^c Biostatistics Consulting Center , Uniformed Services University of the Health Sciences, Bethesda, MD

^d Translational Medicine Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD

Abstract

Background—Patients with tuberous sclerosis complex (TSC) are predisposed to developing ungual fibromas and other acral lesions.

Objective—To determine the numbers, types, and locations of acral skin lesions in TSC.

Methods—Examination and photography of 76 adult women with TSC.

Results—The age of the patients ranged from 20 to 69 years, with a mean age of 39 ± 11 years. Ungual fibromas were observed in 61/76 (80%) patients. Periungual fibromas were more common than subungual fibromas, were more common on the feet than the hands, and showed the greatest frequency on the 5th toe. Longitudinal grooves in the nails occurred with or without a visible fibroma. Longitudinal short red streaks -lesions that we term “red comets”-were observed in 22 patients (29%). Longitudinal leukonychia was observed in 14 patients (18%). One patient had isolated digital overgrowth and one patient had pachydermodactyly.

Limitations—No men and children were included in this study.

Conclusions—Examination of patients for skin lesions of TSC could be improved by including inspection for longitudinal nail grooves, red comets, longitudinal leukonychia, and splinter hemorrhages in addition to ungual fibromas. The anatomical distribution of TSC ungual fibromas is not random and appears consistent with trauma-promoted tumor formation.

Keywords

tuberous sclerosis complex; periungual fibroma; subungual fibroma; fingernails; toenails

Correspondence and reprint requests: Thomas N. Darling, MD, PhD, Department of Dermatology, Uniformed Services University of Health Sciences, 4301 Jones Bridge Rd, Bethesda, MD 20814, tdarling@usuhs.mil.

*co-first author

Conflict of Interest Disclosure: None declared.

INTRODUCTION

Patients with TSC have a mutation in a tumor suppressor gene, either *TSC1* or *TSC2*.¹ Tumor formation in multiple organs is accompanied by a somatic mutation that inactivates the wild-type allele², in accord with Knudson's two-hit hypothesis.³ Tumors have been reported in the brain, heart, lungs, kidneys, and skin of TSC patients. The skin tumors include facial angiofibromas, forehead plaques, shagreen patches, and ungual fibromas.⁴ Ungual fibromas are a major diagnostic criterion for the diagnosis of TSC and a concern to patients because of pain and distortion of the nail.^{5, 6} The most recent consensus criteria stipulated that ungual fibromas must be non-traumatic to serve as a major criterion⁷, since single ungual fibromas occur in the general population in response to trauma.^{8, 9}

The frequency of ungual fibromas varies in studies, from 15%¹⁰, 22%¹¹ to 52%.⁵ This variability appears mostly attributable to different age compositions of study populations. Ungual fibromas are among the last skin lesions to appear in TSC, with onset typically in the second decade¹⁰ and as late as the fifth decade.¹² In one study, ungual fibromas were not observed in TSC children under age 5 years, and the percentage with ungual fibromas increased with age in older children and adults (23% of TSC patients ages 5–14; 68% ages 15–29; and 88% ages 30 and older).¹²

Ungual fibromas are described as periungual (arising under the proximal nail fold) and subungual (originating under the nail plate). The typical patterns of distribution are important for recognition and diagnosis, and may have implications for their pathogenesis. For example, it is known that fibroblast-like cells in periungual fibromas contain second-hit mutations, since they exhibit allelic deletion of *TSC2*.¹³ The histological changes that characterize these tumors, including an epidermis that is acanthotic with a thickened horny layer, and a stroma that contains capillaries surrounded by collagen fibers¹⁴, appear to be orchestrated by these fibroblast-like cells^{13, 15}. If tumor formation were simply the result of randomly occurring second-hit mutations, then one might anticipate an equal distribution of lesions among different fingers and toes. To define the distribution and types of acral lesions in TSC, we tabulated the locations of all acral skin lesions according to digit and nail region. We report notable associations of TSC with "red comets", splinter hemorrhages, and longitudinal leukonychia. The distribution of acral lesions is not random. Lesions predominate on fingers and toes that are more likely subject to trauma.

PATIENTS AND METHODS

Patients were recruited to the Clinical Center at the National Institutes of Health, a tertiary referral center, for studies of TSC and lymphangioleiomyomatosis (LAM). Informed consent was obtained according to protocols approved by the National Heart, Lung, and Blood Institute Institutional Review Board (protocols 00-H-0051, 95-H-0186 and/or 82-H-0032). Patients were diagnosed with TSC according to current clinical criteria. Seventy-six patients had skin examinations and photography. One author (TND) evaluated all patients. The dermatological consult notes and photographs were retrospectively reviewed by four authors (SA, C-HH, LG, and TND). The types and locations of each lesion were recorded. The types of lesions included were periungual fibromas, longitudinal nail grooves without a visible periungual fibroma, subungual fibroma, red comets, longitudinal leukonychia, and splinter hemorrhages. Each lesion was located by digit and region of the nail. The nail regions were divided visually into thirds longitudinally, and recorded as ulnar or fibular, middle, and radial or tibial.

The chi square goodness-of-fit test was used to compare the observed distribution of fibromas to that expected if fibromas were equally distributed among locations. To compare the frequency of lesions among digits, data were compared to expected numbers equally distributed

without or with accounting for different sizes of nails . To determine relative nail width and area, ten randomly selected pictures of patient hands and feet were imported into OpenLab 5.0 (Improvision Inc, a Perkin Elmer Company, Waltham, MA). The software was used to measure total surface area and width of each toenail or fingernail, and the ratio for each digit compared to digit 1 on the hands or feet of each patient . The widths of nails 1 to 5, relative to the first digit, were 1.00, 0.62, 0.57, 0.55, and 0.39 for toenails, and 1.00, 0.78, 0.85, 0.77, and 0.60 for fingernails. The areas of nails 1 to 5, relative to the first digit, were 1.00, 0.47, 0.30, 0.30, and 0.19 for toenails, and 1.00, 0.68, 0.71, 0.64, and 0.42 for fingernails.

RESULTS

The 76 patients with TSC ranged in age from 20 to 69 years, with a mean age of 39 (standard deviation 11 years). All patients were adult women, since this patient population had been recruited for studies of LAM, a pulmonary disease in TSC that occurs almost exclusively in women.¹⁶ Three males in a previous study¹⁷ were excluded, since the frequency of ungual fibromas may differ in males and females.¹⁸

Sixty-one patients had ungual fibromas, of which 15 had a solitary lesion and 46 had multiple ungual fibromas (Figure 1A). The number of ungual fibromas ranged from 0 to 45, with a mean of 6.3 ± 8.8 . Most patients had ungual fibromas on one to eight digits, and one patient had them on all 20 digits (Figure 1B). The mean number of digits with one or more fibromas was 3.6 ± 4.5 . About half of the patients with ungual fibromas had both periungual and subungual lesions, with periungual fibromas predominating overall (Figure 1C).

Periungual fibromas were pink papules originating from under the proximal or lateral nail fold (Figure 2A). Their shapes resembled garlic cloves (Figure 2B), or were globoid (Figure 2C), fusiform (Figure 2D), or vermiform (Figure 2E). Most had a hyperkeratotic tip, sometimes with punctuate hemorrhage just proximal to the tip . The underlying nail plate had a longitudinal groove that usually approximated the width of the fibroma. Nails distorted by multiple large periungual fibromas were dystrophic or absent (Figure 2A , 2nd and 5th digits). Longitudinal nail grooves were also observed in the absence of any visible periungual fibroma (Figures 2C and 2F). As these grooves typically did not develop visible fibromas over several years of observation, they were counted separately and not included as periungual fibromas. Nails of some patients had multiple longitudinal striations.

Subungual fibromas were pink papules originating under the nail plate. Those located more distally protruded from beneath the nail plate as focal areas of hyperkeratosis (Figure 2B) or larger papules (Figure 2G) . More proximal or larger fibromas lifted the nail plate and were accompanied by subungual hyperkeratosis (Figure 2H). Small subungual fibromas did not protrude, but were visible under the nail as oval, red or white discolorations.

In addition to these classic TSC findings, some patients had subungual “red comets”, splinter hemorrhages, and longitudinal leukonychia. Red comets were partially blanchable red longitudinal streaks that had a larger distal head with a narrowing proximal tail (Figure 3A). They were solitary (Figure 3B) or multiple (Figure 3D), and were made more evident with light pressure applied to the nail (Figure 3C, E). Some comets had a whitish halo around the distal portion of the comet (Figure 3F). Most patients were unaware of their presence. Comets were frequently associated with splinter hemorrhages, within and distal to the comet (Figure 3A, F) . Longitudinal leukonychia appeared as white streaks extending from the nail matrix to the end of the nail (Figure 3G, H). Red comets, splinter hemorrhages, and longitudinal leukonychia were observed in 29%, 46%, and 18% of patients, respectively. These were less common than periungual fibromas, longitudinal nail grooves without a visible fibroma, and subungual fibromas (71%, 68%, and 50% of patients, respectively) (Table 1). In addition, one

patient had overgrowth of her left index finger and one patient had increased thickness of the skin overlying the proximal interphalangeal joints consistent with pachydermodactyly. Macroductyly¹⁹ and pachydermodactyly²⁰ are infrequent findings in TSC.

To determine whether lesions were randomly distributed, the numbers of lesions were tabulated by location. Toenails had significantly more periungual fibromas than fingernails (282 vs. 86, $p < 0.001$), compared to the numbers of lesions expected assuming equal distribution to feet or hands. Subungual fibromas and comets showed the opposite distribution, with significantly more subungual fibromas and comets on fingernails than toenails (71 vs. 45, $p = 0.016$, and 93 vs. 4, $p < 0.001$, respectively). Non-random distribution of lesions was also apparent when location was divided into where they were found on the nail (Figure 4A and 4B). Periungual fibromas were less numerous than expected in the central region of fingernails, based on equal distribution into the three regions ($p < 0.001$) (Figure 4A). In contrast, subungual fibromas and red comets were more numerous in the central region of fingernails ($p = 0.043$ and $p = 0.001$, respectively), and subungual fibromas were more numerous in the central region of toenails ($p = 0.017$) (Figure 4B).

Comparisons were also made by digit, summing right and left since there were no significant differences in numbers between sides (data not shown). Total numbers of lesions on each digit are shown in Figure 4C and 4D. For statistical analysis, calculations were made assuming that the expected distribution is proportional to nail size, with expected numbers of periungual fibromas and grooves proportional to nail width, and expected numbers of subungual fibromas and comets proportional to nail area. Periungual fibromas were more numerous than expected on the 5th toes ($p < 0.001$). Longitudinal grooves without periungual fibromas were less frequent than expected on the thumbs ($p < 0.001$), whereas subungual fibromas and red comets were both more numerous than expected ($p < 0.001$ for each). Statistically significant differences in each of these comparisons remained even when equal distribution to each nail, without correcting for nail size, was assumed.

DISCUSSION

Acral skin lesions are present in most adults with TSC. Periungual and subungual fibromas are the most widely known. We found that periungual were more common than subungual fibromas, and that longitudinal nail grooves without a visible fibroma were almost as common as periungual fibromas. In addition, we documented the occurrence of red comets, longitudinal leukonychia, and splinter hemorrhages in TSC patients.

Longitudinal nail grooves are generally thought to be the result of prolonged insult to the nail matrix. Periungual fibromas may exert pressure on the matrix to cause nail grooves, in much the same way as postulated for digital myxoid cysts.^{21, 22} However, we and others¹² have observed nail grooves in TSC with no visible periungual fibroma. These probably result from cryptic fibromas impacting the matrix, but further studies are needed to rule out the possibility of defective nail formation in the absence of an initiating fibroma.

Red comets were observed in about one-fourth of adult TSC patients. Red comets are partially blanchable, suggesting the presence of telangiectasias with extravasated blood. They are variable in size but most appear stable over time. They differ from splinter hemorrhages by the frequent presence of an enlarged distal end with an associated rim of pallor and by their persistence. In addition, red comets tended to extend from the mid into the distal third of the nail without involving the free edge, whereas splinter hemorrhages are most often confined to the distal third of the nail and usually extend to the free edge.²³ They differ from longitudinal erythronychia by not spanning the nail from matrix to distal tip.²⁴ They can be distinguished from glomus tumors by the presence of longitudinal red lines rather than a reddish spot, and

the absence of pain typical for glomus tumors.²⁵ Red comets may be characteristic of TSC, as we have not seen them in 20 patients with sporadic LAM, which is not associated with TSC.

Longitudinal leukonychia was documented in 18% of TSC patients. It is not a specific finding, however, as longitudinal leukonychia is present in most patients with Hailey-Hailey disease²⁶, and white streaks together with red streaks are found in Darier disease.^{22, 27} Longitudinal leukonychia is a relatively uncommon finding in TSC, and its utility in diagnosis must take into account these other conditions.

Splinter hemorrhages were found in almost half of the TSC patients, and are the least diagnostic of TSC, since they occur commonly after minor nail trauma.^{23, 28} They are also associated with skin diseases such as psoriasis or onychomycosis, systemic diseases such as subacute bacterial endocarditis or antiphospholipid antibody syndrome, and treatment with kinase inhibitors such as sorafenib.^{29–32} It is important to recognize the association of splinter hemorrhages with TSC since this may avoid needless evaluation for other conditions. For example, one of our patients had undergone several imaging studies to evaluate possible bacterial endocarditis. The finding of splinter hemorrhages should prompt a closer examination for small subungual fibromas, red comets and other signs of TSC.

Periungual fibromas were more common on the toes than fingers, as earlier reported.^{10, 12} This propensity for toenail lesions prompted early speculation that pressure from shoes stimulated their growth.³³ For further analysis we divided the distribution into digit and location on the digit. Periungual fibromas were most common on the 5th toe, and subungual fibromas on the central one-third of the thumb. The non-random distribution could reflect trauma-promoted tumor formation, either repeated trauma from shoes impacting the smallest toe or lifting trauma to the thumbnail. The role of trauma in ungual fibroma formation is also supported by patient history, since some of our patients reported developing periungual fibromas on the fingernails after crushing injury. This might be a result of trauma-induced production at the wound site of MCP-1³⁴, a paracrine factor that can promote TSC skin tumorigenesis.¹⁵

These observations suggest that the history of preceding trauma should not be used to discount the possibility of TSC in a patient presenting with an ungual fibroma, and such patients should be examined for additional skin manifestations of TSC. If no other diagnostic skin findings are observed, we believe that the presence of red comets and longitudinal grooves in other nails should increase clinical suspicion of TSC. Fifteen of our TSC patients had only one ungual fibroma, but 10 of these 15 patients also had either red comets or longitudinal grooves without a visible associated fibroma. Ungual fibromas are the only cutaneous manifestation of TSC in some patients¹², and physician recognition can lead to the correct diagnosis.

Acknowledgments

This work was supported by a Clinical Scientist Development Award from the Doris Duke Charitable Foundation, R01 CA100907, and the Intramural Research Program of the National Institutes of Health, National Heart, Lung, and Blood Institute. We thank the Tuberous Sclerosis Alliance and The LAM Foundation for patient referral. We thank Drs. Leonard Sperling and Martha Vaughn for helpful discussions and critical review of the manuscript.

Funding Sources: R01 CA100907, and the Intramural Research Program of the National Institutes of Health, National Heart, Lung, and Blood Institute.

Abbreviations used

TSC	tuberous sclerosis complex
LAM	lymphangioleiomyomatosis

References

1. Crino PB, Nathanson KL, Henske EP. The tuberous sclerosis complex. *N Engl J Med* 2006;355:1345–56. [PubMed: 17005952]
2. Darling TN. Hitting the mark in hamartoma syndromes. *Adv Dermatol* 2006;22:181–200. [PubMed: 17249302]
3. Knudson AG Jr. Mutation and cancer: statistical study of retinoblastoma. *Proc Natl Acad Sci U S A* 1971;68:820–3. [PubMed: 5279523]
4. Schwartz RA, Fernandez G, Kotulska K, Jozwiak S. Tuberous sclerosis complex: advances in diagnosis, genetics, and management. *J Am Acad Dermatol* 2007;57:189–202. [PubMed: 17637444]
5. Nickel WR, Reed WB. Tuberous sclerosis. Special reference to the microscopic alterations in the cutaneous hamartomas. *Arch Dermatol* 1962;85:209–26. [PubMed: 14479476]
6. Aste N, Pau M, Aste N, Biggio P. Tuberous sclerosis with unusual giant ungual fibromas. *J Eur Acad Dermatol Venereol* 2003;17:100–1. [PubMed: 12602986]
7. Roach ES, Gomez MR, Northrup H. Tuberous sclerosis complex consensus conference: revised clinical diagnostic criteria. *J Child Neurol* 1998;13:624–8. [PubMed: 9881533]
8. Carlson RM, Lloyd KM, Campbell TE. Acquired periungual fibrokeratoma: a case report. *Cutis* 2007;80:137–40. [PubMed: 17944173]
9. Zeller J, Friedmann D, Clerici T, Revuz J. The significance of a single periungual fibroma: report of seven cases. *Arch Dermatol* 1995;131:1465–6.
10. Jozwiak S, Schwartz RA, Janniger CK, Michalowicz R, Chmielik J. Skin lesions in children with tuberous sclerosis complex: their prevalence, natural course, and diagnostic significance. *Int J Dermatol* 1998;37:911–7. [PubMed: 9888331]
11. Nevin NC, Pearce WG. Diagnostic and genetical aspects of tuberous sclerosis. *J Med Genet* 1968;5:273–80. [PubMed: 5713638]
12. Webb DW, Clarke A, Fryer A, Osborne JP. The cutaneous features of tuberous sclerosis: a population study. *Br J Dermatol* 1996;135:1–5. [PubMed: 8776349]
13. Li S, Takeuchi F, Wang JA, Fan Q, Komurasaki T, Billings EM, et al. Mesenchymal-epithelial interactions involving ephregulin in tuberous sclerosis complex hamartomas. *Proc Natl Acad Sci U S A* 2008;105:3539–44. [PubMed: 18292222]
14. Kint A, Baran R. Histopathologic study of Koenen tumors. Are they different from acquired digital fibrokeratoma? *J Am Acad Dermatol* 1988;18:369–72. [PubMed: 3346418]
15. Li S, Takeuchi F, Wang JA, Fuller C, Pacheco-Rodriguez G, Moss J, et al. MCP-1 overexpressed in tuberous sclerosis lesions acts as a paracrine factor for tumor development. *J Exp Med* 2005;202:617–24. [PubMed: 16129702]
16. Steagall WK, Taveira-DaSilva AM, Moss J. Clinical and molecular insights into lymphangiomyomatosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2005;22 (Suppl 1):S49–66. [PubMed: 16457017]
17. Sparling JD, Hong CH, Brahim JS, Moss J, Darling TN. Oral findings in 58 adults with tuberous sclerosis complex. *J Am Acad Dermatol* 2007;56:786–90. [PubMed: 17239986]
18. Au KS, Williams AT, Roach ES, Batchelor L, Sparagana SP, Delgado MR, et al. Genotype/phenotype correlation in 325 individuals referred for a diagnosis of tuberous sclerosis complex in the United States. *Genet Med* 2007;9:88–100. [PubMed: 17304050]
19. Norman-Taylor F, Mayou BJ. Macrodactyly in tuberous sclerosis. *J R Soc Med* 1994;87:419–20. [PubMed: 8046733]
20. Lo WL, Wong CK. Localized pachydermodactyly in tuberous sclerosis. *Clin Exp Dermatol* 1993;18:146–7. [PubMed: 8481991]
21. Lin YC, Wu YH, Scher RK. Nail changes and association of osteoarthritis in digital myxoid cyst. *Dermatol Surg* 2008;34:364–9. [PubMed: 18177395]
22. Nicolopoulos J, Goodman GJ, Howard A. Diseases of the generative nail apparatus. Part I: Nail matrix. *Australas J Dermatol* 2002;43:81–90. quiz, 1–2. [PubMed: 11982563]
23. Dowling RH. Sub-ungual splinter haemorrhages. *Postgrad Med J* 1964;40:595–600. [PubMed: 14220406]

24. de Berker DA, Perrin C, Baran R. Localized longitudinal erythronychia: diagnostic significance and physical explanation. *Arch Dermatol* 2004;140:1253–7. [PubMed: 15492189]
25. Moon SE, Won JH, Kwon OS, Kim JA. Subungual glomus tumor: clinical manifestations and outcome of surgical treatment. *J Dermatol* 2004;31:993–7. [PubMed: 15801264]
26. Burge SM. Hailey–Hailey disease: the clinical features, response to treatment and prognosis. *Br J Dermatol* 1992;126:275–82. [PubMed: 1554604]
27. Cooper SM, Burge SM. Darier's disease: epidemiology, pathophysiology, and management. *Am J Clin Dermatol* 2003;4:97–105. [PubMed: 12553850]
28. Young JB, Will EJ, Mulley GP. Splinter haemorrhages: facts and fiction. *J R Coll Physicians Lond* 1988;22:240–3. [PubMed: 3230540]
29. Robert C, Faivre S, Raymond E, Armand JP, Escudier B. Subungual splinter hemorrhages: a clinical window to inhibition of vascular endothelial growth factor receptors? *Ann Intern Med* 2005;143:313–4. [PubMed: 16103482]
30. Autier J, Escudier B, Wechsler J, Spatz A, Robert C. Prospective study of the cutaneous adverse effects of sorafenib, a novel multikinase inhibitor. *Arch Dermatol* 2008;144:886–92. [PubMed: 18645140]
31. Saladi RN, Persaud AN, Rudikoff D, Cohen SR. Idiopathic splinter hemorrhages. *J Am Acad Dermatol* 2004;50:289–92. [PubMed: 14726890]
32. Goodman GJ, Nicolopoulos J, Howard A. Diseases of the generative nail apparatus. Part II: nail bed. *Australas J Dermatol* 2002;43:157–68. quiz 69–70. [PubMed: 12121391]
33. Butterworth T, Wilson M. Dermatologic aspects of tuberous sclerosis. *Arch Dermatol Syphilol* 1941;43:1–41.
34. Swift ME, Burns AL, Gray KL, DiPietro LA. Age-related alterations in the inflammatory response to dermal injury. *J Invest Dermatol* 2001;117:1027–35. [PubMed: 11710909]

Figure 1.

Most adult TSC patients have multiple ungual fibromas involving several digits . A) The number of patients with the specified numbers of ungual fibromas. B) The number of patients with ungual fibromas on the specified numbers of digits. C) The number of patients with no ungual fibromas, subungual fibromas (SF) alone, periungual fibromas (PF) alone, or subungual and periungual fibromas.

Figure 2.

Periungual and subungual fibromas in TSC. A) Ungual fibromas involving all nails. B) Close-up of the 3rd digit in A shows a clove-like periungual fibroma, a nail-like periungual fibroma, and a subungual fibroma. C) Close-up of the 4th digit in A shows a globoid periungual fibroma and a longitudinal groove without a visible fibroma. D) Three fusiform periungual fibromas fill one longitudinal groove. E) Vermiform periungual fibromas. F) A longitudinal groove without a visible fibroma. G) Subungual fibroma protruding from under the nail plate. H) Elevation of the nail plate from a subungual fibroma.

Figure 3.

Red comets and longitudinal leukonychia in TSC. A) Multiple nails with red comets. B) Two red comets are barely visible (arrows) until the nail is blanched (C) with light pressure. D) Multiple red comets are (E) partially blanchable. F) Several red comets show a rim of pallor and splinter hemorrhages. G) Longitudinal leukonychia (arrow) as an isolated finding. H) Longitudinal leukonychia (arrow) together with red comets and splinter hemorrhages.

Figure 4.

Acral lesions in TSC show a non-random distribution. Numbers of periungual fibromas, grooves without a visible fibroma (A and C), and those of subungual fibromas and red comets (B and D) are shown for the region of the nail (A and B) or digit (C and D) in which they were found. Regions are divided into fibular (Fib) or radial (Rad), central (Cen), and tibial (Tib) or ulnar (Uln).

Table I

Numbers and percentages of TSC patients with acral lesions, and mean numbers of lesions by location.

Lesion Type	Hand			Foot			Total		
	# patients	(%)	# lesions/pt	SD	# patients	(%)	# lesions/pt	(%)	SD
Periungual fibroma	26	34%	3.3	4.7	52	68%	5.4	71%	8.2
Groove (no visible fibroma)	43	57%	3.2	3.1	45	59%	3.3	68%	4.9
Subungual fibroma	33	43%	2.2	1.7	20	26%	2.3	50%	2.8
Red comet	22	29%	4.2	6.0	4	5%	1.0	29%	6.2
Splinter hemorrhage	32	42%	3.8	3.2	10	13%	1.6	46%	3.4
Longitudinal leukonychia	12	16%	1.4	1.0	4	5%	1.5	18%	1.2

Numbers of lesions/patient are the mean numbers for those with at least one of that type of lesion (excluding those with none). Pt, patient; SD, standard deviation.