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Recurrent Familial Digital Fibrokeratoma: A Case Report

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ABSTRACT

Digital fibrokeratoma (DF) is an uncommon, benign, soft tissue tumor. It usually occurs sporadically in adult males, and its recurrence is rare when treated by means of surgical removal. To the best of our knowledge, we report here the first case of recurrent female familial DF. The mother's first DF, on her right hallux, was removed when she was 32 years of age, and her second fibrokeratoma, on the left fifth toe, was removed when she was 49 years of age, and then relapsed 3 years later. The daughter's first DF, on her left fifth toe, was excised when the daughter was 24 years of age and recurred 1 year later. Both the mother's and daughter's recurrent lesions were surgically excised and pathologically diagnosed as DF. Because both the mother's and daughter's DF occurred at relatively early ages, we believe that genetic factors might play a role in the tumorigenesis of DF in this family.

Digital fibrokeratoma (DF) was first established as a clinical entity in 1968 (1). It is a rare, benign, firm, solitary, fibrous lesion, commonly presenting in the acral portions of the extremities. It most frequently occurs in fingers and toes but is also found in the soles, heels, palms, and other sites (1–4). In feet, it mainly localizes to the great toe (3,5), whereas occurrences on other toes, especially on fifth toe, are rare (5,6). The tumor usually occurs sporadically and predominantly in adult males (4). There are no known racial differences, as cases have been reported in different populations (7,8). Although it is a benign lesion, it does not regress spontaneously, and therefore surgical excision is required (9,10). Recurrence after excision is uncommon (8). To the best of our knowledge, we report here the first recurrent familial fibrokeratoma on the left fifth toe, found in both mother and daughter. Because both mother and daughter had experienced recurrence after excision of DF on the same toe, the development of the lesion in these patients may be associated with heredity, and we present this report to raise awareness of the condition.

Case Reports

Case 1

A 52-year-old white female presented for evaluation of a symptomatic growth on her left fifth toe, the lesion having been present for 3 years. Her medical history included depression, anxiety disorder, bipolar disorder, anemia, and hypothyroidism.

She had minimal pain with the left fifth toe lesion, except when direct pressure was applied to the area. The pain was also aggravated by contact during standing and walking, and her shoes consistently showed an uneven wear pattern, in which they contacted the left fifth toe and quicker than usual breakdown at this site. She described a history of another similar lesion that she experienced at the same site when she was 49 years of age, which was excised by her dermatologist (no pathology was available after inquiry for the same). Moreover, when she as 32 years of age, a firm, white tissue mass, measuring $8 \times 2 \times 2$ mm, was removed from the medial periungual area of her right great toe, which was diagnosed pathologically as an acquired (acral) DF.

Physical examination revealed that only one half of the left fifth toenail remained along the medial aspect, and the lateral aspect of the nail bed had 3 stalk-like masses protruding from the nail bed, beneath the proximal nail fold (Fig. 1). The 3 masses measured $6 \times 3 \times 3$ mm, $4 \times 3 \times 3$ mm, and $2.0 \times 1.2 \times 1.2$ mm, respectively. Each mass was firm, flesh-colored, and without active drainage, and they were tender on palpation. Three radiographic views of left foot did not show any

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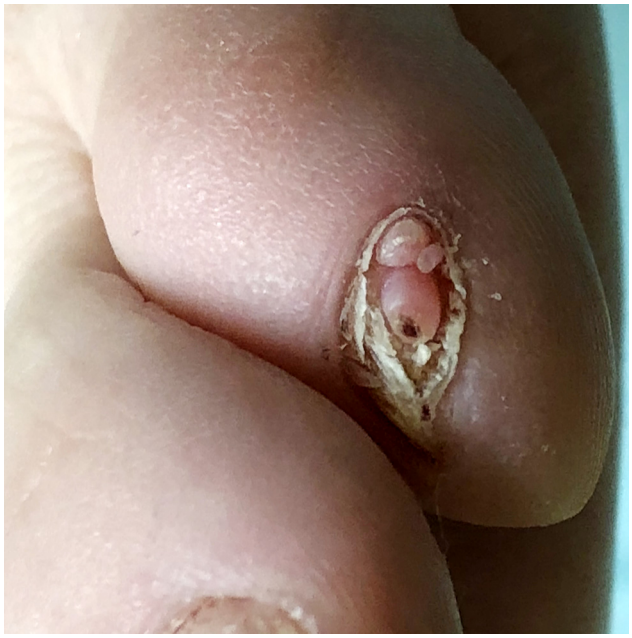

Fig. 1. Surgical picture of the mother's digital fibrokeratomas showing 3 different sized, skin colored, firm, protruding stalk-like masses from the fifth nail bed.

signs of osseous erosion, fracture, subluxation, dislocation, or osseous involvement (Fig. 2). After discussion with the patient, including review of the suspected diagnosis of DF, treatment options, and prognosis, the decision was made to excise the lesions.

At the time of the surgery, the patient's left fifth toe was prepped with iodophor and anesthetized with local injection of 0.5% bupivacaine with epinephrine diluted 1:200,000. An incision around the bases of the 3 tumor stalks was made and revealed that the bases of each were not connected with any underlying osseous tissues. The 3 tumors were totally separated from adjacent tissues, using a curette, and completely removed and placed in 10% buffered formalin for fixation and pathological examination. Subsequent hematoxylin and eosin sections showed 3 polypoid structures, with hyperkeratotic epidermis, and a central core of fibrovascular tissue and dilated vessels beneath the epidermis, but without adnexal or neural structures (Fig. 3). The proliferated fibroblasts, collagen, and vascular vessels were bundled together and aligned perpendicularly to the surface of the epidermis. The 3 masses had similar morphologies, and each was diagnosed as a DF. After the surgery, the patient healed unremarkably with no sign of lesion recurrence at 12 months postoperatively.

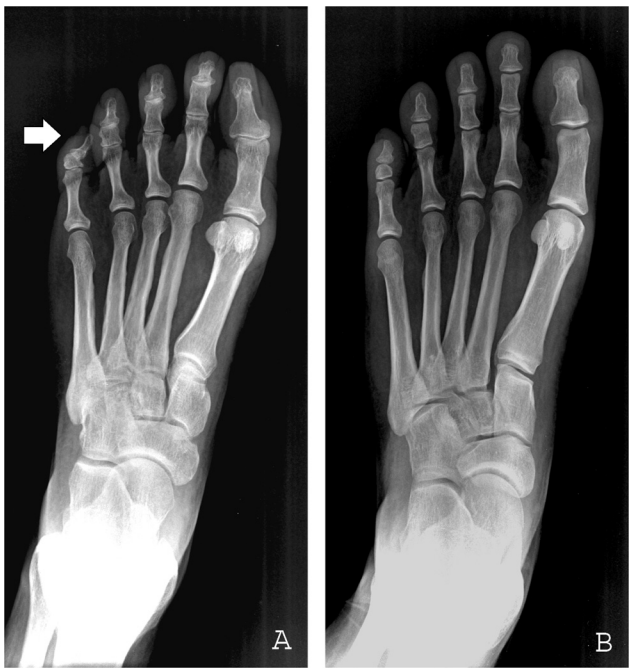

Fig. 2. Anteroposterior radiograph images of the left feet from both mother (*A*) and daughter (*B*) revealing no signs of acute fracture, subluxation, dislocation, osseous erosion, periosteal reaction, or destruction on the left fifth toes. Mother's radiograph (*A*) showing adductovarus hammertoe contracture on the left fifth digit (*arrow*).

Case 2

The 25-year-old daughter of the earlier mentioned patient presented with a recurrent mass on her left fifth toe, present for ~5 years. One year earlier, a dermatologist had removed the growth, which was identified clinically as DF, and the base of the lesion was treated with a laser to eradicate tumor. This treatment did not resolve the problem, as it returned and was larger and more painful than it had been previously. The pain increased, gradually, to a level of 8 on a 0-to-10 scale (0 = no pain, 10 = most severe pain), and it was aggravated by standing and walking, with nothing providing relief. The patient wore appropriately fitted shoes. Her medical history was significant for gastroesophageal reflux disease, headaches, migraines, seizures, and epilepsy.

Physical examination revealed that only one third of the nail plate on the left fifth toe was present along the lateral nail fold, with the remainder of the toenail absent and with a fleshy, solid, firm, soft tissue mass measuring $7 \times 4 \times 3$ mm, with a slightly raised cauliflower appearance and a dry, crusty, hemorrhagic appearance. The lesion was painful on palpation. The remainder of her neuromuscular exam was within normal limits. Radiographs of her involved foot failed to reveal osseous involvement or any other pathologic changes (Fig. 2). After consideration of the treatment options, the mass was surgically removed using the same procedure as was used to treat her mother's left fifth toe lesion.

Histologically, the surface of the lesion displayed epidermal hyperkeratosis and acanthosis. No dysplastic changes or mitotic figures were noticed. The underlying skin featured proliferation of fibroblasts and collagen fibers forming thick, dense, closely packed bundles arranged vertically, perpendicular to the surface of the skin. Marked vascular proliferation was found in parallel with the collagen bundles (Fig. 3). The morphological changes were consistent with a diagnosis of DF. After the surgery, the patient healed unremarkably with no sign of lesion recurrence at 11 months postoperatively. After discussion of the potential benefits of added information regarding the genetic nature of the etiology of the lesion, the daughter and her mother both declined to pursue genetic testing.

Discussion

In this report, we describe the clinical presentations, histopathology, and treatment of what we believe to be the first reported cases of recurrent, familial, acral DF occurring in a mother and daughter. The uniqueness of this report is that both the mother and daughter presented with their first mass at the early ages of 20 to 30 years, and the daughter's first and the mother's second DF recurred on the left fifth digit 1 to 3 years after the initial surgical removal.

Clinically, DF usually presents as a solitary, fleshy mass, <1 cm in diameter. Variants including multibranched rod-like nodules (11,12), and giant DF >1 cm in diameter have also been described (7). Here, we reported another variant with 3 stalk-like, firm, flesh-colored masses protruding from the nail bed, beneath the proximal nail fold.

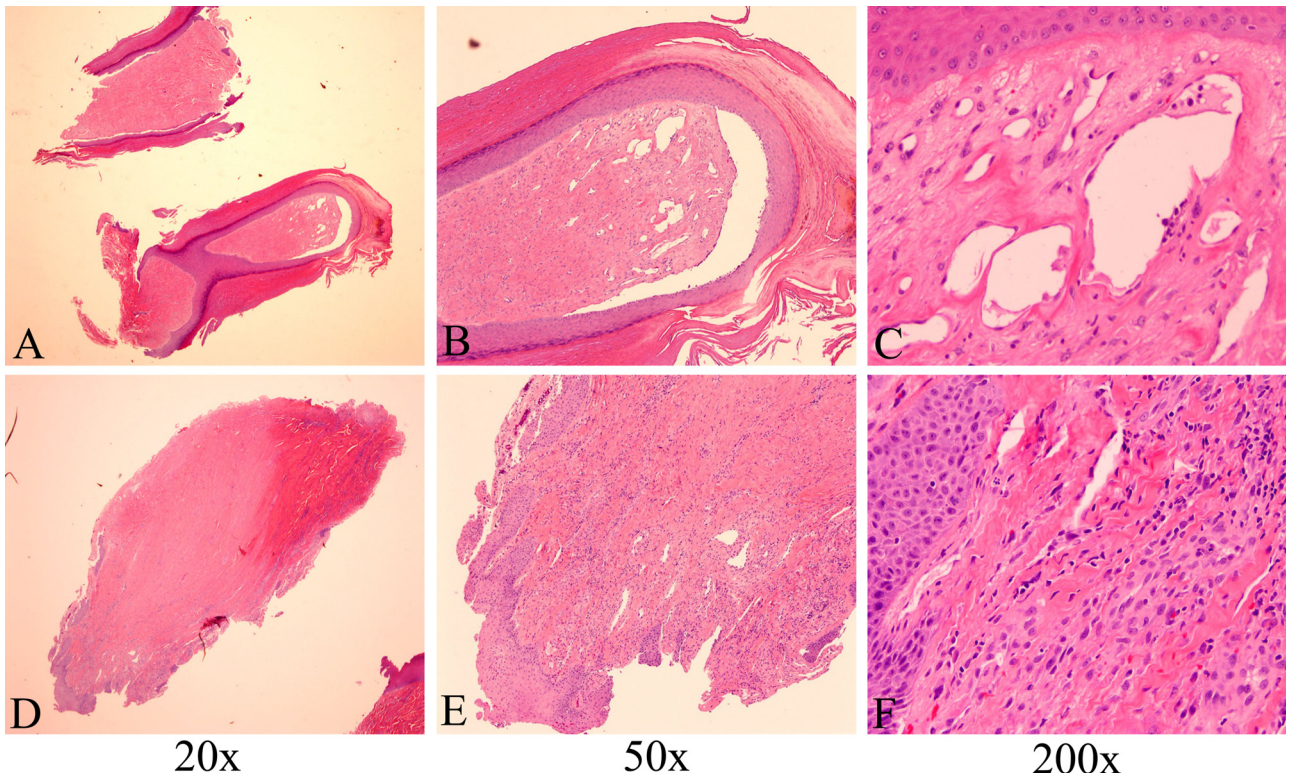

Fig. 3. Hematoxylin and eosin microfilms showing morphology of the digital fibrokeratoma from both mother (*A*, *B*, *C*) and daughter (*D*, *E*, *F*) at different magnifications. Note the hyperkeratosis and acanthosis in the epidermis and highly proliferated fibrovascular tissues bundled together in the dermis, which were arranged longitudinally to the axis of the masses.

Histologically, DF is characterized by proliferation of fibroblasts and collagen fibers in the dermis, with epidermal acanthosis. According to the different components of stromal tissues, Kint et al (2) further divided DF into 3 different types: type I, densely and closely packed thick collagen bundles with elastic fibers forming a core arranged longitudinally to the surface of the hyperkeratotic epidermis and numerous capillaries in the dermis; type II, increased number of fibroblasts but reduced elastic fibers; and type III, poor cellular structure with edematous changes and a lack of elastic fibers (2). In our report, the mother's tumor was classified as type I and the daughter's as type II.

Although DF is a benign lesion, it needs to be differentiated from other lesions, including Koenen's tumor, rudimentary supernumerary digit, acrochordon, cutaneous horn, verruca vulgaris, pyogenic granuloma, eccrine poroma, fibroma, dermatofibroma, superficial acral fibromyxoma, and more severely, squamous cell carcinoma and aggressive digital papillary adenocarcinoma. Clinical presentations, pathological examinations, and immunohistochemistry with different biomarkers can aid in making an accurate diagnosis.

The recurrent DFs from both mother and daughter, and the daughter's medical history with epilepsy, also raised concern for the differential diagnosis of tuberous sclerosis complex (TSC) in this family. TSC is an autosomal dominant genetic disease caused by mutations of either *TSC1* or *TSC2* gene encoding hamartin and tuberin, respectively. Hamartin and tuberin form complexes involved in regulating cellular growth and division. Dysfunctions of either *TSC1* or *TSC2* lead to multiple organ disorders (13). TSC is most often diagnosed at an early age (infants and children) (14). Koenen's fibroma, one of the major manifestations of TSC, most often involves at least 2 digits and is histologically characterized by prominent stellate atypical myofibroblasts, rich ectatic blood vessels, and a lack of epidermal changes (15), which differentiates it from fibrokeratoma. In the patients who we described in this report, the physical examinations did not reveal facial angiofibromas, shagreen patches, or adenoma sebaceum (16), and there were no other major symptoms; therefore, the diagnosis of TSC was unlikely. However, the possibility of TSC could not be completely excluded because both patients declined to do any genetic testing.

The pathogenesis of DF is not clear. It is suggested that trauma, repeated contact pressure, infection with *Staphylococcus aureus*, and increased expression of factor XIIIa in tumor tissues, which drives the proliferation of fibroblasts, may be involved in the development of DF in some cases (1,17–19). In our case report, the mother's shoes were worn unevenly and easily broken down, suggesting that repeated pressure may be associated with the formation of the tumor in the mother. In this report, the mother had her first DF removed on her right hallux at 32 years of age, and the second DF on her left fifth toe was removed when she was 49 years of age, whereas the daughter had her first DF on her left fifth toe removed when she was 24 years of age. Both the mother's and daughter's DFs on their left fifth toes were recurrent after surgical excision. Because both mother and daughter presented with DF, at relatively early ages, we believe that genetic factors were likely strongly influential in these cases. Genetic tests, including next-generation gene sequencing, could potentially reveal the genes responsible for the tumorigenesis of DF. Such tests, however, were not obtained for either the mother or daughter described in this report.

References

1. Bart RS, Andrade R, Kopf AW, Leider M. Acquired digital fibrokeratomas. Arch Dermatol 1968;97:120–129.
2. Kint A, Baran R, De Keyser H. Acquired (digital) fibrokeratoma. J Am Acad Dermatol 1985;12:816–821.
3. Verallo VV. Acquired digital fibrokeratomas. Br J Dermatol 1968;80:730–736.
4. Zakopoulou N, Bokotas C, Frangoulis M, Karypidis D, Hatziolou E, Papadopoulos O. Giant tumour of the heel: acquired fibrokeratoma. Clin Exp Dermatol 2009;34:605–606.

5. Hwang S, Kim M, Cho BK, Park HJ. Clinical characteristics of acquired ungual fibrokeratoma. Indian J Dermatol Venereol Leprol 2017;83:337–343.
6. Tower DE, Hammond JR. Acral fibrokeratoma: a rare pedal soft-tissue mass. J Am Podiatr Med Assoc 2018;108:172–177.
7. Ali M, Mbah CA, Alwadiya A, Nur MM, Sunderamoorthy D. Giant fibrokeratoma, a rare soft tissue tumor presenting like an accessory digit, a case report and review of literature. Int J Surg Case Rep 2015;10:187–190.
8. Shih S, Khachemoune A. Acquired digital fibrokeratoma: review of its clinical and dermoscopic features and differential diagnosis. Int J Dermatol 2019;58:151–158.
9. Lee CY, Lee KY, Kim KH, Kim YH. Total excision of acquired periungual fibrokeratoma using bilateral proximal nail fold oblique incision for preserving nail matrix. Dermatol Surg 2010;36:139–141.
10. Yelamos O, Alegre M, Garces JR, Puig L. Periungual acral fibrokeratoma: surgical excision using a banner flap. Actas Dermosifiliogr 2013;104:830–832.
11. Moriue T, Yoneda K, Moriue J, Nakai K, Kubota Y. Multibranched acquired periungual fibrokeratoma. JAMA Dermatol 2014;150:456–457.
12. Goktay F, Altan ZM, Haras ZB, Gunes P, Yasar S, Aytekin S, Haneke E. Multibranched acquired periungual fibrokeratomas with confounding histopathologic findings resembling papillomavirus infection: a report of two cases. J Cutan Pathol 2015;42:652–656.
13. Northrup H, Krueger DA. International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Consensus Conference. Pediatr Neurol 2013;49:243–254.
14. Randle SC. Tuberous sclerosis complex: a review. Pediatr Ann 2017;46:e166–e171.
15. Zeller J, Friedmann D, Clerici T, Revuz J. The significance of a single periungual fibroma: report of seven cases. Arch Dermatol 1995;131:1465–1466.
16. Portocarrero LKL, Quental KN, Samorano LP, Oliveira ZNP, Rivitti-Machado MCDM. Tuberous sclerosis complex: review based on new diagnostic criteria. An Bras Dermatol 2018;93:323–331.
17. Sezer E, Bridges AG, Koseoglu D, Yuksek J. Acquired periungual fibrokeratoma developing after acute staphylococcal paronychia. Eur J Dermatol 2009;19:636–637.
18. Amarouch H, Aitourghoui M, Ramli I, Zaouri H, Senouci K, Hassam B. Post-staphylococcal acquired digital fibrokeratoma: a new case. Presse Med 2015;44:843–845.
19. Nemeth AJ, Penneys NS. Factor XIIIa is expressed by fibroblasts in fibrovascular tumors. J Cutan Pathol 1989;16:266–271.