



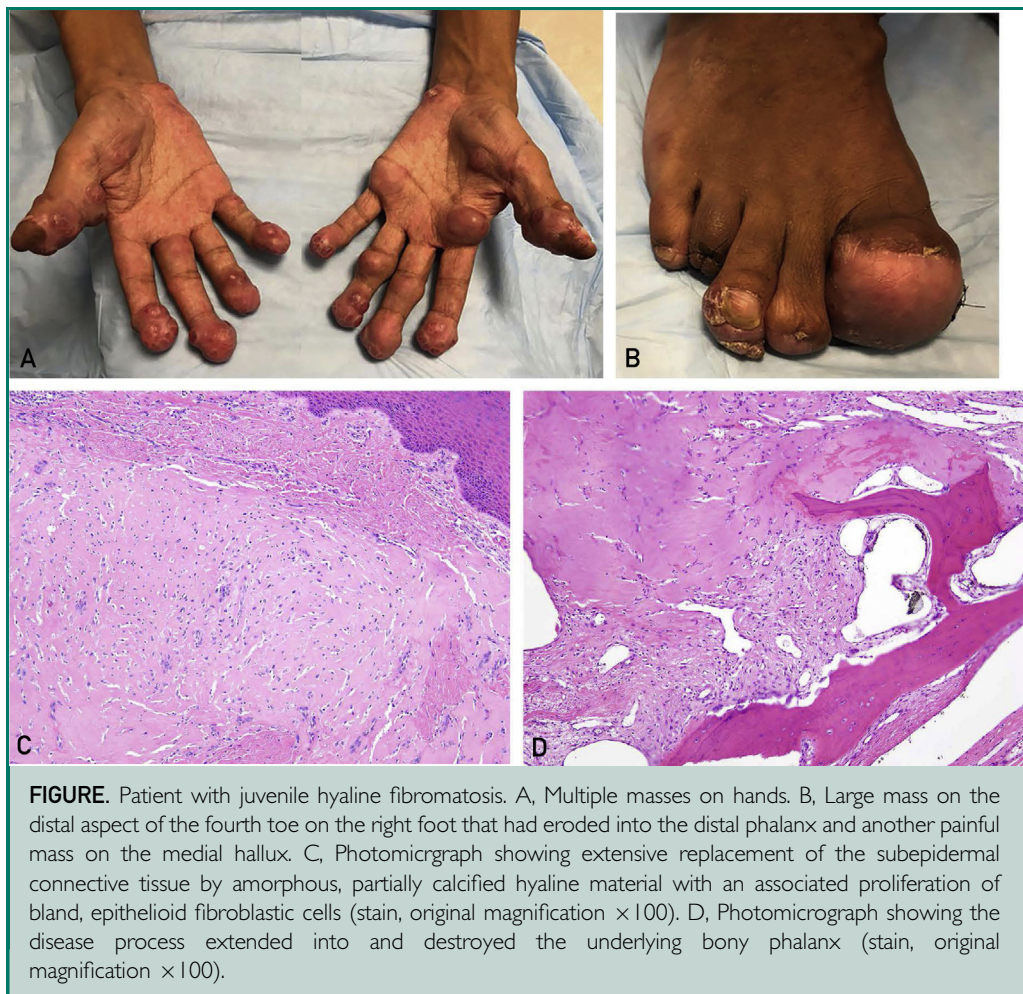
# Juvenile Hyaline Fibromatosis

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**A** 27-year-old African American man presented to an orthopedic surgeon with a painful mass on his left fourth toe, which impaired ambulation and the wearing of closed footwear. His medical history was notable for juvenile hyaline fibromatosis diagnosed at age 4 years and for multiple prior operations to remove symptomatic masses on his face and extremities. Physical examination revealed multiple masses of varying size on his face and all extremities (Figure A), with a large mass on the distal aspect of the fourth toe on the right foot that had eroded into the

distal phalanx and another painful mass on his medial hallux (Figure B). A right fourth toe partial amputation and excision of the hallux mass were performed. Histologic examination of the amputation specimen revealed extensive replacement of the subepidermal connective tissue by amorphous, partially calcified hyaline material with an associated proliferation of bland, epithelioid fibroblastic cells, diagnostic of juvenile hyaline fibromatosis (Figure C). This process extended into and destroyed the underlying bony phalanx (Figure D).



Juvenile hyaline fibromatosis is a very rare genetic disorder with an autosomal recessive pattern of inheritance, first described by Murray in 1873 as “mollusum fibrosum.”<sup>1</sup> It is genetically related to a similar (but not identical) condition termed *infantile systemic hyalinosis*.<sup>2</sup> Patients with juvenile hyaline fibromatosis present in childhood with joint contractures, gingival hyperplasia, osteopenia, osteolytic bone lesions, and papular and nodular skin lesions.<sup>3</sup> The skin lesions vary widely in number and size, are slow growing and usually painless, and tend to recur following excision. Both juvenile hyaline fibromatosis and infantile systemic hyalinosis are caused by sequence variations in the *ANTXR2* gene (*ANTXR* cell adhesion molecule 2; gene name alias, capillary morphogenesis gene 2 [*CMG2*]), which codes for a protein involved in basement membrane matrix assembly, in particular collagen type VI homeostasis, and morphogenesis of endothelial cells.<sup>4</sup> Distinct mutations are seen in juvenile hyaline fibromatosis and infantile systemic hyalinosis, suggesting a

genotypic-phenotypic correlation. The prognosis for these diseases is variable, with survival into adulthood for patients with juvenile hyaline fibromatosis and early death from intractable diarrhea and recurrent infections in infantile systemic hyalinosis.

**Potential Competing Interests:** Dr Folpe is a consultant for Ultragenyx Pharmaceutical and Epizyme, Inc. The other authors report no competing interests.

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