Juvenile hyaline fibromatosis: an unusual clinical presentation

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Abstract

Juvenile hyaline fibromatosis is a recessive autosomal hereditary disorder characterized by abnormal growth of hyalinized fibrous tissue. Its clinical presentation is marked by tumors of the skin, bone lesions, joint contractures, and gingival hyperplasia. We report a localized form of juvenile hyaline fibromatosis, a rare disease with several cases reported in the worldwide literature. A 23-year-old man presented with multiple tumors, joint contractures, and osteolytic bone lesions, but without gingival hyperplasia in one year of follow-up. Although, the onset of this condition is commonly in early childhood with progression, his unusual clinical presentation began at eight years of age with late progression in adolescence.

Keywords: juvenile hyaline fibromatosis, late progression, surgical excision

Introduction

Juvenile hyaline fibromatosis (JHF) was first described by Murray in 1873 as molluscum fibrosum [1]. It is a rare disease with recessive autosomal heredity that is characterized by abnormal growth of hyalinized fibrous tissue [2-4]. Juvenile hyaline fibromatosis is clinically characterized by tumors, bone lesions, joint contractures, gingival hyperplasia, and normal intelligence [1, 5, 6]. Most tumors involve head, back, and extremities. The lesions are painless, but cosmetically unacceptable [4]. It is most commonly diagnosed in early childhood, even though there are some reports of new diagnosis in adult life [5]. It is a progressive disease and the manifestations tend to be additive with age. There is no gender or ethnic predilection. One-third of affected children are siblings and several have been born to consanguineous parents [6, 7]. Variable penetrance is present and two distinct forms of JHF has been postulated: a localized form with very slow growth and a diffuse form with large and rapidly growing tumors [4, 5]. The treatment is not satisfactory. Early surgical excision is recommended, but recurrences are frequent [8]. We report a patient with juvenile hyaline fibromatosis without gingival hyperplasia and onset at 8 years old with late progression in adolescence.

Case Synopsis

A 23-year-old man, born of unrelated parents, presented with multiple tumors. At 8 years of age, he developed a single nodule on the face. At 15 years, he began to develop other multiple nodules involving the head, back, abdomen, extremities, and perianal area. He also reported stiffness and limitation in moving the shoulders. The nodules were uncomfortable and interfered with sleep. Parents, brothers and sisters were healthy and denied any dermatologic disease.

On dermatologic examination, he exhibited multiple firm tumors variable in size. Most were located on the face, back, abdomen and extremities (**Figure 1**). These lesions were also restricting the function of the joints, mainly the shoulders. There were no oral findings (**Figure 1**). Computed tomography showed osteolytic lesions in the shoulders and hip related to tumor compression.

Several tumors were excised from the back and have not recurred (**Figure 2**). Histopathological findings showed poorly circumscribed masses of eosinophilic, hyalinized, periodic acid-Schiff-positive and diastase-resistant material in dermis and subcutaneous tissue. A hypocellular spindle cell proliferation, with hyperchromatic nuclei was seen without evidence of mitosis (**Figure 3**). Congo red stain was negative. Immunohistochemical studies showed that the spindle cells were positive for collagen III, vimentin, smooth muscle actin, HHF35, and beta catenin (not shown). A panel of special stains and immunostains with results was listed in **Tables 1, 2**.

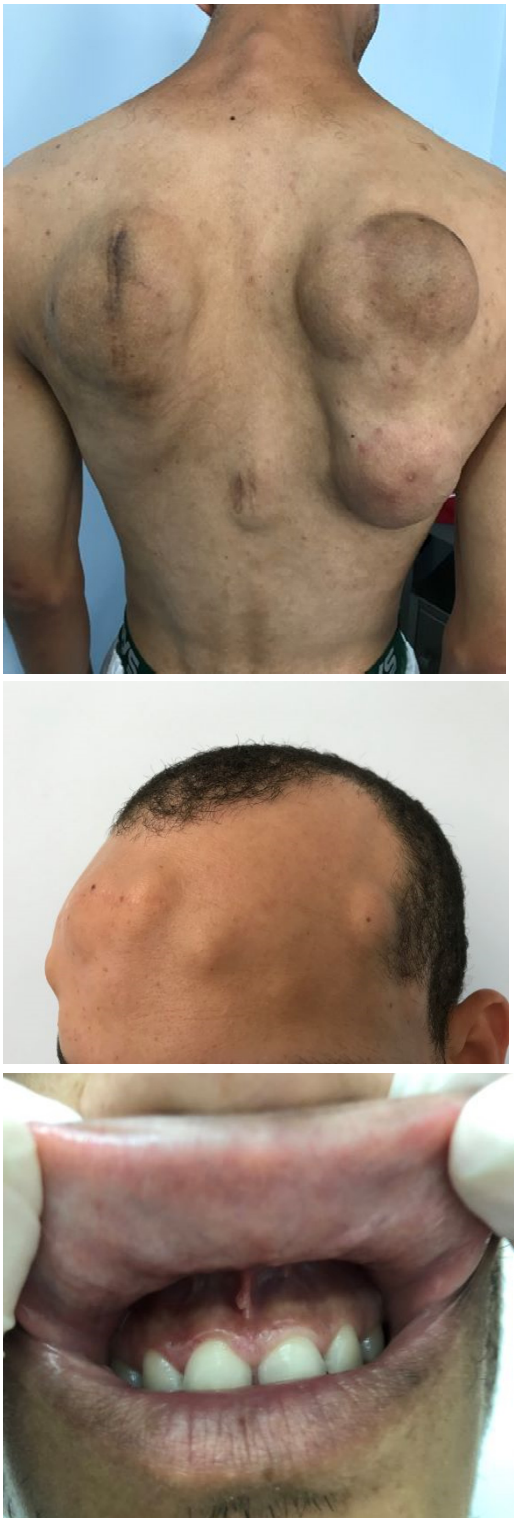

Figure 1. *Multiple tumorous skin lesions involving forehead and back. Gingival hyperplasia is absent.*

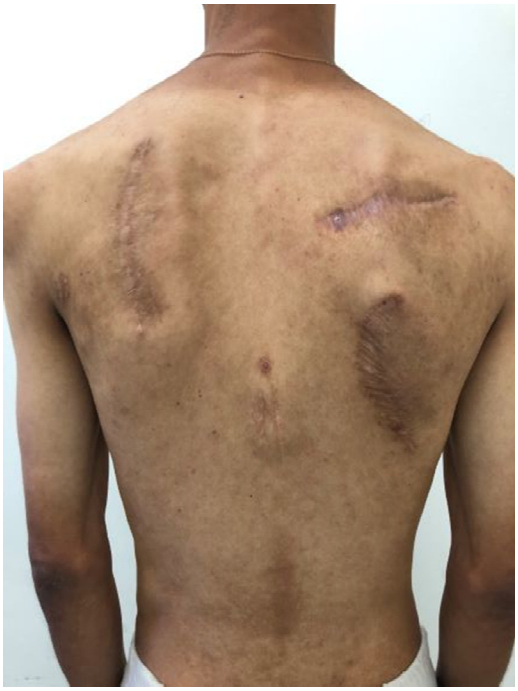

Figure 2. *One-year follow-up after first surgical excision, without recurrence to the present.*

Table 1. *Staining results of biopsy.*

Matrix stains	Result
PAS with diastase	Positive
Congo red	Negative

Table 2. *Immunohistochemical stains of biopsy.*

Immunohistochemistry of cellular component	Result
Colagen III	Positive
Vimentin	Positive
Smooth muscle actin	Positive
HHF 35	Positive
Beta catenin	Positive
AE1AE3	Negative
S100	Negative
CD34	Negative
Caldesmon	Negative
Ciclin D1	Negative

Case Discussion

Juvenile hyaline fibromatosis was first reported by Murray in 1873 as molluscum fibrosum, but the current name was provided by Kitano in 1976. It is a rare recessive autosomal hereditary disease that arises from abnormalities of the gene *ANTXR2* located in chromosome 4q21. Variable penetrance is described and patients can express partial disease. Several pathogenetic mechanisms have been proposed including impaired synthesis of procollagen or tropocollagen, increased synthesis of glycosaminoglycans by fibroblasts, and impaired collagen IV metabolism. More recently, decreased type III collagen metabolism and a secondary increase in type I collagen metabolism have been suggested [4, 9]. The authors speculated that this abnormal collagen metabolism leads to instability and intracellular accumulation, and may explain the clinical manifestations of JHF.

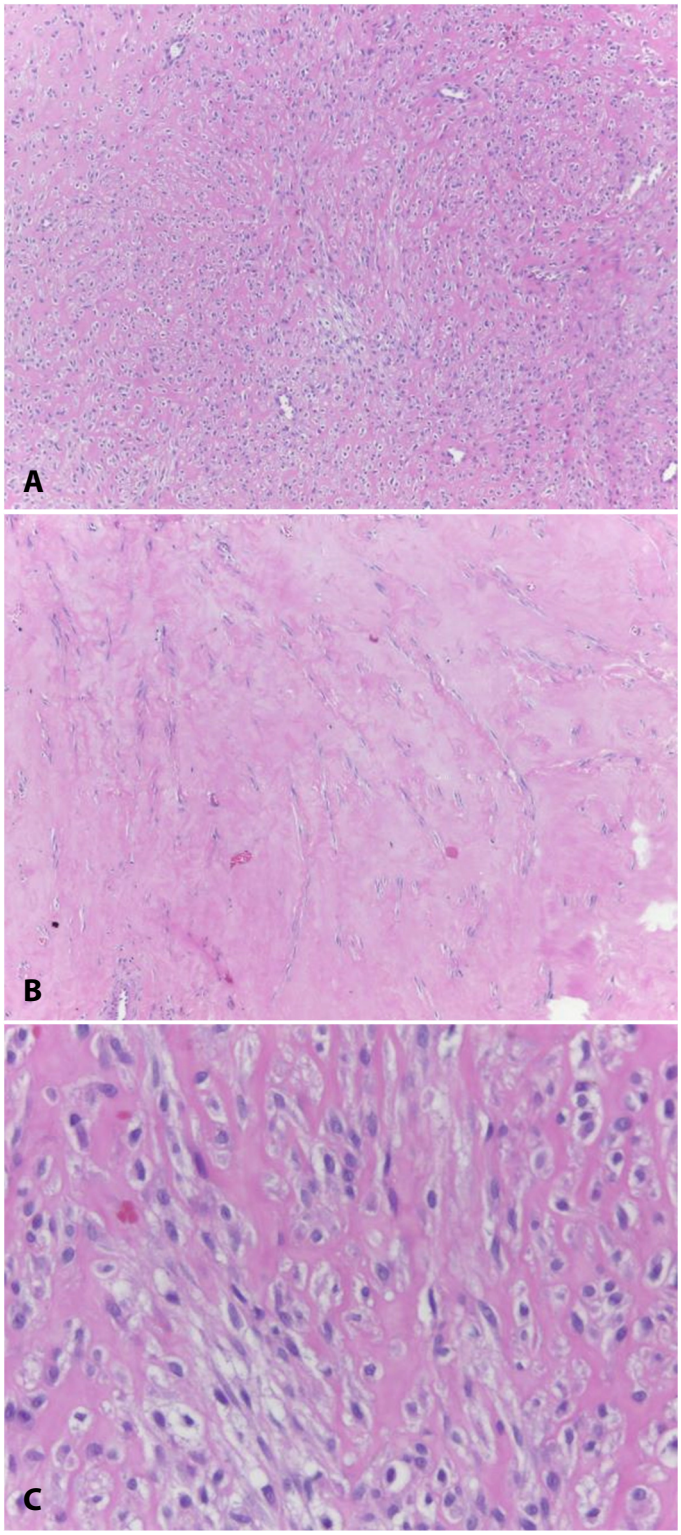

Figure 3. *Histopathological findings: hyalinized PAS-positive and diastase resistant material, permeating monomorphic hypocellular spindled cells proliferation. H&E,* ***A)*** *40×;* ***B)*** *100×;* ***C)*** *400×.*

We report a localized form with limited cutaneous involvement, slow growth, and normal life expectancy. The diagnosis was based on the presence of typical skin tumors, osteolytic bone lesions, joint contractures, and histopathological findings. He did not exhibit gingival hyperplasia. However, he may develop these complications in the future.

The first signs are often lesions on the skin and soft tissue, although joint manifestations could be primary. Juvenile hyaline fibromatosis is not a disorder known to undergo malignant transformation and the related primary morbidity is a result of joint contractures that limit movement, and may result in patients becoming wheelchair-bound in early adulthood. Large cutaneous nodules may develop ulceration and secondary infection or pain [1, 6, 10]. Gingival overgrowth may result in poor oral hygiene and dental infections [3].

A similar condition, infantile systemic hyalinosis, should be considered in the differential diagnosis. It is characterized by the above findings with further visceral involvement. The main difference is the age of presentation and the prognosis. Carriers of this diffuse form are usually dead by early childhood, owing to intractable diarrhea because of hyalinized growths in the gastrointestinal tract. Many authors consider that JHF and ISH are in a spectrum of one disorder, hyaline fibromatosis syndrome, with differing penetrance and phenotypic expression [1].

Other conditions in the differential diagnosis that should be included are: Winchester syndrome, neurofibromatosis, nodular amyloidosis, and Farber disease. Winchester syndrome is characterized by joint contractures, osteoporosis, corneal opacities, and dwarfism. Skin nodules are uncommon and there is no deposition of hyaline matrix. Neurofibromatosis is also commonly characterized by dermal and soft tissue tumors, although joint contractures and gingival hypertrophy are not usual. Furthermore, neural differentiation is consistently absent in the skin lesions of juvenile hyaline fibromatosis [1]. Farber disease is a disorder of lipid metabolism characterized by nodular swelling around the joints, short stature, and delayed mental development. Nodular amyloidosis shows a hyalinized and paucicellular matrix as does JHF, but Congo red is positive. Congo red stain was negative in our case, distinguishing it from amyloidosis. The pattern of hyaline material and the monomorphic fusocellular proliferation with low mitotic rate supports the diagnosis of JHF.

Conclusion

Juvenile hyaline fibromatosis is a rare disease and requires multidisciplinary care. It is particularly important for the dermatologist to recognize the early development of nodules to allow surgical intervention and familial genetic counselling with an aim to minimize the impact of the disease. The main treatment for JHF is surgical excision of subcutaneous nodules, although local recurrence is common. There is a limited response to intralesional corticosteroid injections in early stages [9]. The functional prognosis for patients with joint contractures is poor. Symptomatic treatment for joint contracture, including capsulotomy, corticosteroids, ACTH and/or physiotherapy may be attempted [4]. Gingivectomy is also commonly suggested for the treatment of gingival hypertrophy [3].

Potential conflicts of interest

The authors declare no conflicts of interests.

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