Atrophic Skin Patches With Abnormal Elastic Fibers as a Presenting Sign of the MASS Phenotype Associated With Mutation in the Fibrillin 1 Gene

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Marfan syndrome (MFS) is a life-threatening autosomal dominant disorder of connective tissue. Chief manifestations include proximal aortic aneurysm, dislocation of the ocular lens, and bone overgrowth.1 Mutations in the FBN1 gene (OMIM 134797), which encodes the matrix protein fibrillin 1, are identified in more than 90% of patients presenting with classic MFS.2,3 The most common skin finding in MFS is striae distensae. Particular individuals referred for suspected MFS who do not completely fulfill the MFS diagnostic criteria are classified as having a MASS phenotype. The acronym represents the following manifestations: a prolapsed mitral valve, myopia, aortic root enlargement, and skeletal and skin manifestations. Mutations in FBN1 have been shown to be associated in some cases with the MASS phenotype. Skin manifestations may be an important clue to the diagnosis of these disorders.

Observations

We studied a patient referred for unusual atrophic skin patches on the buttocks. Results of histopathological examination and electron microscopy demonstrated markedly abnormal elastic fibers. Subsequent medical genetics evaluation led ultimately to the diagnosis of the MASS phenotype and the discovery of an underlying FBN1 mutation.

CONCLUSIONS AND RELEVANCE

Although the clinical suspicion and diagnosis of MFS and related disorders are usually established by its main associated clinical features, including ophthalmologic, skeletal, and vascular involvement, clinicians should be aware of the associated skin manifestations, including unusual atrophic patches with abnormal elastic fibers that can sometimes be the first noted sign of the genetic disorder.

Report of a Case

Dermatologic Evaluation

A man in his late 50s was referred for atrophic patches on the buttocks. One atrophic patch had been present on the left buttock since 15 years of age. The second patch appeared on the right buttock some months prior and was noted to be painful (Figure 1). His medical history was unremarkable. Skin examination revealed 2 erythematous large atrophic patches on both buttocks and an additional smaller skin-colored atrophic patch on the left buttock. The older erythematous patch on the left buttock was 10 cm in diameter, whereas the newer one on the right buttock measured 5 cm in diameter (Figure 1). All 3 lesions were soft and nontender on palpation.

Ultrastructural evidence of markedly abnormal elastic fibers. These findings led to the diagnosis of the MASS phenotype with an underlying FBN1 mutation. We further discuss this unusual skin finding not previously reported in patients with MFS or the MASS phenotype.

IMPORATANCE Marfan syndrome (MFS) is a dominantly inherited disorder of connective tissue caused by mutations in the fibrillin 1 gene (FBN1). The most common skin finding in MFS is striae distensae. Particular individuals referred for suspected MFS who do not completely fulfill the MFS diagnostic criteria are classified as having a MASS phenotype. The acronym represents the following manifestations: a prolapsed mitral valve, myopia, aortic root enlargement, and skeletal and skin manifestations. Mutations in FBN1 have been shown to be associated in some cases with the MASS phenotype. Skin manifestations may be an important clue to the diagnosis of these disorders.
Skin biopsy specimens were obtained from the centers of the 2 larger lesions. The biopsy from the large lesion on the left buttock revealed large eosinophilic colloidlike aggregations in the papillary dermis (Figure 2A). Higher magnification revealed clumps of curly eosinophilic fibers within the colloidlike aggregates. In addition, we noted an apparent increase in the number of small blood vessels throughout entire dermis. Elastic tissue stain demonstrated large clumps of curly elastic fibers within the colloidlike aggregates (Figure 2B). In the dermis, large areas were devoid of elastic fibers with occasional short “chopped” thick elastic fibers and increased numbers of small blood vessels. Some bundles of densely packed curly elastic fibers were seen in the lower dermis. The biopsy from the lesion on the right buttock demonstrated an increased number of small blood vessels throughout the dermis. A Verhoeff–van Gieson elastic tissue stain revealed an increased number of thick elastic fibers. Higher magnification demonstrated short or chopped elastic fibers and bundles and aggregates of thick wavy elastic fibers (Figure 2C). Results of the Congo red and von Kossa stains did not show amyloid or calcium, respectively.

A biopsy specimen for electron microscopy was obtained from the uninvolved normal-looking skin on the buttock. The ultrastructural study performed as previously described revealed normal-looking collagen fibrils intermingled with abnormal-looking fragmented elastic fibers (Figure 3A). The elastic fibers had the appearance of numerous cracks and holes at their peripheries, which produced a network reminiscent of a cobweb (Figure 3). At a higher magnification, numerous fibrils were present at the borders of the cobweblike formations (Figure 3B). Owing to the marked histopathological and ultrastructural abnormalities of the elastic fibers observed, a medical genetics consultation was requested for evaluation of a possible underlying disorder of connective tissue.

Figure 1. Clinical Presentation of an Atrophic Skin Lesion

An erythematous atrophic patch on the right buttock.

Figure 2. Histopathological Examination of the Atrophic Skin Lesion

A, A biopsy specimen obtained from the atrophic lesion on the left buttock. The epidermis is normal looking, and colloidlike aggregates in the papillary dermis consist predominantly of dense aggregates of eosinophilic fibers. An increased number of small blood vessels is also present (hematoxylin-eosin, original magnification ×200). B, An elastic tissue stain demonstrates that the colloidlike aggregates in the upper dermis are made largely of dense round aggregates of curly elastic fibers (Verhoeff–van Gieson [VVG] stain, original magnification ×200). C, A biopsy specimen obtained from the atrophic lesion on the right buttock. Short elastic fibers are seen along with thick and wavy irregular bundles of elastic fibers (VVG stain, original magnification ×400).
Medical Genetics Evaluation

The patient reported a history of clumsiness and recurrent falls during childhood but no significant joint laxity, joint dislocations, or fractures. He was diagnosed with mild scoliosis during his teenage years but had not needed any corrective measures. Bruising and scar formation were normal. He also reported having high myopia since childhood. His parents were nonconsanguineous and both died of heart disease late in the seventh decade of life. Results of the physical examination revealed a slender man (Figure 4A) with nondysmorphic facial features. Oral examination revealed a single uvula, normal palate, and missing teeth due to poor oral hygiene, although no periodontal disease was noted. No pectus carinatum or excavatum deformity was found, although a mild bone dysplasia was noted at the clavicles and ribs. Joint hypermobility was noted at the fingers, although thumb and wrist signs were negative for MFS. At the elbows, contractures were observed (Figure 4B), and the patient was unable to extend his elbows. At the back, a mild ky-
Discussion

The atrophic skin patches in our patient clinically resembled antedoderma and middermal elastolysis. Both defects are characterized by a loss of elastic tissue without an increased amount of abnormal elastic fibers, as in our patient. Increased amounts of elastic tissue may be seen in solar elastosis, pseudoxanthoma elasticum, elastosis perforans serpiginosa, and isolated elastomas. The non-sun-exposed location of the lesions, the lack of calcium with a von Kossa stain, the lack of transepidermal elimination, and the clinical presentation, respectively, precluded these possibilities.

The most common skin manifestation of MFS and the MASS phenotype are striae. Striae distensae consist of bands of thin, wrinkled skin that are red, then purple, and finally white. The histopathological features of striae associated with MFS and other conditions are similar: the epidermis is thin and flattened, and the upper dermis is decreased in thickness and characterized by straight thin collagen bundles arranged parallel to the skin along with elastic fibers that are arranged similarly. The elastic fibers are present in greater quantity than in the surrounding skin, possibly as dense bundles of parallel fibers. Below this zone, a localized absence of elastic fibers may be noted, and in the borders between the striae and normal skin, curled, broken, and reticular elastic fibers are sometimes evident. For these reasons, striae distensae are considered scars. In the present case, the biopsy findings of the specimen taken from the centers of the lesions did not show the characteristic histopathological features or structure of striae distensae, and the ultrastructural study demonstrated elastic fibers with markedly abnormal structure.

The ultrastructural findings in this case resembled those described in the normal-looking skin of a 15-year-old girl with MFS. The main finding in the younger patient was fragmentation of elastic fibers at their peripheries with subdivision into many fine fibers, ultimately giving them a cobweblike appearance. This ultrastructural resemblance encouraged us to pursue a medical genetics evaluation, which resulted in the diagnosis of the MASS phenotype and a mutation in the FBN1 gene.

Conclusions

Although the diagnosis of inherited disorders of connective tissue is usually established by the skeletal, vascular, and ophthalmologic manifestations, clinicians should be aware of the associated skin findings. These findings include unusual atrophic patches with abnormal elastic fibers, which can sometimes be the first noted sign of the genetic disorder.
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REFERENCES


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Case Report/Case Series

Research