Familial Syringomas: An Example of Gonadal Mosaicism

COL Kathleen J. Smith, MC, USA, Bethesda, Maryland
Henry G. Skelton, MD, Herndon, Virginia

Multiple syringomas may be inherited as an autosomal dominant trait or may occur as segmental or unilateral lesions limited to one generation. We present a man with diffuse involvement whose mother also has unilateral syringomas. No previous generations were affected. We believe that this case represents an example of an autosomal dominant postzygotic mutation that resulted in gonadal mosaicism in the mother.

Syringomas most commonly appear in adult women, usually as multiple papules on the lower eyelids and cheeks.[1] Less common locations include the vulva, penis, forehead, and scalp.[2-5] Familial syringomas also have been reported, as well as unilateral or segmental syringomas and eruptive syringomas.[6-13] Although the etiology of localized syringomas is unknown, factors within the local environment leading to occlusion of the upper eccrine ducts probably play a role. However, familial and unilateral syringomas and at least some cases of eruptive syringomas result from mutations either within zygote or later postzygotic somatic mutations, which may or may not affect gonadal mosaicism in the affected patient.

Case Report

A 19-year-old white man presented with diffuse skin-colored to slightly yellowish papular lesions, most prominent on the ventral trunk (Figure 1). The patient's mother had first noticed these lesions when he was approximately 2 years old. His mother had similar lesions that were restricted to the left side of her body, also most prominent on the ventral trunk. The patient had one sibling who had not developed similar lesions, and there had been no prior history of the lesion in any other maternal or paternal ancestors. Both the mother's and the son's lesions had remained asymptomatic.

We performed 5-mm punch biopsies on 2 lesions selected from the son. The findings of both biopsies were similar: numerous small ducts lined by 2 rows of epithelial cells. The surrounding dermis showed moderate fibrosis, and the bulk of the area of epithelial proliferation extended down to approximately the midreticular dermis (Figure 2A). Some of the ducts had small, commalike tails of epithelial cells. There also were solid strands of epithelial cells independent of the ducts (Figure 2, A and B). Mainly within the upper portion of the lesion, there were cystic ductal lumina filled with keratin and lined by cells containing keratohyaline granules. The biopsies of both lesions revealed that the lower portion of the eccrine ducts, from which the syringomas appeared to arise, was morphologically normal and closely followed a hair follicle (Figure 2B).

Comment

Familial syringomas may rarely be inherited as an autosomal dominant trait.[6,7,14] In addition, there are reports of unilateral or segmental syringomas with no family history.[8-10] These lesions may result from autosomal dominant, but spontaneous, somatic mutations that do not involve germ cells and cannot be passed on to the next generation. Eruptive syringomas also may represent either germ line or somatic mutations, and most cases become manifest when patients are young, about the time of puberty.[11-13]

The initial mutation in the family we are reporting probably occurred in the mother. Her lesions were and had always been unilateral, suggesting that it was postzygotic mutation. Although variable penetrance may explain variation in the manifestation of genetic traits between individuals

Dr. Smith is from the Department of Dermatology and Pathology, National Naval Medical Center, Bethesda, Maryland. Dr. Skelton is from the Laboratory Corporation of America, Herndon, Virginia.
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Reprints: Henry G. Skelton, MD, 2047 Vestavia Park Ct, Vestavia Hills, AL 35216.

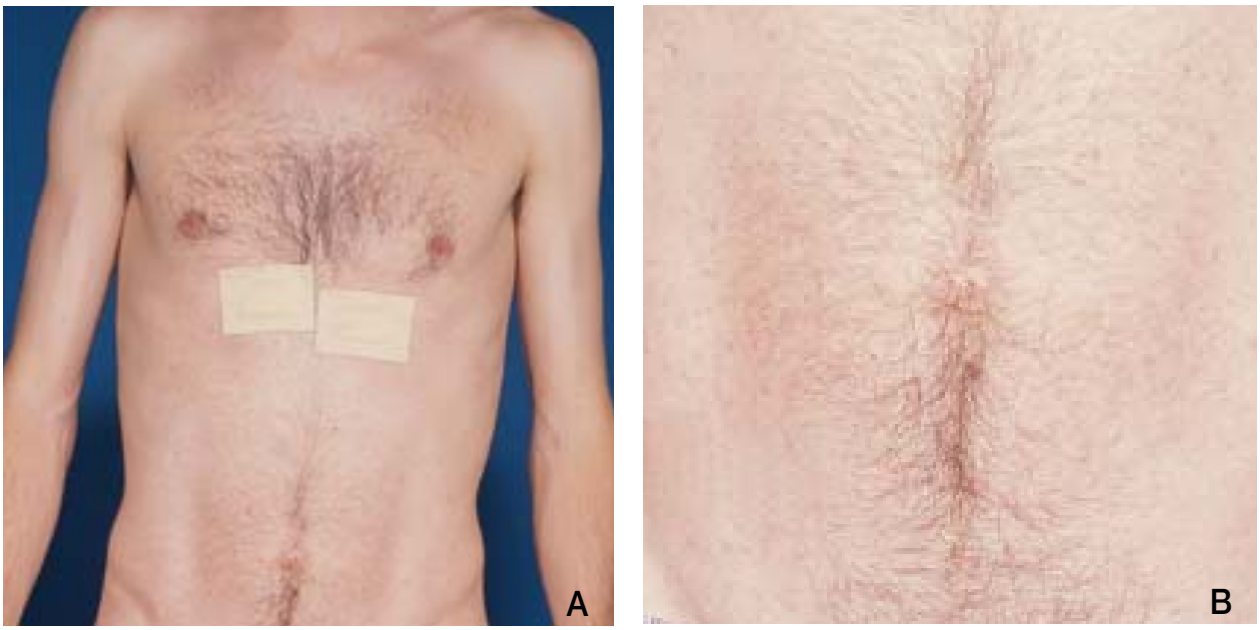

Figure 1. Numerous skin-colored to slightly yellowish papules diffused over the abdomen (A). Higher magnification of the lesions (B).

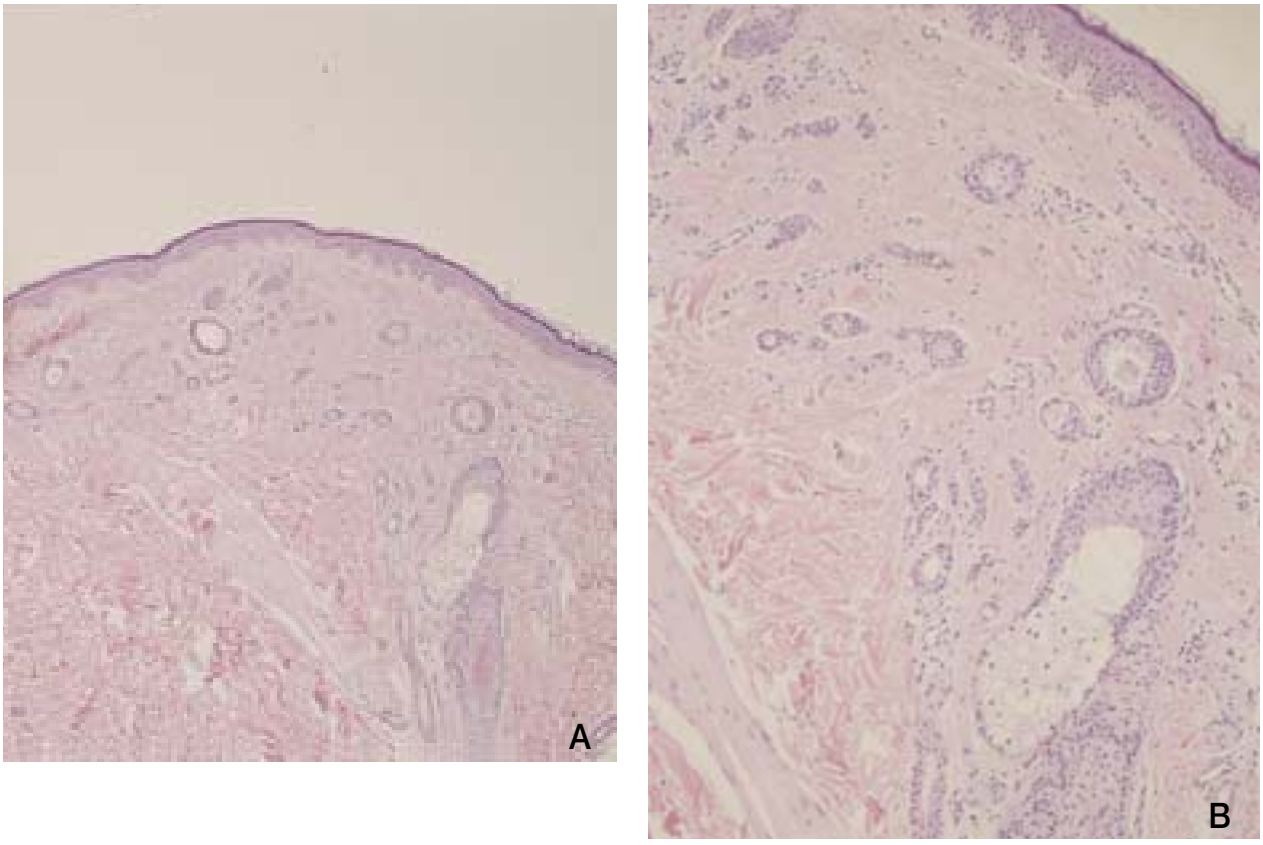

Figure 2. Numerous small ducts lined by 2 rows of bland epithelial cells (A). The syringomas seem to arise from the lower portion of eccrine ducts, which appear morphologically normal (B)(H&E, original magnifications ×75 and ×300).

who carry the mutated gene, it would be unlikely that it could explain the strictly unilateral pattern seen in the mother, with a diffuse pattern seen in the son. The subsequent passage of the defective gene to her son could have occurred if the postzygotic mutation in the mother resulted in formation of germ cells on the affected side, leading to gonadal mosaicism.

As in local syringomas, the mechanism for the production of these lesions is not known. Keratin plug within the upper portion of the ducts over morphologically normal eccrine ducts deep within the dermis may result from a primary defect in the upper portion of the eccrine ducts. The resulting obstruction may lead to secondary ductal proliferation that induces stromal fibrosis.

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