JAMA Dermatology Clinicopathological Challenge

# Multiple Atrophic Papules and Plaques on the Trunk and Extremities of a Young Man

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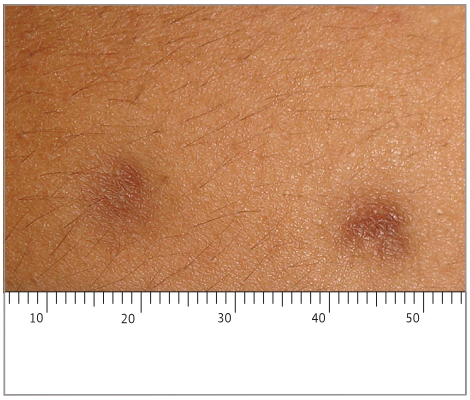
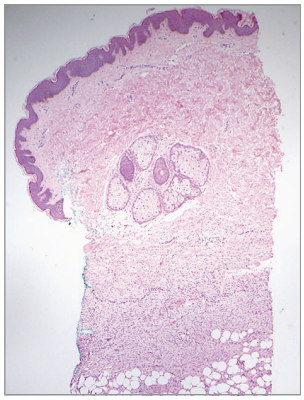
A Atrophic plaques




B Original magnification ×40



C Original magnification ×200

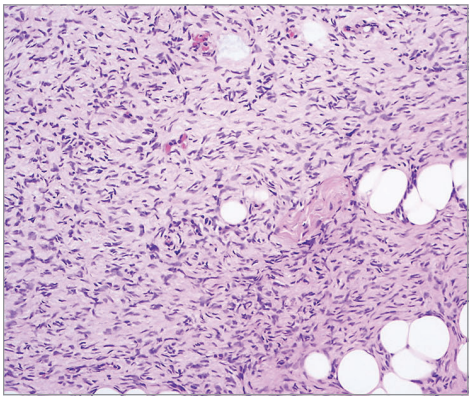


**Figure.** A, The patient presented with 2 distinct, smooth-surfaced, 0.5- to 1.0-cm atrophic plaques with overlying hyperpigmentation on the left thigh. Both lesions exhibited the buttonhole sign on palpation. B and C, Histopathology shows poorly circumscribed hypercellular proliferation of spindle cells occupying the lower reticular dermis with lacelike infiltration of the subcutaneous fat (hematoxylin-eosin). The somewhat whorled, uniform appearing spindle cells with mildly hyperchromatic, elongated, wavy nuclei surrounded by pale cytoplasm. Mitotic figures and nuclear pleomorphism are uncommon.

**A young man** in his late teens presented with numerous atrophic papules and plaques on his trunk and extremities that developed gradually over several years. Although most were asymptomatic, the patient was concerned about the ongoing appearance of new lesions and the associated pain that some lesions were causing. His medical history was significant for adenosine deaminase–deficient severe combined immunodeficiency (ADA-SCID), which had been managed since childhood with twice weekly intramuscular injections of pegademase bovine enzyme replacement, thrice weekly trimethoprim-sulfamethoxazole for *Pneumocystis* prophylaxis, and monthly infusions of intravenous immunoglobulin. Physical examination revealed 9 smooth-surfaced, skin-colored to hyperpigmented, 0.5- to 1.5-cm atrophic papules and plaques that exhibited the buttonhole sign on palpation (Figure, A). The multicentric lesions were located on the left knee, left thigh, bilateral chest, and back. Punch biopsies of lesions on his trunk and extremities were sent for histopathological examination with hematoxylin-eosin (H&E) staining (Figure, B and C), immunohistochemical (IHC) studies, and molecular evaluation with reverse transcription polymerase chain reaction.

**WHAT IS YOUR DIAGNOSIS?**

- **A.** Neurofibroma
- **B.** Anetoderma
- **C.** Dermatofibrosarcoma protuberans, atrophic variant
- **D.** Medallionlike dermal dendrocyte hamartoma

## Diagnosis

**C.** Dermatofibrosarcoma protuberans, atrophic variant

## Microscopic Findings

Histopathological examination with H&E revealed a hypercellular proliferation of spindle-shaped fibroblastic cells occupying the reticular dermis and infiltrating the subcutis (Figure, B and C). The elongated, wavy nuclei were mildly hyperchromatic but otherwise bland, and mitotic figures were uncommon. Immunohistochemistry showed strong, diffuse positivity for CD34 and vimentin, whereas factor XIIIa and S100 were negative. Reverse transcription polymerase chain reaction confirmed the presence of a COL1A1-PDGFβ fusion transcript. These features were consistent with dermatofibrosarcoma protuberans (DFSP), specifically the variant known as atrophic DFSP.

## Discussion

Dermatofibrosarcoma protuberans is a rare malignant mesenchymal tumor of the dermis and subcutis found most commonly on the trunk and proximal extremities. Its incidence is up to 4.5 cases per million population per year,[1] but it is rarer among children. Autosomal recessive ADA-SCID (OMIM 102700) is a genetic disorder of

humoral and cellular immunity. In 2011, Kesserwan et al[2] first described an association between ADA-SCID and DFSP, highlighting the latter's unique features of multicentricity, early age at onset, and tendency to manifest as small atrophic plaques. The mechanism underlying the development of multiple atrophic DFSP lesions in patients with ADA-SCID has not been fully elucidated. The natural history of DFSP in this setting is unknown because until recently, few patients with ADA-SCID survived into adulthood.[2]

Diagnosis of childhood DFSP is frequently delayed because of its subtle, asymptomatic presentation, indolent growth, and potentially ambiguous histology.[3,4] At a minimum, routine histopathologic and IHC evaluation of tissue obtained via full-thickness punch biopsy is required.[5] On histopathologic assessment with H&E, DFSP lesions appear as deeply infiltrative, poorly circumscribed spindle cell tumors with a storiform or fascicular pattern. Tumor cells often exhibit enlarged nuclei, but pleomorphism and mitotic activity are low. Of note, DFSP lesions associated with ADA-SCID may lack this classic pattern.[2]

Dermatofibrosarcoma protuberans lesions typically express CD34, nestin, and apolipoprotein D and are negative for factor XIIIa, cathepsin K, stromelysin 3, HMGA1, HMGA2, tenascin, D2-40, and CD163, although some tumors do not fully conform with the predicted IHC pattern.[5,6] When H&E and IHC findings are inconclusive, cytogenetic fluorescence in situ hybridization analysis can assess for the (17;22)(q22;q13) chromosome translocation characteristic of DFSP. Reverse transcription polymerase chain reaction can identify its resultant COL1A1-PDGFβ fusion transcript.[7] These 2 studies are critical in differentiating DFSP from medallion-like dermal dendrocyte hamartoma (MDDH), another rare infiltrative CD34+ spindle cell neoplasm that has been described most commonly in children and adolescents. Unlike DFSP, however, MDDH is known to follow a benign course.[8]

Clinical examination and histologic features can help differentiate DFSP from other atrophic papules. In addition to MDDH, the differential diagnosis for atrophic DFSP includes neurofibroma and anetoderma. Neurofibromas, particularly those in patients with neurofibromatosis type 1, can present as small, skin-colored to violaceous, or hyperpigmented atrophic papules that demonstrate the buttonhole sign. Histologically these dermal tumors are composed of Schwann cells, fibroblasts, and mast cells. Other cutaneous manifestations of neurofibromatosis type 1, including café-au-lait macules and axillary or inguinal freckling, may accompany the presence neurofibromas. Anetoderma is a disorder of elastic tissue that also presents as an atrophic papule. Histology demonstrates characteristic loss of elastic tissue, differentiating anetoderma from DFSP.

The natural history of DFSP in the setting of ADA-SCID is unclear, and there are no standard management guidelines. Extensive imaging and laboratory evaluations are not usually indicated, because DFSP lesions rarely metastasize. Patients with ADA-SCID may develop multiple slow-growing atrophic DFSP lesions despite adenosine deaminase enzyme replacement therapy or allogeneic hematopoietic cell transplant.[2] Because of their multicentricity, bland histologic features, and generally indolent nature, one could argue for excision of only those atrophic DFSP lesions that are considerably increasing in size, causing morbidity, or are symptomatic. On the basis of these changing features, we removed some of the patient's lesions with Mohs micrographic surgery. However, with the multicentric lesions and the potential for poor cosmetic and functional outcome from repeated excisions, the patient declined surgical management of all DFSP lesions. Instead, he preferred to have the lesions closely monitored during frequent follow-up visits. Patients with DFSP and ADA-SCID should be examined at least every 12 months for life, with inspection and palpation of known lesions, new lesions, and the scars at excision sites.[5,6]

## ARTICLE INFORMATION

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