Dermatofibrosarcoma Protuberans in Two Patients with Acquired Immunodeficiency Syndrome

Allen N. Sapadin, MD, New York, New York
J. M. Gelfand, MD, Boston, Massachusetts
K. L. Howe, MD, New York, New York
R. G. Phelps, MD, New York, New York
D. Grand, MD, New York, New York
D. Rudikoff, MD, New York, New York

GOAL

To describe the characteristics of dermatofibrosarcoma protuberans (DFSP) in conjunction with the acquired immunodeficiency syndrome.

OBJECTIVES

1. To discuss the location and clinical appearance of DFSP.
2. To delineate other dermatologic conditions associated with DFSP.
3. To identify the preferred therapy for DFSP.

CME Test on page 77

Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive cutaneous tumor of intermediate malignancy. Most commonly, it arises as an asymptomatic, indurated plaque on the trunk within which protuberant nodules develop over time. We describe its occurrence in two patients with human immunodeficiency virus, a previously unreported association. The first patient, a 41-year-old woman, complained of painful lesions around the left shoulder that developed within a scar from previous trauma to the area. The second patient, a 50-year-old man, developed a recurrent DFSP within the scar from a previous surgical procedure. Dermatofibrosarcoma protuberans was confirmed in both cases by the histopathologic and immunohistochemical findings.

From the Departments of Dermatology and Pathology, Mount Sinai School of Medicine, New York, New York; Mount Sinai Medical Center, New York, New York; and the Department of Dermatology, Beth Israel Medical Center of the Albert Einstein College of Medicine, New York, New York.
REPRINT REQUESTS to Box 1048, The Mount Sinai Medical Center, One Gustave L. Levy Place, New York, New York 10029-6574 (Dr. Sapadin).

Infection with the human immunodeficiency virus (HIV) has been associated with numerous mucocutaneous manifestations. An increased risk of skin malignancy is well recognized. A variety of cancers, including Kaposi's sarcoma and non-Hodgkins lymphoma, have frequently been described in the HIV-infected population. After Kaposi's sarcoma, basal cell carcinoma (BCC) is the most frequent skin cancer.[1] Other primary cutaneous malignant lesions that have been described in this population include squamous cell carcinoma[2,3] and malignant melanoma.[3,4] Bowen's disease, intraepithelial dysplasia of the anus[5] and cervix,[6] and conjunctival squamous cell carcinoma[7] have also been documented.

Soft tissue malignancies have been reported infrequently in HIV-infected patients. There is a possible increase in leiomyosarcoma in HIV-1-infected children

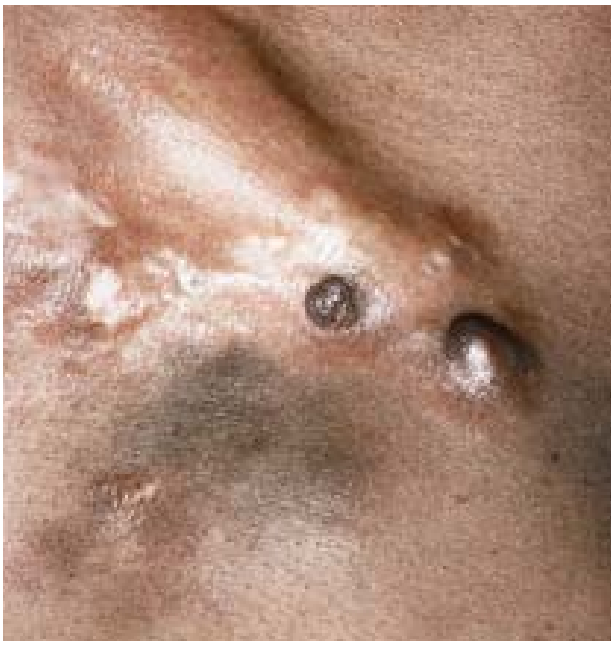

FIGURE 1. Case I. Ill-defined dermatofibrosarcoma protuberans at the left infraclavicular area. Protuberant, soft, hyperpigmented nodules were located at the lateral-most aspect of the atrophic hypopigmented plaque. An area of hyperpigmentation extended inferiorly.

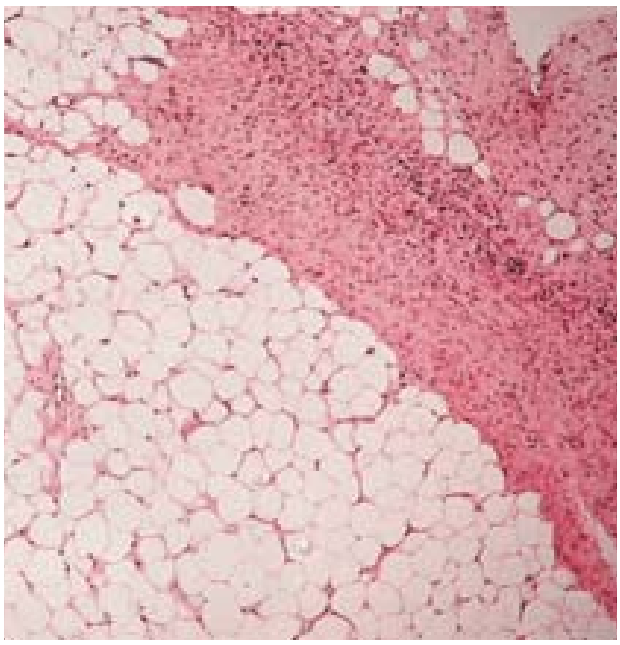

FIGURE 2. Case I. Subcutaneous fat shows infiltration with and replacement by dermatofibrosarcoma protuberans in a characteristic lace-like array. Note the fusiform cells without significant atypia, characteristic of this neoplasm (H&E; original magnification, X 50).

as compared with the general pediatric population.[8] This resulted in its inclusion as an indicator for severe immunosuppression in the 1994 classification system of pediatric HIV disease.[9] We report two HIV-infected patients who developed dermatofibrosarcoma protuberans (DFSP), the first such report in this population.

Case Reports

Case I—A 41-year-old HIV-positive black woman complained of painful lesions around the left shoulder that developed within a previous scar. Several years prior to presentation, the patient had sustained blunt trauma to the chest. The "scar" increased in size over the previous 2 months. The patient also reported darkening of the surrounding skin and sharp pain that radiated downward in the area. Three years prior to presentation, the patient had been treated for pulmonary tuberculosis. The patient's peripheral CD4+ T cell count was 48/mm^3.

Examination revealed a morphologically complex and ill-defined lesion at the left infraclavicular area (Figure 1). Medially, there was a 5 by 3 cm atrophic, depressed area with mottled pigmentary changes. Two protuberant, soft, hyperpigmented nodules were located nearby at the lateral-most aspect of the clavicle. An area of hyperpigmentation extended inferiorly.

A skin biopsy specimen revealed an infiltrating cellular fibrohistiocytic neoplasm that extended from superficial dermis to deep subcutaneous fat. Superficially, the tumor showed only sparse cellularity. Polygonal and stellate-appearing cells were present in a loose myxomatous stroma. The tumor replaced large parts of subcutaneous fat, with remnants of adipocytes being displaced to the periphery. In the deeper portions of the subcutis, cells with a delicate fusiform cytoplasm and thin wavy nuclei infiltrated the fat in a lace-like array (Figure 2). Both the myxomatous and spindle cell areas stained strongly with CD-34 (Figure 3), while staining for S-100 protein, muscle cell actin, and smooth muscle actin was negative. On the basis of the clinical, histopathologic, and immunohistochemical findings, a diagnosis of DFSP (myxoid variant) was made.

Case II—A 50-year-old HIV-positive man developed several asymptomatic papules within a surgical scar on his upper back. Four years previously, he had undergone excision of a BCC in this location. This was the fourth BCC that had been treated since he was diagnosed with HIV. Histopathologic examination at that time revealed a DFSP adjacent to the BCC. Re-excision was performed with wide surgical margins, and no residual DFSP was evident. Medical history was significant for HIV infection since 1986. His medications included zidovudine and lamivudine. There was no history of opportunistic infections. The patient's peripheral CD4+ T cell count was 180/mm^3.

Examination revealed a 13 by 2 cm linear scar in a right para-vertebral location. At the superior-most

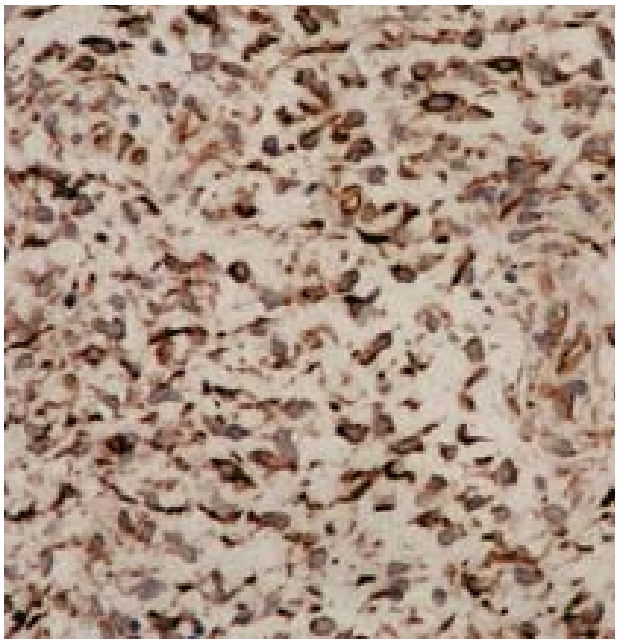

FIGURE 3. Case I. Myxoid area of the tumor shows strong cytoplasmic staining for CD-34 (original magnification, X 100).

aspect of the scar was a 1.2 cm firm, skin-colored nodule. Inferior to this nodule and also within the scar were three firm papules, measuring 2 mm in diameter.

A biopsy specimen from the nodule revealed recurrent DFSP. Immunohistochemical staining was strongly positive for CD-34, while factor XIIIa, S-100, muscle cell actin, and smooth muscle actin staining were negative.

The patient was treated with Mohs' micrographic surgery, at which time the tumor was found to have peripheral and deep extension beyond its clinical boundaries. The tumor was completely extirpated in eight stages.

Comments

Dermatofibrosarcoma protuberans is a skin tumor of intermediate malignancy characterized by slow, infiltrative growth and a propensity for local recurrence after surgical excision.[10] Although commonly referred to as a fibrohistiocytic tumor, its exact cell of origin is a matter of controversy. Alternative evidence implicates the fibroblast,[11] histiocyte,[12] and neural cells.[13] It accounts for less than 0.1% of all malignancies and has an estimated incidence of 0.8 cases per million persons per year.[14,15] More than one-half of the cases arise on the skin of the trunk,[14,16-18] and in 25% of these, the site of origin is the chest or shoulder areas.[14,17,19] The proximal extremities and head and neck are less frequently affected sites.[14,18]

Initially, DFSP presents as an asymptomatic, indurated plaque with a violaceous, skin-colored, or red-brown discoloration. Nodules develop within the plaque over months to years. This occurrence often heralds a phase of accelerated growth that may be associated with pain, ulceration, or hemorrhage.[14,16,20]

Of note, one of our patients had a history of blunt trauma and scar formation in the area in which DFSP developed. The second patient developed recurrent DFSP in the surgical scar of the prior excision. Whether or not a causal relationship exists between preceding trauma and DFSP is controversial but suggested by several remarkable case reports of DFSP developing in burn scars,[17] surgical scars,[21] and at the site of previous immunizations.[22]

Depressed and atrophic lesions have been reported as a rare clinical variant of DFSP.[23-25] These may mimic morphea, morpheaform BCC, anetoderma, and atrophic scars. The DFSP of our first patient was morphologically unusual and closely resembled a lesion reported by Lambert *et al.*[23] Four of the five patients with "dermatofibrosarcoma non-protuberans" reported in their series had depressed lesions without a nodular or protruding component. Case five initially presented with a depressed lesion, but subsequently developed overlying mottled pigmentary changes and protuberant nodules nearby, as did our patient. Since the depressed area was not biopsied in our patient, no comment can be made with regard to the histopathologic findings.

Multiple BCCs,[26] as well as squamous cell carcinomas,[27] may occur in patients with HIV infection and may appear synchronously. They can behave aggressively and may rarely metastasize.[28] Our second patient had a history of multiple (total of four) BCCs that developed after HIV seroconversion. The original DFSP in this patient was not clinically suspected. Rather, it was found juxtaposed to a BCC upon histopathologic examination of the upper back specimen. The concurrence of DFSP and BCC in the same surgical specimen has not been reported previously. The DFSP recurrence in the excision scar is also noteworthy. The efficacy of Mohs' micrographic surgery in the treatment of DFSP has been well established[29] and was successfully employed in this case. To date, there has been no recurrence of his tumor.

REFERENCES

1. Smith KJ, Skelton HG, Yeager J, *et al.*: Cutaneous neoplasms in a military population of HIV-1 infected patients: Military Medical Consortium for the Advancement of Retroviral Research. *J Am Acad Dermatol* 29: 400-406, 1993.
2. Lobo DV, Chu P, Grekin RC, *et al.*: Nonmelanoma skin cancers and infection with the human immunodeficiency virus. *Arch Dermatol* 128: 623-627, 1992.

3. Tindall B, Finlayson R, Mutimer K, *et al.*: Malignant melanoma associated with human immunodeficiency virus infection in three homosexual men. *J Am Acad Dermatol* 20: 587-591, 1989.
4. Van Ginkel CJ, Sang RT, Blaauwgeers JL, *et al.*: Multiple primary malignant melanomas in an HIV positive man. *J Am Acad Dermatol* 24: 284-285, 1991.
5. Palefsky JM, Gonzales J, Greenblatt RM, *et al.*: Anal intraepithelial neoplasia and anal papillomavirus infection among homosexual males with group IV HIV disease. *JAMA* 263: 2911-2916, 1990.
6. Vermund SH, Kelley KF, Klein RS, *et al.*: High risk of human papillomavirus infection and cervical squamous intraepithelial lesions among women with symptomatic human immunodeficiency virus infection. *Am J Obstet Gynecol* 165: 392-400, 1991.
7. Ateenyi-Agaba C: Conjunctival squamous cell carcinoma associated with HIV infection in Kampala, Uganda. *Lancet* 345: 695-696, 1995.
8. Rabkin CS, Yellin F: Cancer incidence in a population with a high prevalence of infection with human immunodeficiency virus type 1. *J Natl Cancer Inst* 86: 1711-1716, 1994.
9. Centers for Disease Control and Prevention: Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. *Morbid Mortal Wkly Rep* 43: 1-12, 1994.
10. Gloster HM: Dermatofibrosarcoma protuberans. *J Am Acad Dermatol* 35: 355-374, 1996.
11. Escalona-Zapata J, Fernandez EA, Escuin FL: The fibroblastic nature of dermatofibrosarcoma protuberans: a tissue culture and ultrastructural study. *Virchows Arch [A Pathol Anat Histopathol]* 391: 165-175, 1981.
12. Ozello L, Hamels J: The histiocytic nature of dermatofibrosarcoma protuberans: tissue culture and electron microscopic study. *Am J Clin Pathol* 65: 136-148, 1976.
13. Alguacil-Garcia A, Unni KK, Goellner JR: Histogenesis of dermatofibrosarcoma protuberans: an ultrastructural study. *Am J Clin Pathol* 69: 427-434, 1978.
14. Pack GT, Tabah EJ: Dermatofibrosarcoma protuberans: a report of thirty-nine cases. *Arch Surg* 62: 391-411. 1951.
15. Bendix-Hansen K, Myhre-Jensen D, Haae S: Dermatofibrosarcoma protuberans: a clinico-pathological study of nineteen cases and review of the world literature. *Scand J Plast Reconstr Surg Hand Surg* 17: 247-252, 1983.
16. Taylor HB, Helwig EB: Dermatofibrosarcoma protuberans: a study of 115 cases. *Cancer* 15: 717-725, 1962.
17. McPeak C, Cruz T, Nicastri A: Dermatofibrosarcoma protuberans: an analysis of 86 cases—five with metastases. *Ann Surg* 166: 803-816, 1967.
18. Enzinger FM, Weiss SW: Soft Tissue Tumors, 2nd ed, pp 252-268. CV Mosby, St Louis, 1988.
19. Hadju SI: Pathology of Soft Tissue Tumors. Philadelphia, Lea and Febiger, 1979.
20. Burkhardt BR, Soule EH, Winkelmann RK, *et al.*: Dermatofibrosarcoma protuberans: study of fifty-six cases. *Am J Surg* 111: 638-644, 1966.
21. Coard K, Branday JM, LaGrenade L: Dermatofibrosarcoma protuberans: a 10 year clinicopathological review of an uncommon tumor. *West Indian Med J* 43: 130-133, 1994.
22. Morman MR, Lin RY, Petrozzi JN: Dermatofibrosarcoma arising in a site of multiple immunizations. *Arch Dermatol* 115: 1453, 1979.
23. Lambert WC, Abramovits W, Gonzalez-Sevra A, *et al.*: Dermatofibrosarcoma non-protuberans: description and report of five cases of a morpheaform variant of dermatofibrosarcoma. *J Surg Oncol* 28: 7-11, 1985.
24. Page EH, Assaad DM: Atrophic dermatofibroma and dermatofibrosarcoma protuberans. *J Am Acad Dermatol* 17: 947-950, 1987.
25. Zelger BW, Ofner D, Zelger BG: Atrophic variants of dermatofibroma and dermatofibrosarcoma protuberans. *Histopathology* 26: 519-527, 1995.
26. Gilson I, Barnett J, Snow S: Basal cell carcinoma in HIV disease [abstract]. *Int Conf AIDS* 5: 252, 1989.
27. Overly WL, Jakubek DJ: Multiple squamous cell carcinomas and human immunodeficiency virus infection. *Ann Intern Med* 106: 334, 1987.
28. Sitz KV, Keppen M, Johnson DF: Metastatic basal cell carcinoma in acquired immunodeficiency syndrome-related complex. *JAMA* 257: 340-343, 1987.
29. Gloster HM Jr, Harris KR, Roenigk RK: A comparison between Mohs micrographic surgery and wide surgical excision for the treatment of dermatofibrosarcoma protuberans. *J Am Acad Dermatol* 35: 82-87, 1996.

FACULTY DISCLOSURE

The Faculty Disclosure Policy of the College of Medicine requires that faculty participating in a CME activity disclose to the audience any relationship with a pharmaceutical or equipment company that might pose a potential, apparent, or real conflict of interest with regard to their contribution to the program.

Dr. Sapadin reports no conflict of interest.