Disseminated Vitiligo Developing Around Kaposi Sarcoma Nodules in an AIDS Patient

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Vitiligo and other autoimmune disorders are increasingly being reported in a background of immunosuppression. Viral-induced immune activation and molecular mimicry are the proposed mechanisms for the development of autoimmune diseases in individuals infected with human immunodeficiency virus (HIV). An association of vitiligo with Kaposi sarcoma (KS) rarely has been reported. The development of vitiligo preferentially around KS lesions in a patient with AIDS is unusual. We report a case of disseminated vitiligo that developed around KS nodules in a patient with AIDS.

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Case Report

A 33-year-old man diagnosed with human immunodeficiency virus (HIV) infection 4 years prior presented to the dermatology department with a nodular skin rash of 4 months' duration that was confirmed to be Kaposi sarcoma (KS). In the last 4 weeks the rash had spread to the face, mouth, and eyelids. He had noticed spontaneous but substantial and progressive vitiligo of the skin around the lesions in the last 3 weeks (Figure 1). His $CD4^+$ T-cell count was 43/mm^3 (reference range, 500–1000/mm^3 and he did not have a history of antiretroviral therapy. He died of septicemia 3 days after admission.

Laboratory studies revealed the following values: hematocrit, 32.6% (reference range, 41%–50%); white blood cell count, 9700/mm^3 (reference range, 4500–11,000/mm^3) (with polymorphonuclear leukocytes, 85% [reference range, 40%–70%]; lymphocytes, 11% [reference, 34%]; eosinophils, 0% [reference, 2.7%]; basophils, 3% [reference, 0.3%]; monocytes, 1% [reference, 4%]); erythrocyte sedimentation rate, 109 mm/h (reference range, 0–20 mm/h); total protein, 6.4 g/dL (reference range, 6.0–8.0 g/dL). Antinuclear antibody and purified protein derivative (tuberculin) skin test results were negative. His $CD4^+$ T-cell count was 43/mm^3.

Skin biopsy results of the nodular lesions demonstrated a nodular dermal proliferation of atypical spindle cells arranged in nests and fascicles. There were slitlike vascular spaces within the spindle cell proliferation with extravasation of red blood cells (Figure 2).

Comment

Numerous skin manifestations have been documented in AIDS patients. Approximately 90% of HIV-infected patients develop cutaneous signs and symptoms[1,2]; therefore, diagnosis and management are vital in recognizing the progression of HIV infection. Common skin infections become increasingly severe and refractory to treatment as the immune system deteriorates, which may signal progression of HIV.[1]

The cutaneous manifestations of HIV infection may be divided into 3 categories: neoplastic, infectious, and others. Vitiligo rarely has been reported in association with HIV infection, and the coincidence of KS and vitiligo in HIV patients has not yet been

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The authors report no conflict of interest.

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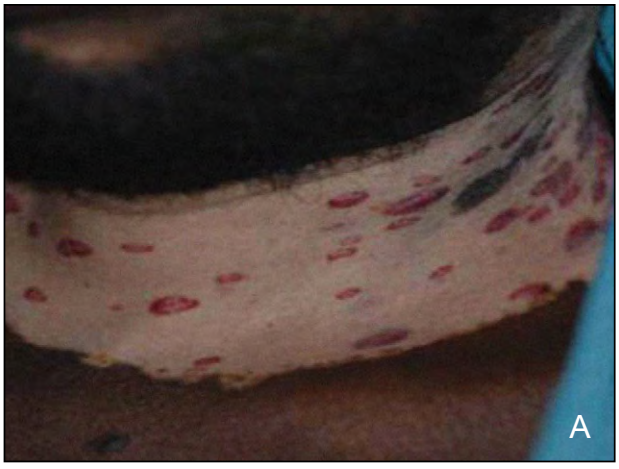

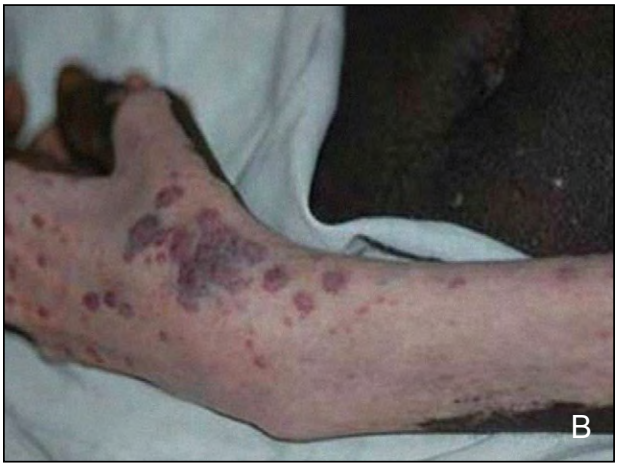

Figure 1. Vitiligo patches around clusters of Kaposi sarcoma nodules (A and B).

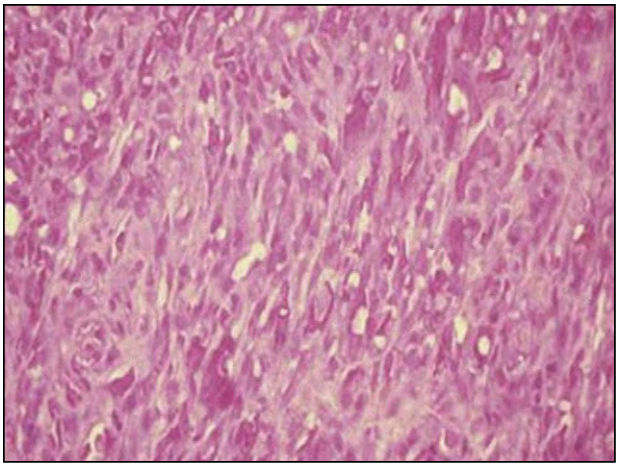

Figure 2. Histopathology of the excised nodule showed spindle cell proliferation and slitlike vascular spaces (H&E, original magnification ×40).

reported to our knowledge.[3] A relationship between HIV infection and the development of vitiligo has been previously described but is not fully established.[4,5] There is some evidence for the association between vitiligo and certain immunologic abnormalities. Chédiak-Higashi syndrome, characterized by parietal oculocutaneous albinism, has been related to impaired host defense mechanisms.[6] The Vogt-Koyanagi-Harada syndrome, characterized by bilateral uveitis associated with meningeal involvement, vitiligo, and dysacusia, has specific antibodies against surface antigens on normal melanocytes.[3]

Kaposi sarcoma is caused by an excessive proliferation of spindle cells thought to have an endothelial cell origin. Despite their heterogeneity, the tumors are predominantly composed of KS human herpesvirus genomic material with immunohistochemical markers of both lymphoid, spindle, and endothelial cells.[7] Although the origin is still unknown, there is increased endothelial factor VIII antigen; spindle cell markers such as smooth muscle α-actinin; and macrophage markers such as ICAM-1 (intercellular adhesion molecule 1), CD68, and CD14 expressed by these spindle cells.[8] Human herpesvirus 8 (HHV-8) genomic sequences have been identified by polymerase chain reaction in more than 90% of all types of KS lesions, including epidemic and endemic forms, suggesting a causative role for this DNA virus. The current working hypothesis is that HHV-8 must be present for the disease to develop. It is transmitted via saliva[9]; blood-borne transmission has yet to be proven. Human immunodeficiency virus considerably increases the risk for immunosuppression. Additionally, these viral sequences have been associated with body cavity–based lymphomas, Castleman disease, and leiomyosarcomas that occur in individuals infected with HIV.[10] Factors that are thought to contribute to the development of KS in individuals infected with HHV-8 and HIV include an abnormal cytokine milieu associated with HIV infection with angiogenic cytokines, such as IL-1β, basic fibroblast growth factor, acidic fibroblast growth factor, endothelial growth factor, and vascular endothelial growth factor.[11]

Vitiligo in association with HIV was first reported by Duvic et al[12] in 1987. Persistent viral infections have been postulated to be trigger factors for the development of autoimmune disease in a genetically predisposed host. Human immunodeficiency virus not only induces immunodeficiency but also is associated with immunodysregulation that may manifest itself as autoimmune reactivity. The mechanism for the development of vitiligo in association with HIV is not clearly understood but several theories have

been proposed.[5] The early phase of HIV infection may be accompanied by immunologic abnormalities that are characterized by lymphadenopathy, polyclonal B-cell activation with hypergammaglobulinemia, and suppressor T-cell activation. If HIV infection and vitiligo are causally related, then polyclonal B-cell activation with production of autoantibodies to melanocytes and/or antibody-dependent cell-mediated cytotoxicity against melanocytes may contribute to the development of vitiligo. Otherwise, it is possible that melanocytes may be directly affected by HIV.[13]

Conclusion

We present a rare case of vitiligo and KS associated with HIV infection. Although the role of HIV infection in these 2 skin lesions is not clear, the immunologic responses that occur early in the course of HIV infection may contribute to the development of both of these skin lesions.

REFERENCES

1. Smith KJ, Skelton HG, Yeager J, et al. Cutaneous findings in HIV-1-positive patients: a 42-month prospective study. Military Medical Consortium for the Advancement of Retroviral Research (MMCARR). *J Am Acad Dermatol*. 1994;31(5, pt 1):746-754.
2. Janniger CK, Gascon P, Schwartz RA, et al. Erythroderma as the initial presentation of the AIDS syndrome. *Dermatologica*. 1991;183:143-145.
3. Pignataro P, Rocha Ada S, Nery JA, et al. Leprosy and AIDS: two cases of increasing inflammatory reactions at the start of highly active antiretroviral therapy. *Eur J Clin Microbiol Infect Dis*. 2004;23:408-411.
4. McGowan JW 4th, Long JB, Johnson CA, et al. Disseminated vitiligo associated with AIDS. *Cutis*. 2006;77:169-173.
5. Antony FC, Marsden RA. Vitiligo in association with human immunodeficiency virus infection. *J Eur Acad Dermatol Venereol*. 2003;17:456-458.
6. Tojo N, Yoshimura N, Yoshizawa M, et al. Vitiligo and chronic photosensitivity in human immunodeficiency virus infection. *Jpn J Med*. 1991;30:255-259.
7. DeVita V. AIDS-related malignancies. In: DeVita V, Vincent T Jr, eds. *Cancer: Principles and Practice of Clinical Oncology*. Vol 8. 5th ed. Philadelphia, PA: Lippincott, Williams, & Wilkins; 2008:2404-2407.
8. Uccini S, Ruco LP, Monardo F, et al. Co-expression of endothelial cell and macrophage antigens in Kaposi's sarcoma cells. *J Pathol*. 1994;173:23-31.
9. Maurer T, Ponte M, Leslie K. HIV-associated Kaposi's sarcoma with a high CD4 count and a low viral load. *N Engl J Med*. 2007;357:1352-1353.
10. Montaner S, Sodhi A, Ramsdell AK, et al. The Kaposi's sarcoma–associated herpesvirus G protein-coupled receptor as a therapeutic target for the treatment of Kaposi's sarcoma. *Cancer Res*. 2006;66:168-174.
11. Grisotto MG, Garin A, Martin AP, et al. The human herpesvirus 8 chemokine receptor vGPCR triggers autonomous proliferation of endothelial cells. *J Clin Invest*. 2006;116:1264-1273.
12. Duvic M, Rapini R, Hoots WK, et al. Human immunodeficiency virus–associated vitiligo: expression of autoimmunity with immunodeficiency? *J Am Acad Dermatol*. 1987;7:656-662.
13. Howanitz N, Nordlund JJ, Lerner AB, et al. Autoantibodies to melanocytes. occurrence in patients with vitiligo and chronic mucocutaneous candidiasis. *Arch Dermatol*. 1981;117:705-708.