Nonepidemic Kaposi Sarcoma: A Case of a Rare Epidemiologic Subtype

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PRACTICE **POINTS**

- Nonepidemic Kaposi sarcoma (KS) is a recently described fifth subtype of the disease that typically occurs in younger men who are HIV-negative without detectable cellular or humoral immune deficiency.
- The cutaneous manifestations of nonepidemic KS are similar to those of classic KS, except that disease extent is limited and the prognosis is favorable in nonepidemic KS.
- Dermatologists should consider KS when a patient presents with clinically representative findings, even in the absence of typical risk factors such as immunosuppression.

To the Editor:

Kaposi sarcoma (KS) is a rare angioproliferative disorder associated with human herpesvirus 8 (HHV-8) infection.[1] There are 4 main recognized epidemiologic forms of KS: classic, endemic, epidemic, and iatrogenic (Table). Nonepidemic KS is a recently described rare fifth type of KS that occurs in a subset of patients who do not fit the other classifications—HIV-negative patients without detectable cellular or humoral immune deficiency. This subset has been described as clinically similar to classic KS with limited disease but occurring in younger men.[2,3] We describe a case of nonepidemic KS in a Middle Eastern heterosexual immunocompetent man.

A 30-year-old man presented for evaluation of a growth on the nose of 3 months' duration. The patient reported being otherwise healthy and was not taking long-term medications. He denied a history of malignancy, organ transplant, or immunosuppressive therapy. He was born in Syria and lived in Thailand for several years prior to moving to the United States. HIV testing 6 months prior to presentation was negative. He denied fever, chills, lymphadenopathy, shortness of breath, hemoptysis, melena, hematochezia, and intravenous drug use.

Physical examination revealed a solitary shiny, 7-mm, pink-red papule on the nasal dorsum (Figure 1). No other skin or mucosal lesions were identified. There was no cervical, axillary, or inguinal lymphadenopathy. A laboratory workup consisting of serum immunoglobulins and serum protein electrophoresis was unremarkable. Tests for HIV-1 and HIV-2 as well as human T-lymphotropic virus 1 and 2 were negative. The CD4 and CD8 counts were within reference range. Histopathology of a shave biopsy revealed a dermal spindle cell proliferation arranged in short intersecting fascicles and admixed with plasma cells and occasional mitotic figures. Immunohistochemistry showed that the spindle cells stained positive for CD34, CD31, and HHV-8 (Figure 2). The lesion resolved after treatment with cryotherapy. Repeat HIV testing 3 months later was negative. No recurrence or new lesions were identified at 3-month follow-up.

Similar to the other subtypes of KS, the nonepidemic form is dependent on HHV-8 infection, which is more commonly transmitted via saliva and sexual contact.[3,4] After infecting endothelial cells, HHV-8 is believed to activate the mammalian target of rapamycin and nuclear factor κB pathways, resulting in aberrant cellular differentiation and neoangiogenesis through upregulation

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of vascular endothelial growth factor and basic fibroblast growth factor.[2,4] Similar to what is seen with other herpesviruses, HHV-8 infection typically is lifelong due to the virus's ability to establish latency within human B cells and endothelial cells as well as undergo sporadic bouts of lytic reactivation during its life cycle.[4]

Types of Kaposi Sarcoma[1-3]

Classic

Occurs mostly in elderly men of Mediterranean, North African, and Eastern European Jewish ancestry

Indolent course with an increased risk for secondary malignancy

Endemic

Associated with notable mortality

Observed primarily in a younger HIV-negative population in East and Central Africa

Epidemic (or AIDS related)

Most aggressive form, primarily affecting HIV-infected patients in Western countries and sub-Saharan Africa

Often accompanied by disseminated mucocutaneous and visceral lesions, fever, weight loss, and diarrhea

Iatrogenic

Occurs in immunodeficient populations, including patients receiving immunosuppression therapy for organ transplantation, chemotherapy, or rheumatologic disease

Nonepidemic

Rare subtype that occurs in a subset of patients who do not fit other classifications including HIV-negative patients without detectable cellular or humoral immune deficiency

Clinically similar to classic Kaposi sarcoma with limited disease but occurring in younger men

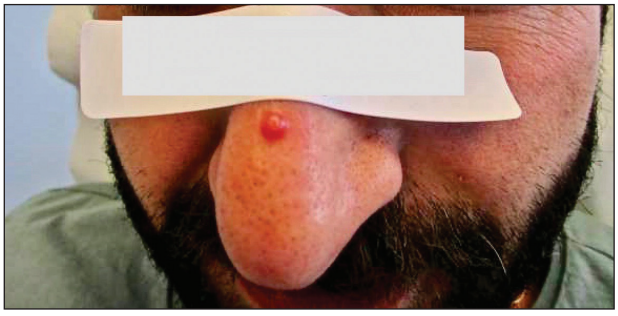

FIGURE 1. Solitary shiny, 7-mm, pink-red papule on the patient's nasal dorsum that was diagnosed as nonepidemic Kaposi sarcoma.

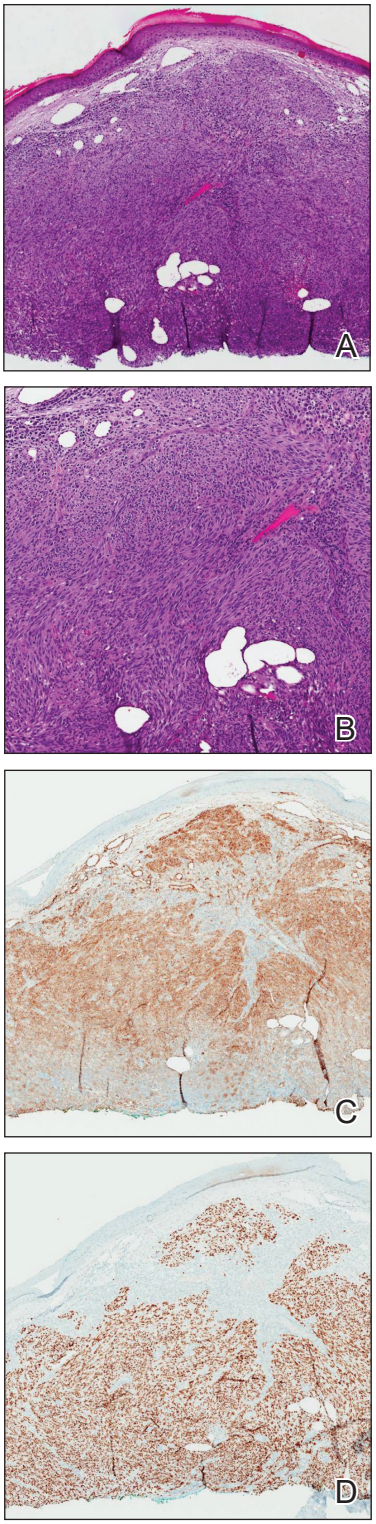

FIGURE 2. Histopathology of Kaposi sarcoma. A and B, A shave biopsy specimen from a nasal lesion revealed a dermal spindle cell proliferation arranged in short intersecting fascicles, admixed with plasma cells and occasional mitotic figures (H&E, original magnifications ×10 and ×20). C and D, Immunohistochemistry demonstrated spindle cells with positive staining for CD31 and human herpesvirus 8, respectively (original magnifications ×10).

Nonepidemic KS resembles other variants clinically, manifesting as erythematous or violaceous, painless, nonblanchable macules, papules, and nodules.[1] Early lesions often are asymptomatic and can manifest as pigmented macules or small papules that vary from pale pink to vivid purple. Nodules also can occur and be exophytic and ulcerated with bleeding.[1] Secondary lymphoproliferative disorders including Castleman disease and lymphoma have been reported.[2,5]

In contrast to other types of KS in which pulmonary or gastrointestinal tract lesions can develop with hemoptysis or hematochezia, mucocutaneous and visceral lesions rarely are reported in nonepidemic KS.[3] Lymphedema, a feature associated with endemic KS, is notably absent in nonepidemic KS.[1,3]

The differential diagnosis applicable to all KS subtypes includes other vascular lesions such as angiomatosis and angiosarcoma. Histopathologic analysis is critical to differentiate KS from these conditions; visual diagnosis alone has only an 80% positive predictive value for KS.[4] The histopathologic presentation of KS is a vascular proliferation in the dermis accompanied by an increased number of vessels without an endothelial cell lining.[4] Spindle cell proliferation also is a common feature and is considered to be the KS tumor cell. Immunostaining for HHV-8 antigen as well as for CD31 and CD34 can be used to confirm the diagnosis.[4]

The management and prognosis of KS depends on the epidemiologic subtype. Classic and nonepidemic KS generally are indolent with a good prognosis. Periodic follow-up is recommended because of an increased risk for secondary malignancy such as lymphoma. The treatment of epidemic KS is highly active antiretroviral therapy. Similarly, reduction of immunosuppression is warranted for iatrogenic KS. For all types, cutaneous lesions can be treated with local excision, cryosurgery, radiation, chemotherapy, intralesional vincristine, or a topical agent such as imiquimod or alitretinoin.[6]

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