Nonepidemic Kaposi sarcoma: A recently proposed category

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INTRODUCTION

Kaposi sarcoma (KS) is an indolent angioproliferative tumor thought to be dependent on viral replication, immune modulation, and inflammatory cytokines produced by infected endothelial and immune cells. Human herpesvirus-8 (HHV-8) is thought to cause KS and is documented in more than 95% of patients with KS. The skin is the most common site of presentation, although visceral disease, most commonly affecting the lungs and the gastrointestinal tract, may also occur. KS typically manifests as violaceous, dark brown or black macules, papules, and nodules on the lower extremities that are prone to bleeding and ulceration. It has a slow-growing course in immunocompetent individuals. We present the unusual case of a HIV-negative yet high-risk man in whom cutaneous KS lesions developed on the face that exhibited a complete response to topical imiquimod and tretinoin. Our patient represents an additional case of the rare, underrecognized category known as *nonepidemic KS*.

Abbreviations used:

HHV-8:	human herpesvirus-8
KS:	Kaposi sarcoma
MSM:	men who have sex with men

CASE REPORT

A 55-year-old previously healthy, homosexual African-American man presented for evaluation of multiple small lesions over his left eyebrow that developed over 3 months. He reported no associated pain, discomfort, or itching, nor did he have a medical history suggestive of immunosuppression. Physical examination found Fitzpatrick type IV skin and six 2- to 3-mm, dome-shaped, umbilicated, flesh-colored papules on the left eyebrow (Fig 1, *A*) and 6 reddish papules on the right tragus (Fig 1, *B*). In addition, after 6 months, he exhibited a second nodular lesion located on the right scapha.

A shave biopsy of a lesion was performed. Laboratory blood testing found no abnormalities, including a normal $CD4^+$ count of 637 cells/μL, $CD8^+$ count of 409 cells/μL, and a $CD4^+/CD8^+$ ratio of 1.56. Results of HIV-1 and HIV-2 enzyme-linked immunosorbent assays and polymerase chain reaction testing were negative. Our presumptive diagnosis was KS in an HIV-negative patient.

The biopsy specimen had spindled and epithelioid cells in the dermis (Fig 2, *A*), and immunohistochemistry for HHV-8 was positive in the dermis (Fig 2, *B*), supporting the diagnosis of KS. Both of his lesions completely resolved without complication after 8 weeks of treatment with topical tretinoin 0.08% gel and imiquimod 3.75% cream. He has remained serologically and virologically negative for HIV 4 years after the initial lesion developed.

DISCUSSION

There are four types of histologically indistinguishable KS: classic, endemic, immunosuppressive therapy related, and epidemic. Classic KS was first

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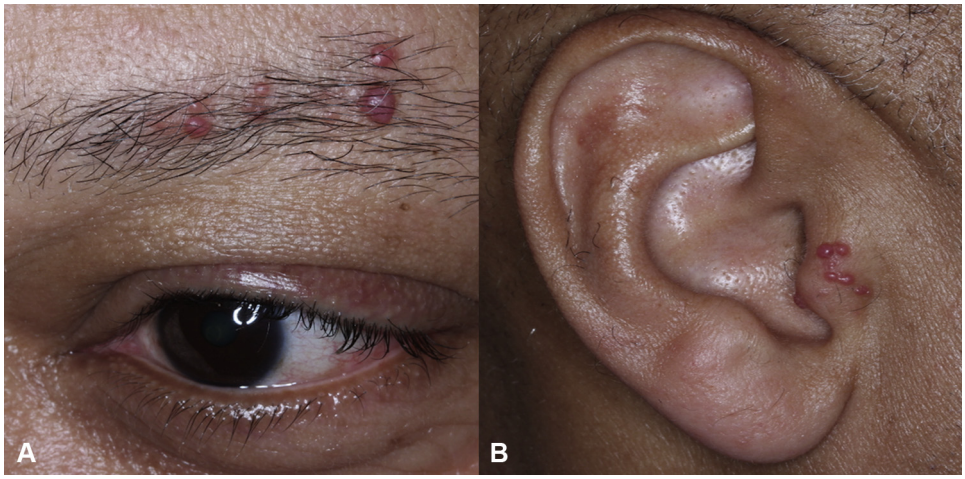

Fig 1. Dome-shaped, umbilicated red papules on the (**A**) left eyebrow and (**B**) right tragus.

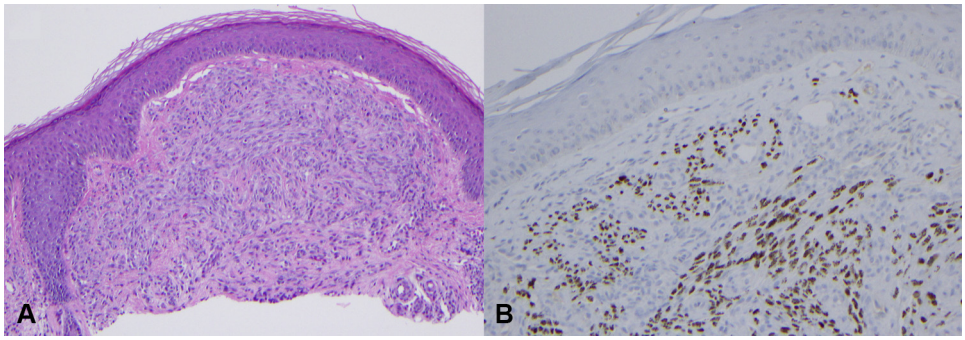

Fig 2. **A**, Spindled and epithelioid cells in the dermis; **B**, Positive immunohistochemistry for HHV-8 in the dermis. (**A**, Hematoxylin-eosin stain: original magnification: ×40.)

described by Moritz Kaposi in 1872 as rarely aggressive and typically found in older men of Mediterranean, North African, or Eastern European Jewish origin.[1] This form of KS is associated with a decreased lymphocyte count and is thought to be promoted by immunosenescence. Signs and symptoms include slow-growing cutaneous red, purple, or brown lesions found most commonly on the ankles or feet.[1] Lesions can also form in the stomach, intestines, and lymph nodes, resulting in gastrointestinal bleeding and blockage of lymph and blood flow.[2]

Endemic KS, in contrast, is more extensive and associated with significant morbidity and mortality. First described in 1914, endemic KS typically affects a younger population compared with the classic type. It occurs most commonly in HIV-negative men in East and Central Africa.[2] A lymphadenopathic subvariant of endemic KS common in young children does not affect the skin. This subvariant spreads through lymph nodes to vital organs, rapidly becoming fatal.[2]

The iatrogenic form of KS occurs in patients receiving immunosuppression for organ transplantation, chemotherapy, or rheumatologic diseases.[2] Iatrogenic KS typically remains localized to the skin, although widespread dissemination with involvement of mucous membranes and viscera may also occur.[2] On average, lesions occur 16 months after transplantation.[2] Management of iatrogenic KS requires balancing complications resulting from KS and those that may result from decreasing or discontinuing the immunosuppressive medication.[2]

Epidemic KS is the most aggressive subtype, and it most commonly affects HIV-infected men who have sex with men (MSM) in Western countries and HHV-8-infected individuals in sub-Saharan Africa.[2] This form is associated with mucocutaneous and visceral lesions in the setting of systemic symptoms including fever, weight loss, and diarrhea.[2] Combined antiretroviral therapy reduces the risk of epidemic KS.[2]

Our report illustrates a rare case of nonepidemic KS, which represents an existing subdivision of KS

with which many dermatologists are not familiar.[1,2] Lanternier et al[1] proposed that this form resembles classical KS with limited disease in most patients; however, it affects younger MSM who lack evidence of cellular or humoral immunodeficiency, including HIV infection.[1,2] It is possible that this clinical entity may be characterized by decreased T-cell function with preserved T-cell counts.[3] The predilection for MSM may be attributable to oral sexual activity, given that HHV-8 DNA has been identified in a high proportion of normal prostate and semen samples.[4] We speculate that our patient's KS was caused by HHV-8 subtypes A5 or B, which have previously been seen in African blacks and individuals of mixed ancestry.[5]

In our case, the patient presented with multiple cutaneous lesions in areas not typically seen in classical KS.[2] This form, according to Lanternier et al,[1] has a good prognosis, as disease is generally limited, but it is associated with lymphoproliferative disease. Despite its more favorable prognosis, treatment of this variant is the same as in classic KS. Isolated lesions can be treated with alitretinoin gel, localized radiation, cryotherapy, or local excision.

Only a few sporadic cases of nonepidemic KS have been reported, mostly between 1986 and 1990.[3,6-8] The most common site of involvement was the lower limbs, and many had coexisting sexually transmitted diseases.[3,6-8] More recently, other investigators have presented similar cases, including a report of an HIV-negative, homosexual man with a KS tumor on the plantar aspect of the foot.[9] A similar clinical presentation in the buccal mucosa was reported by Kua et al.[10] In both cases, lymphoproliferative disease was not found. These reports, together with our additional case, show that clinicians must recognize cutaneous KS in high-risk yet HIV-negative patients to prompt proper evaluation and advise patients of its more favorable prognosis.

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