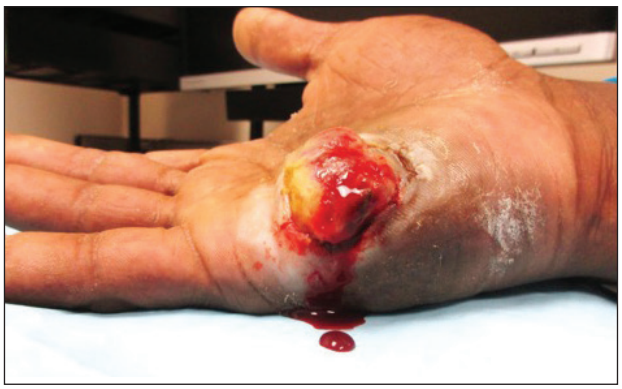
Well-Circumscribed Tumor on the Hand

John F. Linabury, DO; John W. Roman, MD



A 52-year-old man presented to the dermatology clinic with a 2×3-cm, fungating, dome-shaped, ulcerative, moist, well-circumscribed tumor with peripheral maceration on the volar aspect of the right hand of 3 months' duration. The tumor was malodorous, painful, and hemorrhaged easily with minimal trauma. The patient's medical history was notable for human immunodeficiency virus and latent syphilis, with elevated rapid plasma reagin titers and a positive *Treponema palladium* antibody on chemiluminescent immunoassay, that was refractory to 3 treatments with penicillin. The patient was not on antiretroviral therapy. He had a $CD4^+$ lymphocyte count of 980 cells/μL (reference range, 359–1519 cells/μL) and a viral load of 8560 copies/mL (reference range, <200 copies/mL). No other skin or systemic concerns were noted, and the patient denied any recent travel, exposure to animals, or constitutional symptoms. A deep shave biopsy of the lesion was performed.

WHAT'S THE **DIAGNOSIS?**

a. bacillary angiomatosis
b. nodular Kaposi sarcoma
c. pyogenic granuloma
d. squamous cell carcinoma
e. syphilis

PLEASE TURN TO PAGE E5 FOR THE DIAGNOSIS

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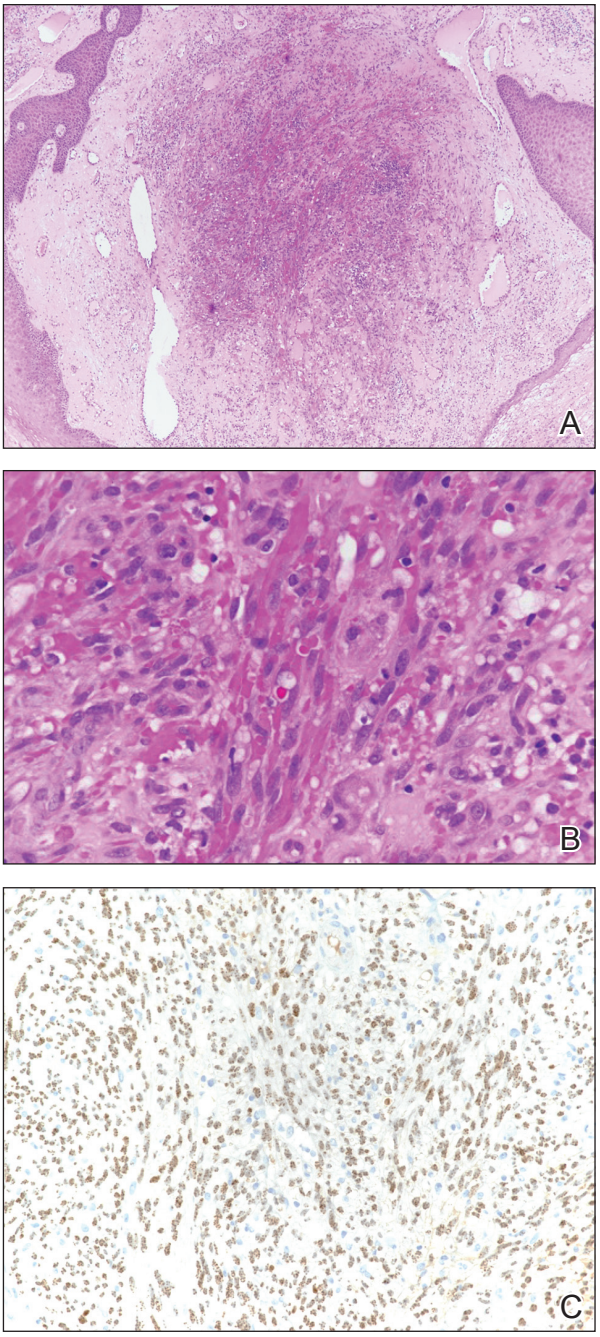
THE **DIAGNOSIS:** Nodular Kaposi Sarcoma

Epidemic Kaposi sarcoma (KS) primarily affects patients with human immunodeficiency virus (HIV) infection. Kaposi sarcoma can appear as brown, red, or blue-black macules, plaques, patches, nodules, or tumors, and it often is observed as multifocal cutaneous lesions located on the head, neck, and upper aspects of the trunk in a fulminant manner. Kaposi sarcoma portends a poor prognosis and is an AIDS-defining malignancy.[1-3] Importantly, antiretroviral therapy does not preclude its consideration in those without AIDS-defining CD4 cell counts and undetectable HIV viremia presenting with cutaneous manifestations.[2,3] A retrospective review by Daly et al[4] reported KS lesions in patients with CD4 lymphocyte counts greater than 300 cells/μL, most of whom were antiretroviral therapy–naïve patients. Also, those with higher CD4 counts tended to have a solitary KS lesion at presentation, while those with CD4 counts less than 300 cells/μL tended to present with multiple foci.[4] Epidemic KS lesions are clinically indistinguishable from other common cutaneous conditions in the differential diagnosis of KS, necessitating biopsy for histopathologic examination. Light microscopy findings help to delineate the diagnosis of KS. Immunohistochemical staining to the latent nuclear antigen 1 of human herpesvirus 8 (HHV-8) confirms the KS diagnosis.[5,6] Our patient's presentation as a solitary acral lesion was atypical for KS.

Light microscopy of our patient's biopsy demonstrated a large tumor on the acral surface of the right hand. Dermal collections of basophilic spindled cells clustered with small slitlike vascular spaces with abundant erythrocyte extravasation and numerous large ectatic vessels at the periphery were seen (Figure, A). At higher magnification, interlaced bundles of spindle cells with slitlike vessels with scattered lymphocytes and plasma cells were seen (Figure, B). An immunohistochemical stain for HHV-8 was positive and largely confined to spindle cells (Figure, C). These findings confirmed KS and met AIDS-defining criteria. Awareness of these histopathologic features is key in differentiating KS from other conditions in the differential diagnosis.

The patient's history of late latent syphilis coinfected with HIV and persistently elevated rapid plasma reagin that was recalcitrant to therapy placed an atypical nodular presentation within reason for the differential diagnosis. Deviations from the typical papulosquamous presentation with acral involvement in an immunocompromised patient mandates a consideration for syphilis with an atypical presentation. Atypical presentations include nodular, annular, pustular, lues maligna, frambesiform, corymbose, and photosensitive distributions.[7,8] Notably, coinfection with HIV modifies the clinical presentation, serology, and efficacy of treatment.[7-10] Atypical presentations are more common in coinfected HIV-positive patients, mandating a high degree of suspicion. Nodular



Kaposi sarcoma. A, Dermal collection of basophilic spindled cells clustered with small slitlike vascular spaces with abundant erythrocyte extravasation and numerous large ectatic vessels at the periphery (H&E, original magnification ×40). B, Interlaced bundles of spindle cells with slitlike vessels with scattered lymphocytes and plasma cells (H&E, original magnification ×400). C, Immunohistochemical staining showed human herpesvirus 8 positivity largely confined to spindle cells (original magnification ×20).

secondary syphilis and the noduloulcerative form (lues maligna) often spare the palmar and plantar surfaces, and patients often have constitutional symptoms accompanying the cutaneous eruptions. In questionable cases, a biopsy lends clarification. Light microscopy on hematoxylin and eosin (H&E) staining may display acanthosis, superficial and deep perivascular swelling, plasma, histiocyte infiltrates, dermoepidermal junction changes, mixed patterns, epidermal hyperplasia, and dermal vascular thickening.[7-9,11] Spirochetes may be observed on Warthin-Starry stain; however, artifact obscuration from melanin granules and reticular fibers or paucity of organisms can make identification difficult. Immunohistochemical staining may prove useful when H&E stains are atypical or have a paucity of organisms or plasma cells or when silver stains have artifactual obscuration.[9] Our patient's solitary palmar lesion without constitutional symptoms made an atypical nodular secondary syphilis presentation less likely. Ultimately, the histopathologic findings were consistent with KS.

Bacillary angiomatosis (BA) is caused by *Bartonella* species and results in vascular proliferation with cutaneous manifestation. It frequently is observed in patients with HIV or other immunosuppressive conditions as well as patients with exposure to mammals or their vectors. Protean cutaneous manifestations and distributions of BA exist. The number of lesions can be singular to thousands. Solitary superficial pyogenic granuloma–like lesions can be clinically indistinguishable from both KS and pyogenic granuloma (PG). Superficial lesions often begin as red, violaceous, or flesh-colored papules that hemorrhage easily with trauma. The morphology of the papule can progress to be exophytic with dome-shaped or ulcerative surface features and is rubbery on palpation.[12] Biopsy is required to differentiate BA from KS. Bacillary angiomatosis on light microscopy with H&E shows protuberant, lobulated, round vessels with plump endothelial cells with or without necrosis. A neutrophil infiltrate in close proximity to bacilli may be noted. Warthin-Starry stain demonstrates numerous bacilli juxtaposed to these endothelial cells. The lack of immunohistochemical staining for HHV-8 also differentiates BA from KS.[12,13]

Pyogenic granuloma is resultant from proliferation of endothelial cells with a lobular architecture. Pyogenic granulomas are benign, rapidly progressive, acquired lesions presenting in the skin and mucous membranes. Pyogenic granuloma often presents as a single painless papule or nodule with a glistening red-violaceous color that occasionally appears with a perilesional collarette. The lesions are friable and easily hemorrhage. Pyogenic granuloma has been associated with local skin trauma and estrogen hormones. Histopathologic examination of PG assists with differentiation from other nodular lesions. Light microscopy with standard H&E staining demonstrates a network of capillaries arranged into a lobule surrounded by a fibrous matrix. Endothelial cells appear round and protrude into the vascular lamina. Mitotic activity is increased. Lack of findings on Warthin-Starry stain assists with differentiating PG from BA, while the microscopy architecture and immunohistochemical staining differentiates PG from KS.[6,13,14]

Squamous cell carcinoma (SCC) is the primary malignant cancer of the hand. The dorsal aspect of the hand is the most common location; SCC less commonly is located on the palmar surface, fingers, nail bed, or intertriginous areas.[15-17] Chakrabarti et al[16] found that these lesions were invasive SCC when located on the palmar surface. Morphologically, SCC takes an exophytic papular, nodular, or scaly appearance with a red to flesh-colored appearance and poor demarcation of the borders. Progression to large ulcerated or secondarily infected lesions also can occur. The inflammatory reaction may cause tenderness to palpation and hemorrhage with trauma. Histopathologic examination of invasive SCC reveals atypical keratinocytes violating the basement membrane and abundant cytoplasm. Our patient's clinical presentation placed invasive SCC low on the differential diagnosis, and the histopathologic and immunohistochemical results eliminated SCC as the diagnosis.

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