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Case Report

Kaposi Sarcoma mimicking pedal osteomyelitis in a patient with HIV

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ABSTRACT

Kaposi Sarcoma (KS) is an angio-proliferative mesenchymal neoplasm that typically affects the skin. In the setting of AIDS, it is usually disseminated, commonly involving noncutaneous sites like oral cavity, lymph nodes, pulmonary, and gastrointestinal systems. Musculoskeletal system involvement by KS is rare, and when encountered, it typically involves the axial skeleton (vertebrae, ribs, sternum, and pelvis) and/or maxillofacial bones. This report describes an unusual case of a 44-year old patient with HIV, who presented with a foot ulcer that fit the typical clinical features of osteomyelitis until MRI of the foot demonstrated atypical findings that challenged the original clinical diagnosis. This case highlights the role that advanced diagnostic imaging plays in the diagnosis of musculoskeletal Kaposi Sarcoma and serves as a reminder to radiologists to include Kaposi Sarcoma in the differential of multifocal osteolytic lesions in patients with HIV.

Introduction

Kaposi Sarcoma is a locally aggressive mesenchymal tumor of blood and lymphatics. It was first described by the Hungarian dermatologist Dr. Moritz Kaposi in 1872, as a primary skin neoplasm with the disseminated form of the disease involving various organ systems. There are 4 major clinical variants of the disease: (1) classic or sporadic, (2) African or endemic, (3) iatrogenic or organ transplant-related, and (4) AIDS-related [1]. AIDS-related and iatrogenic KS differ clinically from the classic and endemic variants, in that they are more often symptomatic and disseminated at presentation and hence require imaging for accurate diagnosis and staging.

Kaposi Sarcoma is the commonest tumor in AIDS patients and is considered to be an AIDS defining illness. The lifetime prevalence of KS may be as high as 50% among homosexual male AIDS patients, and the overall risk of developing AIDS-related KS is 20,000 times greater in patients with AIDS than in the general population and 300 times greater than in other

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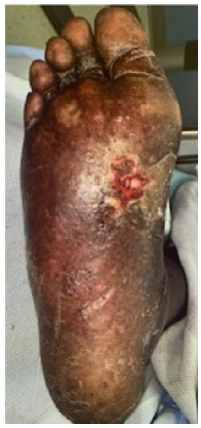

Fig. 1 – A nondraining superficial ulcer was noted on the plantar aspect of the right foot, with granulation tissue at the base and surrounding areas of raised fibrous tissue.

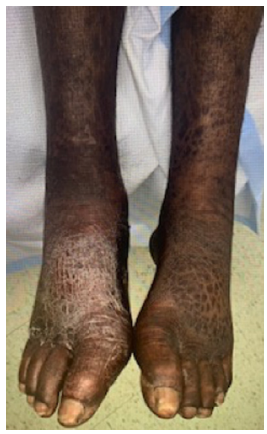

Fig. 2 – Edema and xerosis extending to the level of the ankle joint were present.

immunosuppressed patients [2]. In an autopsy series by Niedt and Schinella, the most common sites for visceral involvement by AIDS-related KS were the lymph nodes (72% of cases), lung (51%), gastrointestinal tract (48%), liver (34%), and spleen (27%) [3]. Musculoskeletal system, especially bone and bone marrow involvement, is uncommon.

Case description

A 44-year old African American male with known history of HIV, hepatitis C treated with Harvoni and hypertension presented to the emergency department (ED) with 1-week onset of right foot pain associated with a skin ulcer. He had no immediate precipitating event or trauma. His past medical history included the diagnosis of HIV in 2000 and treatment for pneumocystis pneumonia in 2015. Social history was positive for half a pack per day cigarette use. Three years prior to the ED visit, he developed a left thigh skin lesion, which was biopsied and proven to be Kaposi Sarcoma. Subsequently, he was treated with 6 cycles of chemotherapy and local radiation therapy for KS. He was on highly active antiretroviral therapy (HAART). However, he admitted to intermittent noncompliance with his HIV treatment. Examination revealed a nondraining ulcer on the plantar aspect of first metatarsal of the right foot, with granulation tissue at the base. Warmth, edema, xerosis, and periwound erythema extending to the level of the ankle joint were present (Figs. 1 and 2).

The patient was admitted by the ED for further evaluation and treatment. Laboratory tests revealed CD4 count of 755 cells/ul and HIV RNA of 36/ml. Radiographs of the right foot showed multifocal erosive and lytic lesions (Figs. 3a and b), new when compared to a radiograph obtained 9 years prior (Fig. 3c). MRI demonstrated multifocal intramedullary enhancing masses associated with cortical erosions and enhancing soft tissue masses throughout several bones of the right foot, with sparing of joint spaces (Figs. 4a–c). Based on the MRI findings, differential diagnosis included atypical infections, lymphoma, and Kaposi Sarcoma. A bone biopsy was recommended. The hospital podiatry service performed bone biopsy of the right cuboid and the right fifth metatarsal base, using a Jamshidi bone biopsy needle. The biopsy report exhibited atypical spindle cells proliferation with positive immunohistochemical (IHC) staining for CD34 and HHV-8; indicating the diagnosis of KS (Figs. 5a and b). Acid fast bacilli (AFB) and GMS stains were negative.

The patient was treated with broad spectrum antibiotics in the hospital for superimposed lower extremity cellulitis. He was discharged following antibiotic treatment with instructions to follow up with his outpatient oncologist for further management of his KS. Additional imaging obtained as an outpatient, included a bilateral lower extremity 99mTc nuclear medicine bone scan and a noncontrast CT of the right lower extremity. The bone scan revealed patchy increased uptake in right foot, right tibial plateau and ipsilateral femoral condyles (Figs. 6a and b). CT showed well defined cortical erosions in proximal tibia (Figs. 7a and b). After a multidisciplinary consultation, a right above knee amputation (AKA) was recommended. The excised tissue confirmed the diagnosis of polyostotic KS and additional cycles of chemotherapy were subsequently prescribed.

Discussion

Kaposi Sarcoma is the commonest tumor in AIDS patients and is considered to be an AIDS defining illness. Human herpes virus 8 (HHV8) and cofactor cytokine kinase induced growth are considered causative factors in the pathogenesis of AIDS-related and iatrogenic KS.

Cutaneous involvement in KS is frequent, but KS involvement of the musculoskeletal system is a rare occurrence, with approximately 70 such cases reported in the literature [4,5]. It occurs more commonly as extension of skin lesions. Musculoskeletal system involvement has been noted in all KS epidemiological forms. While patients with osseous KS lesions are often asymptomatic, they can present with bone pain, functional impairment and even pathologic fractures. African

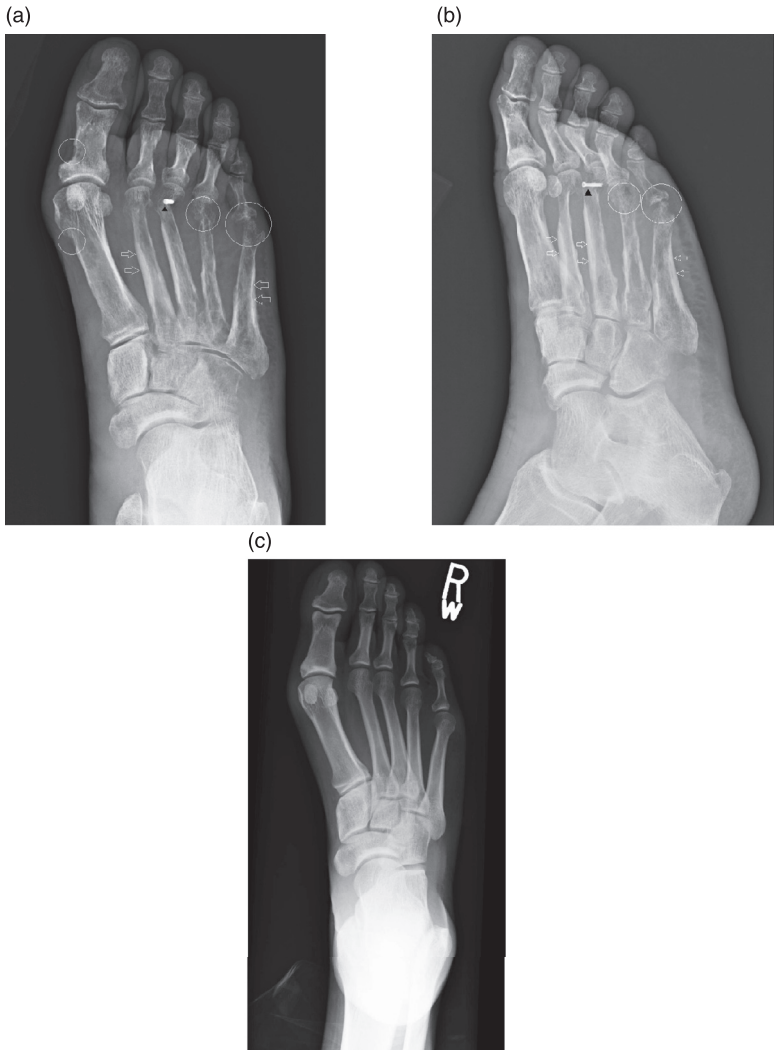

Fig. 3 – Anteroposterior (a) and oblique (b) right foot radiographs show multiple areas of osteopenia and cortical erosions (white circles ○) and periosteal reactions in metatarsals (white arrows ⇨). A screw fixation (black arrowhead ▲) noted at the third metatarsal head. Anteroposterior right foot radiograph (c) of the same patient 9 years prior to current presentation, performed for an unrelated problem, was normal. (Color version of figure is available online.)

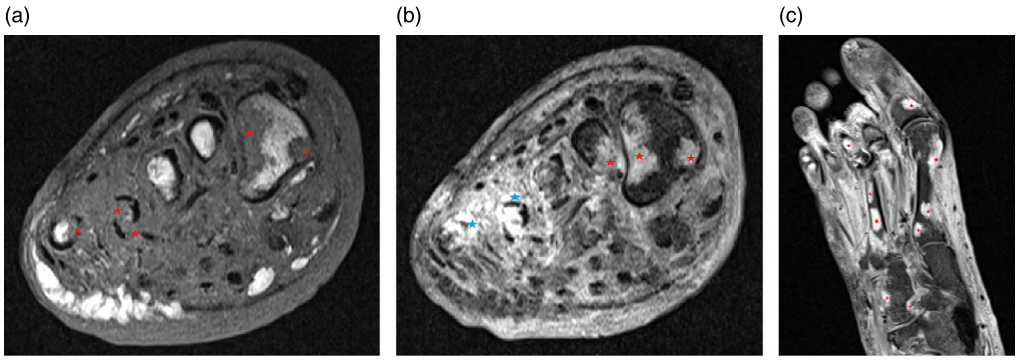

Fig. 4 – T1-weighted precontrast (a) and postcontrast (b) axial MR images of right foot at the proximal metatarsal level demonstrate multiple hypointense lesions (red asterix ★) with intense enhancement of the lesions and adjacent soft tissues (blue asterix ★) on intravenous injection of gadoterate meglumine. Proton density fat saturated coronal MR image of right foot (c) demonstrates multifocal hyperintense erosive lesions (red asterix ★) with sparing of joint spaces. (Color version of figure is available online.)

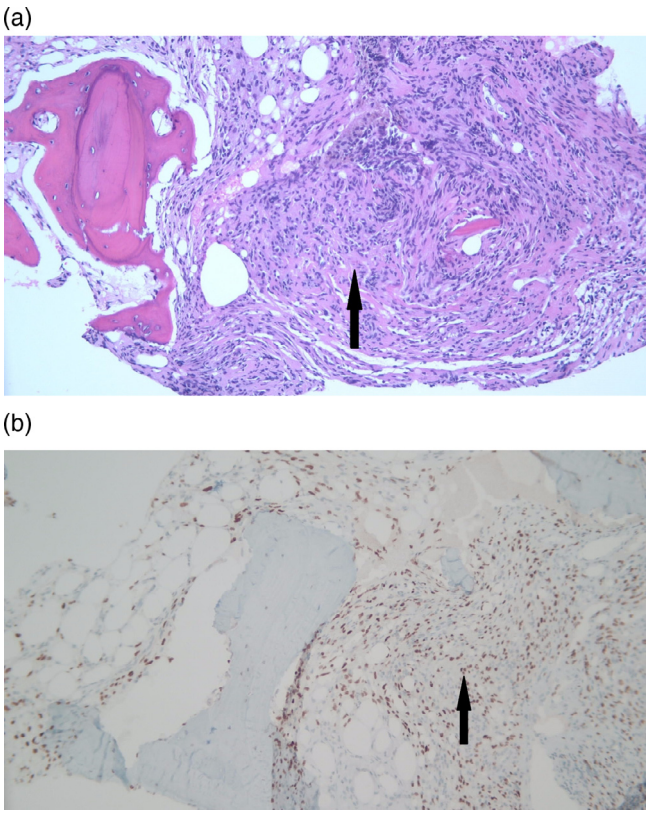

Fig. 5 – Neoplastic slit- like vascular channels with spindle cell proliferation (black arrow ➡) involving bone is seen on H&E stain (a). The tumor cells are immunoreactive for HHV-8 (nuclear staining demonstrated by black arrow) on immunohistochemical stain (b).

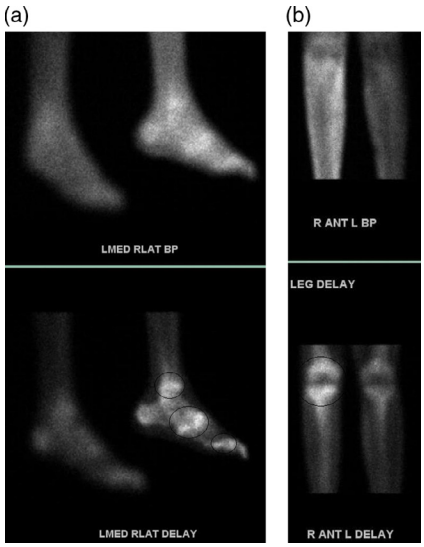

Fig. 6 – Bilateral lower extremity 99Tc bone scan demonstrates increased tracer uptake (black circles ⬭) in the foot (a), tibial plateau and femoral condyles (b) of right lower extremity.

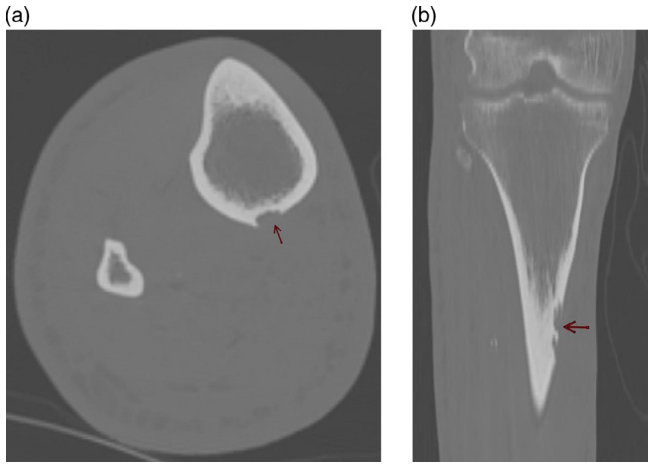

Fig. 7 – Axial (a) and coronal (b) CT scan of right lower extremity shows cortical erosions (red arrows ↖) in proximal tibia. (Color version of figure is available online.)

and Classic KS lesions tend to involve the peripheral skeleton, whereas AIDS-related KS more commonly involves the axial skeleton (vertebrae, ribs, sternum, and pelvis) and/or maxillofacial bones [6]. Other bones reported to be involved by KS, include the long bones of the extremities (humerus, radius, ulna, femur, tibia, and fibula), as well as those of the hands (metacarpals) and feet (talus, calcaneus, and the 3rd, 4th, and 5th metatarsals).

The primary differential diagnosis for aggressive osteolytic lesions in immunocompromised patients can be broadly categorized as typical infectious entities, atypical infectious entities, and neoplastic processes. The most common infectious entity is *Staphylococcus aureus* osteomyelitis. Atypical infectious etiologies in HIV patients include, Bacillary angiomatosis, *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare*, *Nocardia asteroides*, and *Neisseria gonorrhea*. Imaging findings seen in classic osteomyelitis are osseous erosions, perilesional marrow edema, periostitis, joint effusions, sinus tracts, sequestra, and soft tissue inflammation and gas.

Neoplastic entities in HIV patients include, primary bone lymphoma, angiosarcoma, hemangioendothelioma, and spindle cell pseudo-tumors. Neoplastic processes often demonstrate osteolytic lesions with ill-defined margins. A special consideration with unpredictable and possibly overlapping features of KS is primary bone lymphoma. Radiographic features of osseous lymphoma are variable, ranging from normal, lytic, mixed lytic/sclerotic, or sclerotic. A lytic destructive appearance with a moth-eaten or permeative wide zone of transition is the most common appearance [7].

Osteolysis is a finding that may be seen with typical pathogens, atypical pathogens, or neoplastic processes. However, the unique features of discontinuous, yet well-defined, multifocal or polyostotic osteolysis, enhancing soft tissue masses, and absence of joint involvement [8], differentiate KS from the aforementioned entities. Majority of the lesions are osteolytic, with or without associated periosteal reaction, but sclerotic lesions have also been reported. MRI is an excellent imaging modality to highlight these features. Gallium scan

may be helpful as it is negative in KS [6], but positive in infection and lymphoma.

Diagnosis of Kaposi Sarcoma is usually established by pathologic examination. Histologically, the tumor shows vascular proliferation in the form of slit-like spaces and spindle cell proliferation with extravasated red blood cells and hyaline globules. IHC is helpful in supporting the diagnosis of KS. The typical IHC profile of KS includes the expression of vascular markers such as CD34 [9] and ERG along with the expression of HHV-8 which labels latency-associated nuclear antigen (LANA). The differential diagnosis includes other vascular lesions such as hemangioma and bacillary angiomatosis, and IHC for HHV-8 (LANA) is crucial to distinguish KS from other entities. Silver staining with Warthin Starry Grocott is positive in bacillary angiomatosis and is negative in KS. Necrosis or granulomas are not seen in KS but can be seen with mycobacterial infections.

The treatment of KS with bone involvement is a tailored combination of surgery, chemotherapy with doxorubicin and local radiation therapy; in addition to antiretroviral therapy in patients with AIDS-related KS.

Conclusion

Radiologists should remember to include Kaposi Sarcoma in the differential diagnosis of multifocal osteolytic lesions in patients with HIV. The unique radiological features of KS that could help radiologists distinguish KS from other entities are, well defined multifocal lytic lesions, intense enhancement of osseous lesions and adjacent soft tissue masses, joint sparing, absence of perilesional marrow edema, and absence of soft tissue gas.

This case report highlights the role that advanced multiparametric imaging plays in the accurate diagnosis of AIDS-related musculoskeletal KS. Imaging can also be helpful for earlier characterization of additional lesions in multifocal Kaposi Sarcoma and evaluation of systemic response to treatment.

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