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Disseminated Kaposi sarcoma with cytokine release in an AIDS patient

KEYWORDS
HIV;
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Kaposi sarcoma inflammatory cytokine syndrome (KICS)

Dear Editor,

In April 2019, a 38-year-old African American man who identified as bisexual presented to the hospital because of a 4-day history of shortness of breath, cough, and right upper quadrant pain. The patient had a long-standing history of human immunodeficiency virus infection/acquired immune deficiency syndrome (HIV/AIDS). He also reported fatigue, poor appetite, and weight loss. He had been non-compliant with antiretroviral medications.

He was afebrile at presentation. Physical examination revealed bilateral axillary and inguinal lymphadenopathy, bilateral decreased breathing sounds, and scattered violaceous papulonodular skin lesions on the trunk (Fig. 1A). His initial complete blood count (CBC) was within the normal limit and had no leukocytosis (Supplementary Table S1). He had normal kidney function, normal transaminase levels, and had no electrolyte abnormalities. The lactate dehydrogenase (LDH) level was 433 units/L. His serum C-reactive protein (CRP) was elevated at 95.4 mg/dL. On admission, his CD4+ T-cell count was 7 cells/mm^3 and his HIV RNA viral load (VL) was 5960 copies/mL. The chest radiograph showed bilateral pleural effusions and infiltrates (Fig. 1B). One of the skin lesions on the upper back was excised and the biopsy result showed plaque stage of Kaposi sarcoma (KS). Computed tomography (CT) of the chest showed peribronchial thickening and nodularity of the bronchovascular bundles (Fig. 1C). Abdominal CT revealed hepatomegaly with numerous partial contrast enhancement hepatic lesions (Fig. 1D). Investigation with bronchoscopy demonstrated airway hypervascularity and raised erythematous mucosal lesions. The cutaneous, pulmonary and hepatic lesions suggested disseminated KS. Bronchoalveolar lavage smear and culture were negative for *Pneumocystis jirovecii*, acid-fast bacilli, bacterial or fungal infection.

He was treated with intravenous (IV) ceftriaxone and azithromycin for presumed community-acquired pneumonia. He also received IV trimethoprim/sulfamethoxazole empirically for the treatment of *Pneumocystis jiroveci* pneumonia (PJP) with adjunctive prednisone due to hypoxia. HIV antiretroviral therapy (ART) was started with emtricitabine 200 mg/tenofovir alafenamide 25 mg and cobicistat 150 mg/darunavir 800 mg daily. His HIV viral load dropped from 5960 to 547 copies/mL in four days, and CRP decreased to 28 mg/dL in a week. The KS lesions were also decreasing in size.

Despite the initial clinical improvement, he became febrile up to 39 °C after experiencing bilateral knee pain without joint effusions. His CRP rose up to 250.9 md/dL, and the chest CT showed worsening infiltrates. He was once again started on broad-spectrum antibiotics (vancomycin, ceftazidime, and doxycycline) for presumed hospital-acquired pneumonia. The patient passed away from acute respiratory distress syndrome (ARDS) within three days after intubation (hospital day 30). No organism was detected in his blood cultures collected in the hospital. The last blood sample drawn before his death showed CD4 count of 63 cells/mm,[3] HIV RNA viral load undetectable (<20 copies/mL), interleukin (IL)-6 level of 62 pg/mL (reference range 0.0—15.2 pg/mL), IL-10 level >2100 pg/mL (reference range < 2 pg/mL) and Kaposi sarcoma-associated herpesvirus (KSHV) DNA viral load of 5,800,000 copies/mL.

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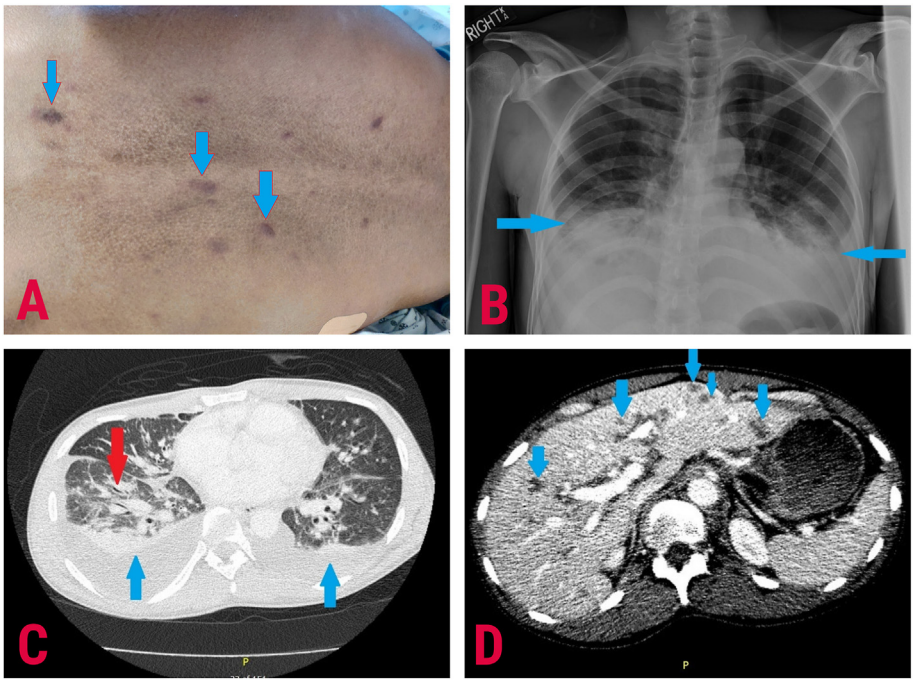

Figure 1. Disseminated Kaposi sarcoma. **1A.** Cutaneous KS lesions on the back: There are numerous violaceous papulonodular skin lesions on the back (blue arrows). Skin biopsy showed plaque stage Kaposi sarcoma. **1B.** Chest X-ray: bilateral pleural effusions (arrows) and infiltrates. **1C.** Chest CT: Peribronchial thickening and diffuse thickening and nodularity of the bronchovascular bundles (red arrow) consistent with pulmonary Kaposi sarcoma. There were also bilateral pleural effusions (blue arrows). **1D.** Abdominal CT with multiple liver nodules: There was hepatomegaly with numerous partial contrast enhancement hepatic lesions (blue arrows), consistent with hepatic Kaposi sarcoma.

In 2010, there was a report of six patients co-infected with HSKV and HIV presenting with IL-6-related systemic inflammatory syndrome but without pathological evidence of KSHV-multicentric Castleman disease (MCD).[1] Based on the case series, a proposed working case definition for this new disease entity called Kaposi sarcoma inflammatory cytokine syndrome (KICS) was created (Supplementary Table S2).[2] In our case, the patient almost fulfilled every single criterion of the definition of KICS, including fever, fatigue, cachexia, respiratory symptoms, gastrointestinal discomfort, arthralgia, neuropathy, anemia, thrombocytopenia, hypoalbuminemia, hyponatremia, lymphadenopathy, hepatomegaly, body cavity effusions, elevated CRP, and elevated KSHV viral load. Both KSHV-MCD and KICS manifest significantly elevated levels of KSHV viral load, IL-6, and IL-10 in comparison to severe or mild KS disease.[2—4] Hence, a lymph node biopsy can help distinguish between KSHV-MCD and KICS. Thus, this case highlights the importance of checking KSHV viral load and performing lymph node biopsy on patients with HIV/AIDS/KS who present with sepsis but without any other evidence of infections. We presumed that our patient had KICS because patients with KICS tend to have a lower CD4 count (<100 cells/mm3) than those with KS-MCD (>200 cells/mm3).[4]

Both KSHV-MCD and KICS belong in the same spectrum of disease and are of high mortality.[3—5] Given the similarities between these two diseases, there are several suggested treatment options for KICS based on the clinical trials for MCD, such as rituximab and liposomal doxorubicin[6] or high-dose zidovudine and valganciclovir.[7]

While KS-MCD and KICS are associated with significant morbidity, these diseases are underdiagnosed and underrepresented (especially KICS) in the current literature. It is crucial to increase the diagnostic capacity and therapy options that aim to reduce cytokine release and KSHV viral burden. Clinicians should remain vigilant for patients with KS/HIV/AIDS who have a septic-like picture or systemic inflammation even in the era of ART. Combination chemotherapy needs to be considered.

Declaration of competing interest

None.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2021.03.019.

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