Acute polyarticular synovitis as a rare presentation of Kaposi sarcoma

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ABSTRACT

Patients with HIV are prone to a number of unusual infectious and malignant conditions, typically resulting from declining immune function. However, there are also a few reports of HIV associated conditions potentially created by viral release of interleukin-6 (IL-6). Herein, we present a case of HIV IL-6-related systemic inflammatory syndrome, a Kaposi sarcoma (KS)-associated syndrome in the absence of multicentric Castleman disease (MCD).

Key words: Kaposi sarcoma, multicentric castleman disease, poly articular synovitis

INTRODUCTION

Kaposi sarcoma (KS)-associated herpes virus (KSHV) infection in HIV patients has been associated with elevated viral interleukin-6 (IL-6), homolog of human IL-6, and IL-10. These inflammatory cytokines are thought to contribute to the systemic symptoms of fevers, cachexia, and laboratory abnormalities including cytopenias, hypoalbuminemia, hyponatremia, and elevated C-reactive protein associated with KSHV induced KS and multicentric Castleman disease (MCD). A subset of patients with severe systemic inflammatory symptoms has been described with HIV and KSHV coinfection, but without MCD. This collection of HIV and KSHV associated inflammatory symptoms has several designations described in the literature such as IL-6-related systemic inflammatory syndrome[1] and KSHV inflammatory cytokine syndrome.[2] This condition has clinical manifestations that resemble those of KSHV associated multicentric Castleman disease (KSV-MCD), but without the lymphadenopathy and pathologic nodal changes of KSHV-MCD.

CASE REPORT

A 55-year-old African American male with HIV on consistent highly active antiretroviral therapy (HAART) therapy with a stable CD4 count of 309, an undetectable viral load, and a history of diffuse B cell lymphoma in remission presented to the hospital with an acute eruption of papules on his palms and elbows that developed over 5 days. In addition to the cutaneous findings; he had associated low grade fever, painful polyarticular synovitis severely limiting his ambulation, conjunctivitis, and painful oral ulcerations that started 2 days prior to the eruption of the palm and elbow lesions.

On cutaneous examination he had multiple pink-purple, firm, non-blanchable papules over both palms and palmar fingers [Figure 1], as well as a few small discrete skin-colored papules over the elbows and wrists [Figure 2]. The mucosa of the lips, gingivae, and tongue had well defined, 2–5 mm discrete ulcers with erythematous borders and a clean base. He did not have any of the above symptoms during the course of his diffuse B cell lymphoma.

Laboratory workup revealed mild microcytic anemia and mild intermittent hyponatremia. The patient also had an elevated erythrocyte sedimentation rate and very mildly elevated rheumatoid factor, with an otherwise normal autoimmune workup including normal antinuclear antibody and anti-citrullinated protein antibody. An infectious workup for cryptococcus, chlamydia, gonorrhea, histoplasma, bartonella, rickettsia, Rocky Mountain spotted fever, and rapid plasma reagin was negative. Epstein-Barr virus and treponema pallidum particle agglutination assay were positive. Of note, IL-6 levels were elevated...
at 139 (normal: 0–5 pg/mL). Arthrocentesis was consistent with inflammatory fluid. Echocardiogram was negative for cardiac vegetations. Joint X-ray imaging was negative for a primary joint pathology.

A biopsy of a palmar lesion revealed KS [Figure 3] with positive staining for human herpes virus-8, also known as KSHV [Figure 4]. Biopsy of a lesion on the elbow was consistent with granuloma annulare [Figure 5]. Prior lymph node and gastrointestinal biopsies showed no evidence of the polyclonal, IgM-lambda restricted plasmacytoid cells in the intrafollicular areas of affected lymph nodes that would normally be seen in MCD.

**DISCUSSION**

The patient's diagnosis was consistent with an IL-6-related systemic inflammatory syndrome, a KS-associated syndrome in the absence of MCD. Patients with this condition present with inflammatory mixed connective tissue disease-like symptoms without a diagnosable mixed connective tissue disease. The systemic inflammatory responses in KS are thought to be secondary to elevated IL-6 inflammatory cytokine levels as was observed in our patient.

The exact etiology of the elevated IL-6 has not been definitively determined, but several mechanisms have been proposed. In HIV affected patients, one possible mechanism for the elevated IL-6 is from KSHV encoded viral IL-6 (vIL-6). This vIL-6 may mimic many activities of human IL-6 (hIL-6). IL-6 has also been directly correlated with HIV viral load. Although increased plasma IL-6 levels have been seen in patients with HIV, there has been no direct association with HIV as the causative factor. Even psychological stress has been proposed as a possible mechanism for the elevation.

Although B cell lymphomas can have a variety of constitutional symptoms, synovitis is not typical. Additionally, immune reconstitution syndrome is an unlikely explanation for the patient's
symptoms given his adherence to HAART therapy and stable CD4 count. The association of systemic inflammation and KS is very rare. The correlation with synovitis is even rarer, thus making this a unique case of KS with synovitis as the presenting symptom.

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