5-2019

A Rare and Newly Recognized Kaposi Sarcoma Herpes Virus-Associated Disease

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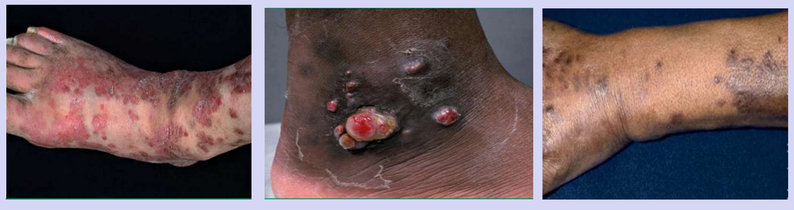
Introduction

- Kaposi sarcoma herpesvirus (KSHV) is associated with Kaposi Sarcoma, primary effusion lymphoma and multicentric Castleman disease (KSHV-MCD) in patients infected with human immunodeficiency virus (HIV).
- A new entity, KSHV inflammatory cytokine syndrome (KICS), identified by the classical signs and symptoms of KSHV-MCD without pathologic evidence of MCD, was recognized in 2010 in HIV infected patients. (2,3,5,7,9)

Case Report

- A 33-year-old African American male with a prior history of syphilis, HIV/ AIDS on Triumeq and stage IV Kaposi Sarcoma on Doxorubicin, presented with worsening fatigue, nausea, vomiting, myalgias, dyspnea and anasarca. His CD4 count remained at 33 cells/ µL despite a low HIV-1 viral load. He was febrile and treated with multiple antibiotics, while extensive workup with cultures ruled out infectious causes.
- He had persistent hyponatremia, hypoalbuminemia, and later developed anemia and thrombocytopenia. Biopsy of his lymph node excluded KSHV-MCD. His significantly increased C-reactive protein and the absence of lymphadenopathy/ splenomegaly on CT images led to the suspicion of KICS. KICS was further confirmed by high KSHV PCR (14855 copies/ ml), massive elevation of cytokines IL-6 and IL-10.
- Despite aggressive immunoglobulin and supportive treatments, he unfortunately died of multi-organ failure one month later.

(1)

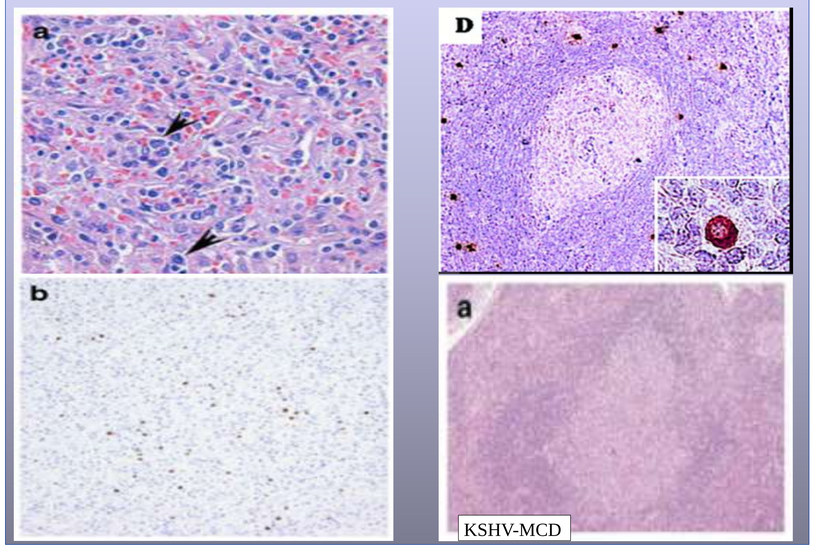


Laboratory Results

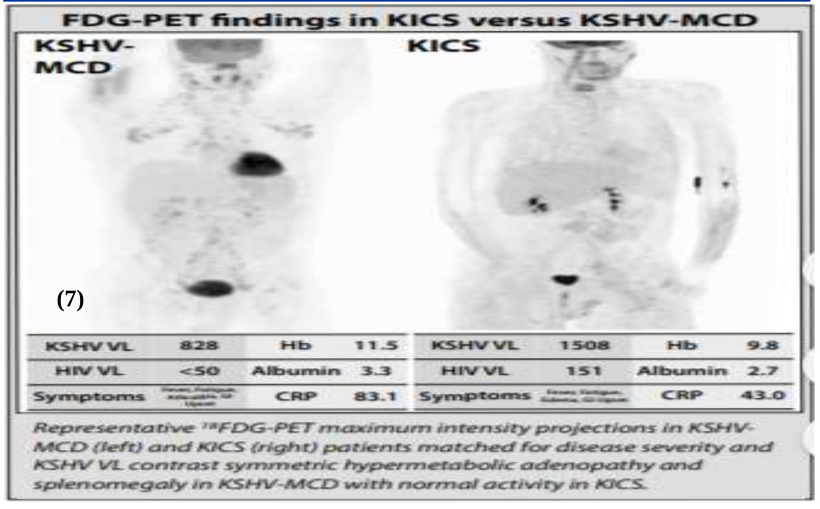
	Range	Actual
C-Reactive Protein	<0.5 mg/dl	17.9
Hemoglobin	13.5-17.0 g/dl	5.7
Albumin	3.2-4.6 g/dl	1.65
Sodium	135-145 mmol/L	121(LL)
Platelet Count	150-450 k/µL	47
Interleukin 10	<=18 pg/mL	2600
Interleukin 6	<=5 pg/mL	52.0
HHV-8 DNA, QN PCR	<1000 copies/mL	14855

Pathology

HHV-8 positive plasmablasts (4) — viral IL-6 in immunoblasts (8)



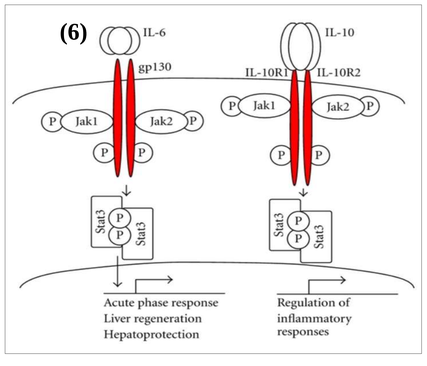
Radiologic Findings



Possible Mechanisms

vIL-6 binds transmembrane protein gp-130, recruits neutrophils, and macrophages, induces tissue damage and production of human IL-6 by uninfected cells. IL-10's production is activated by KSHV-associated microRNAs. Clinical manifestations are due to proinflammatory cytokine deregulation.

(6)



Diagnostic Criteria

- Clinical manifestations: Symptoms maybe fever, fatigue, edema, cachexia, dyspnea, nausea, anorexia, abdominal discomfort, altered bowel habit, arthralgia, myalgia, altered mental state and neuropathy. Lab abnormalities include anemia, thrombocytopenia, hypoalbuminemia and hyponatremia. Radiologic abnormalities may include lymphadenopathy, splenomegaly, hepatomegaly and body cavity effusions.
- Evidence of systemic inflammation: Elevated C-reactive protein
- Evidence of KSHV lytic activity: Elevated KSHV viral load in peripheral blood mononuclear cells (>100 copies/ 10-to-the-6th-power)
- No evidence of KSHV-MCD: Exclusion of MCD requires pathologic assessment of lymphadenopathy, if present (2,3)

Treatment

- Standard treatment is still under investigation due to its rarity and high mortality. (2,3,5,7,9)
- A combination of Rituximab to kill B cells that may harbor KSHV or be producing cytokines, and liposomal Doxorubicin to kill KS spindle cells, may lead to clinical remission.
- High-dose Zidovudine plus Valganciclovir have also been evaluated.

Highlights

- Although both disorders exhibit signs of substantial inflammation, KICS is a different entity from KSHV-MCD. KICS is defined with no lymphadenopathy/splenomegaly and negative pathologic nodal changes in the setting of low CD4 count (<100 cells/µL).
- Standard therapy is still under investigation due to its rarity and high mortality, whereas a combination treatment of Rituximab and Doxorubicin may be used.
- Symptoms at times can be confused with sepsis. KICS is therefore a diagnosis of exclusion.Early identification and treatment initiation are crucial to improve survival of this under-recognized KSHV-associated disease. (2,3,5)

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