"Purple-Xed" by a baffling bleed – A clinical care conundrum

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Abstract

Human retro-viral disease and the myriad opportunistic infections associated with it continue to pose a diagnostic challenge to clinicians. Disseminated Kaposi sarcoma (KS) and KS-associated immune reconstitution inflammatory syndrome (IRIS) are entities that can be associated with adverse clinical outcomes unless recognized early by the treating physician. We present the case of a 36-year-old homosexual HIV-positive male who presented with unusual symptoms of KS and KS IRIS with lower gastrointestinal bleeding and respiratory distress devoid of any cutaneous manifestations.

Key words: HIV, immune reconstitution inflammatory syndrome, Kaposi sarcoma

Introduction

Kaposi's sarcoma (KS) is an angioproliferative spindle-cell tumor that is associated with human herpes virus-8 (HHV-8). It commonly affects mucocutaneous sites while the disseminated form can involve lymph nodes and other visceral organs.[1] The incidence of KS has reduced to as low as 5% with the introduction of Anti retroviral therapy (ART).[2]

Initiation of ART may rarely lead to an immune reconstitution inflammatory syndrome (IRIS), which can be fatal. While IRIS due to opportunistic infections is common, KS-associated IRIS is rare and not readily recognized, thus delaying the necessary treatment and hence associated with high mortality. This is a case report of disseminated KS in the context of IRIS in an HIV-positive male on ART.

Case Report

A 36-year-old male, diagnosed with human retroviral disease and initiated on antiretroviral treatment (ART) for 3 months, presented with passage of frank blood per rectum of 2 months and a cough with expectoration of 3 weeks. He had also developed multiple oral and genital ulcers over the past 2 weeks. His CD4 count was 134 cells/mm^3 at admission.

On examination, he had a BMI of 17.2 kg/m^2. Pulse oximetry saturation of 88% confirmed hypoxia. There was generalized lymphadenopathy, multiple snail track ulcers in the oral cavity, and a solitary painless penile ulcer. The rest of the systemic examination was unremarkable. The patient had undergone a colonoscopy previously which detected an ulcero-proliferative lesion in the anal canal suspicious of malignancy. Laboratory investigations revealed severe anemia, thrombocytopenia, and negligible viral load with an elevated D-Dimer. Microbiological examination of the sputum was negative for bacteria and acid-fast bacilli. Persistent hypoxia prompted us to do a computed tomography chest with pulmonary angiogram that showed no evidence of pulmonary embolism. However, it revealed bilateral parenchymal nodules (peri-lymphatic) with central and peri-broncho vascular ground glass opacities, bilateral mild pleural effusion, and interlobular septal with fissural thickening, suggestive of lymphangitis carcinomatosis [Figure 1]. This clinical presentation compelled us to initiate treatment for *Pneumocystis jirovecii* pneumonia. Nonetheless, he failed to respond to the treatment and hypoxia persisted. A *Treponema pallidum* Hemagglutination test was done as a part of workup for the penile ulcer, which turned positive. He was diagnosed to have secondary syphilis and was started on benzathine penicillin for the same. At this point, a differential diagnosis of primary anorectal malignancy with lymphangitis carcinomatosis vs. pulmonary syphilis was considered. Meanwhile, the patient continued to have bleeding per rectum and therefore underwent a repeat colonoscopy which confirmed the persistence of an ulcer-proliferative lesion and a biopsy was taken. The patient's clinical condition rapidly deteriorated with worsening hypoxia and he succumbed to massive hemoptysis on the third day of his illness. The biopsy report revealed a spindle cell proliferation in the lamina propria with the spindle cells showing mild atypia, suggesting KS [Figures 2 and 3]. This was further confirmed by a positive

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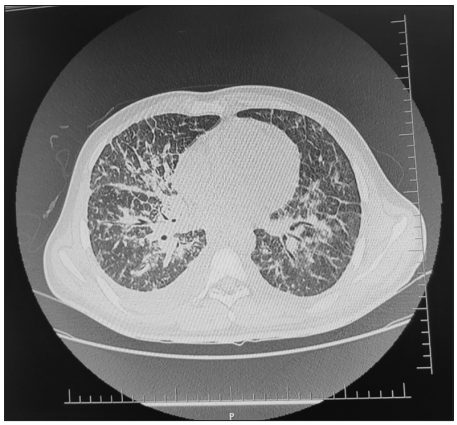

Figure 1: Computed tomography chest showing bilateral peri-lymphatic nodules and peri-broncho-vascular ground glassing

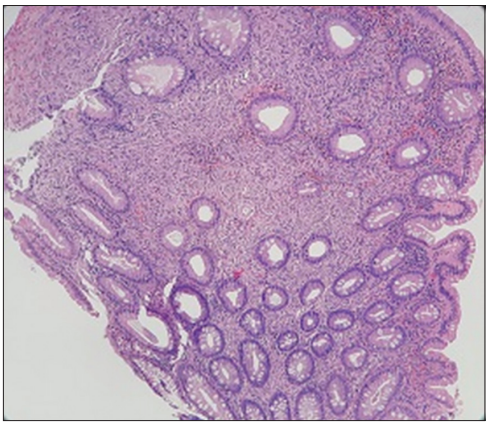

Figure 2: Rectal mucosa with proliferating vascular channels

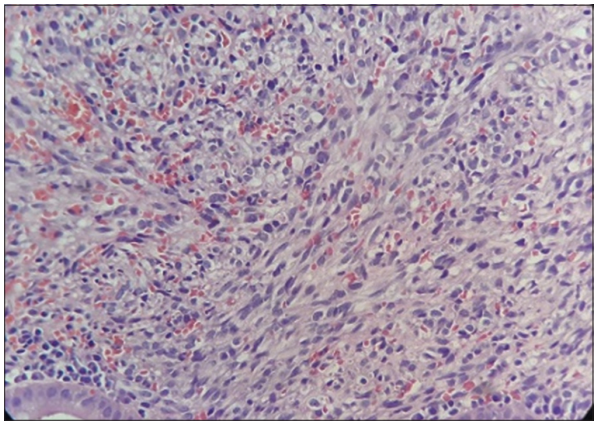

Figure 3: Spindle cell proliferation with vascular channels

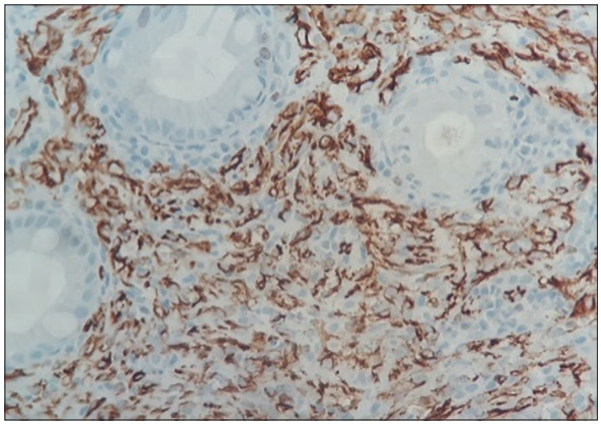

Figure 4: CD34 stain highlighting vascular channels

CD34 staining of the biopsy specimen which subsequently confirmed the diagnosis of KS [Figure 4].

Discussion

KS-IRIS refers to either an abrupt clinical worsening of a previously existing KS or a new presentation of a previously unknown KS in temporal association with initiation or re-initiation of ART or a change to a more active regimen. KS-IRIS occurrence is associated with a concomitant reduction of at least 1 $\log_{10}$ in the HIV RNA level, OR with two of the following three minor criteria: (a) a two-fold increase in the CD4+ T-cell count after ART, (b) an increase in the immune response (KSHV-antibodies), and (c) a spontaneous resolution of disease without specific chemotherapy with the continuation of ART.[3] In our patient, there was the occurrence of new pulmonary and gastrointestinal lesions suggestive of KS along with a reduction in the HIV RNA level. Therefore, this case meets the diagnostic criteria of KS-IRIS. Cutaneous manifestations represent the most common presentation of KS.[4] Our patient presented with disseminated KS devoid of cutaneous manifestations and lower GI bleeding as the initial manifestation that posed a perplexing diagnostic challenge.

The background of immunosuppression also urged us to consider various overlapping differentials including opportunistic infections such as pulmonary syphilis and pneumocystis pneumonia. KS presenting with lower GI bleed has been infrequently reported. Albeit rare, this case demonstrates that GI bleeding from KS may be the initial presenting sign of HIV infection. Classical pulmonary KS presents frequently with hypoxemia and hemoptysis. This constellation of symptoms is typical of disseminated KS, as demonstrated in our patient.

AIDS-associated disseminated KS is a rare condition, especially in our country due to the low prevalence of HHV-8 infections in the Indian population.[2] Further, the low HIV viremia, CD4 counts being >50cells/ul, and temporal association with ART aided in our diagnosis of KS-IRIS. The treatment of KS involves targeted therapy which should be initiated based on disease severity and patient characteristics. Localized or minimally disseminated cutaneous KS mostly respond to highly active antiretroviral therapy (HAART) and surgical resection of the lesion, cryotherapy, or radiotherapy. ART causes partial or complete resolution of KS lesions due to a decrease in HIV viremia and improvement in the CD4 counts. Disseminated disease with visceral involvement requires treatment with chemotherapy agents, such as paclitaxel and liposomal doxorubicin.

IRIS does not indicate failure of ART or a need for changes in antiretroviral regimen.

Chemotherapy in association with ART can be effective in the management of this condition. Pomalidomide along with liposomal doxorubicin has shown promising results. Although considerable advances have been made in the effective management of HIV, more studies to identify therapeutic options for KS and KS IRIS are the need of the hour.

Conclusion

This case highlights an unusual presentation of

disseminated KS which posed a diagnostic challenge due to the absence of cutaneous features, rapid progression of disease, and massive hemoptysis with the development of IRIS that eventually turned out to be fatal.

This case highlights a medical emergency that is often under-recognized. The immuno-deficient state led us to consider several other opportunistic infections which are often indistinguishable from KS that further confounded the diagnosis. The high index of suspicion and constant vigilance is of paramount importance in the early recognition and prompt treatment of this condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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