Journal of Microbiology, Immunology and Infection (2013) 46, 309—312

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CASE REPORT

Immune reconstitution inflammatory syndrome of Kaposi's sarcoma in an HIV-infected patient

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Received 28 November 2011; received in revised form 30 December 2011; accepted 11 January 2012

KEYWORDS
Combination antiretroviral therapy;
HIV infection;
Human herpes virus 8;
Immune reconstitution inflammatory syndrome;
Kaposi's sarcoma

We present a case of Kaposi's sarcoma-related immune reconstitution inflammatory syndrome in an HIV-infected patient who developed fever, worsening pulmonary infiltrates with respiratory distress, and progression of skin tumors at the popliteal region and thigh that resulted in limitation on movement of the right knee joint at 3.5 months following a significant increase of CD4 count after combination antiretroviral therapy.

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1684-1182/$36
doi:10.1016/j.jmii.2012.01.006

Introduction

Kaposi's sarcoma (KS) was first described in 1872 by Mortiz Kaposi. Before the introduction of combination antiretroviral therapy (cART) in 1996, HIV-infected individuals had a 20,000-fold higher risk of developing KS compared to HIV-uninfected individuals.[1] Men who have sex with men are at a significantly higher risk compared to patients who acquired HIV via other routes.[1] After the introduction of cART, the standardized incidence rate of KS has decreased from 2628.5 per 100,000 person-years in 1992–1995 to 356.3 per 100,000 person-years in 2000–2003 in the United States.[2] In a survey conducted at a major hospital for HIV care in Taiwan, the crude incidence of KS has decreased from 20.3% to 2.7% after the introduction of cART in 1997.[3] However, KS remains the most common HIV-associated malignancy in the cART era.[2,4]

Skin manifestations such as pink to purple patches or plaques are the most common presentations of KS,[5] followed by visceral involvement that occurs in more than 25% of cases.[6] Of visceral KS, KS of the gastrointestinal tract is most frequently seen, followed by pulmonary KS.[5] The pathogenesis of KS in HIV-infected patients involves the interactions between human herpes virus 8 (HHV-8), HIV infection, cytokines, and angiogenic factors.[7–9] The decrease in the incidence of KS can be explained by the sustained suppression of HIV replication by cART with resultant immune reconstitution, the decrease of its angiogenic Tat protein, and the reduction of cytokines that trigger the production of angiogenic factors.[10]

With the widespread use of cART, immune reconstitution inflammatory syndrome (IRIS) associated with KS (KS-IRIS) is increasingly reported in HIV-infected patients.[11–15] In this report, we describe a case of clinically deteriorating KS of the lungs and skin at 3.5 months after cART despite an increase of CD4 lymphocyte counts. KS regressed successfully with continuation of chemotherapy and cART.

Case report

A 50-year-old homosexual male with HIV infection sought medical attention at our hospital due to rapidly progressive, painful ecchymosis at the right thigh for 2 weeks. The patient had a diagnosis of HIV infection and AIDS at a hospital 5 months before this evaluation, when he presented with multiple, purplish maculo-papular rashes and nodules that involved the face and trunk. The lesions gradually involved the skin of the four limbs and oral cavity, and he experienced a weight loss of 20 kg in 5 months. A chest radiograph revealed multiple fluffy nodular infiltrates at the bilateral lung fields (Fig. 1A). His baseline CD4 count was 46 cells/μL and plasma HIV-1 RNA load was 93,000 copies/ml. A diagnosis of KS of the skin, oral cavity, and lungs was made. He began to receive cART with efavirenz, lamivudine, and abacavir, and chemotherapy (liposomal doxorubicin, 30 mg, administered every 3 weeks). CD4 count increased to 119 cells/μL 2 months after cART, and KS of the lungs and skin regressed after four courses of chemotherapy (Fig. 1B), and he started to gain weight after cART was initiated.

Six weeks before admission, he began to notice an ill-defined purplish and hard ecchymosis at the right thigh that developed insidiously in the beginning and rapidly progressed to involve the right knee joint, which resulted in pain despite the use of analgesics (Fig. 2). He denied a history of trauma to this region. Follow-up CD4 count and plasma HIV-1 RNA load was 154 cells/μL and <40 copies/mL, respectively. Computed tomography of the lower limbs disclosed hematoma and subcutaneous tissue swelling at the right medial thigh. Pain improved initially with acetaminophen treatment, but ecchymosis worsened in association with thrombocytopenia and rapidly increasing infiltrates of the bilateral lungs in chest radiography (Fig. 1C). He also had several episodes of hemoptysis and fever that resulted in exertional dyspnea and hypoxia.

Upon examination, he appeared acutely ill. He was afebrile with a temperature of 36.7°C, pulse rate of 109 beats/minute, blood pressure of 121/68 mmHg, and respiratory rate of 22 breaths/minute. Several purplish nodules were noted at the upper palates without oral candidiasis. The chest wall expanded symmetrically with bibasilar crackles. An ecchymosis of ill-defined border extended from the right medial thigh to the right posterior knee,

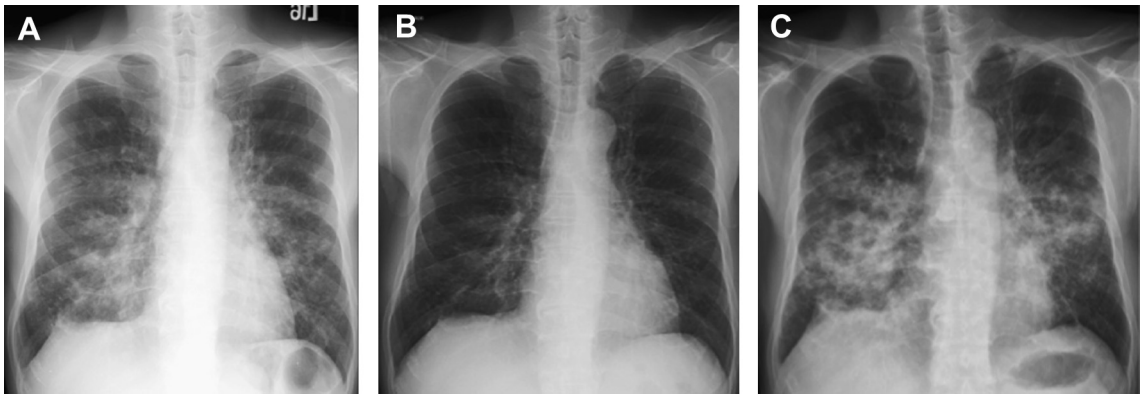

Figure 1. (A) Chest radiography at the time of HIV diagnosis showing several nodular infiltrates at both lungs. (B) Follow-up chest radiography after four courses of chemotherapy and 2.5 months of cART showing significant regression of KS of the lung. (C) Follow-up chest radiography at the time of deteriorating cutaneous lesion. cART = combination antiretroviral therapy; KS = Kaposi's sarcoma.

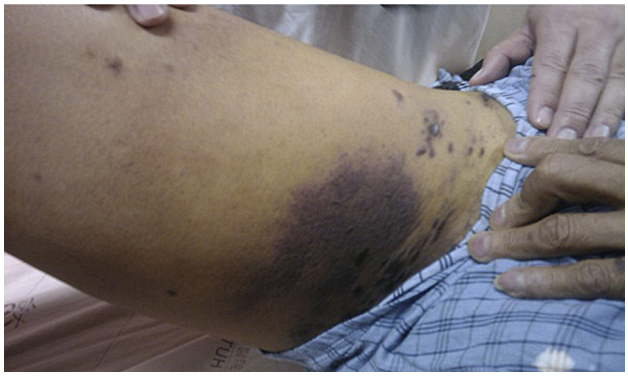

Figure 2. Newly developed Kaposi's sarcoma (KS) at the inguinal region and inner thigh.

which caused pain on extension of the knee joint. Several enlarged, movable lymph nodes were noted at the bilateral submandibular and right peri-auricular regions. White blood cell count was 4540/μL, hemoglobin 11.8 g/dL, and platelet count 110,000/μL.

A thoracentesis yielded bloody pleural effusion (total red blood cell count, 210,000 cells/μl; neutrophil count, 500 cells/μl with 74% lymphocytes), and HHV-8 DNA was detectable in a pleural effusion specimen using real-time polymerase chain reaction assay.[16] The bronchoscopy revealed no endobronchial lesion or active bleeder, but the pathology of transbronchial lung biopsy and sonography-guided lung biopsy specimens showed spindle cells with occasional slit-like spaces adjacent to the unremarkable alveolar tissues. Immunohistochemically, these biopsied tissues were positive for CD31 and HHV-8, which was consistent with KS. Further courses of chemotherapy (liposomal doxorubicin, 35 mg per course) were administered, and hemoptysis ceased; the right leg pain and hematoma gradually improved, while the follow-up platelet count increased to 120,000/μL. Follow-up chest radiography 15 days after three courses of chemotherapy showed a significant regression of the bilateral lung infiltrates. The serial CD4 counts, plasma viral loads, and HHV-8 viral loads are shown in Fig. 3.

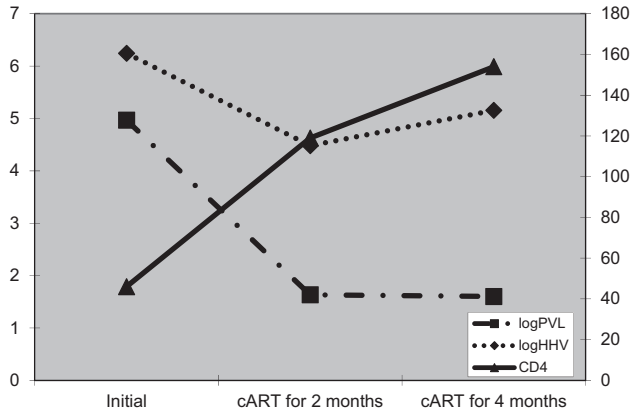

Figure 3. Changes in CD4 count and plasma HHV-8 viral load at baseline and 2 and 4 months after cART. cART = combination antiretroviral therapy; HHV-8 = human herpes virus 8.

Discussion

In the era of cART, cases of KS-IRIS are increasingly reported, and the incidence rate ranges from 6% to 12% among HIV-infected patients who initiate cART.[17–19] A prospective study conducted in Mozambique identified the predictors of KS-IRIS in the cART era, which included pretreatment KS, high plasma HIV RNA load, detectable plasma HHV-8 DNA before cART, and a hemotocrit <30%.[18] The risk may reach its peak during the first 2 months of cART.[11] All four risk factors for KS-IRIS are present in our patient, who had a rapid increase of CD4 count 2.5 months after cART. The immune reconstitution following cART caused KS-IRIS.

Previous studies have shown that HHV-8 DNA levels decreased and the anti-HHV-8 antibody titers increased in patients who developed KS-IRIS.[12,18] However, our patient had an initial decline of the HHV-8 viral load with chemotherapy and cART, followed by an increase of the HHV-8 viral load when KS-IRIS was detected. The temporal relationship between the increase of his CD4 count and rapid worsening of KS at 3.5 months after cART is consistent with the diagnosis of KS-IRIS.

The appropriate management of IRIS-KS remains unclear because the number of such cases is small. A review of the literature suggests that chemotherapy will cause successful regression of pulmonary KS.[11] Therefore, continuation of cART and reinstitution of chemotherapy with liposomal doxorubicin should be considered, especially in patients with visceral involvement.[12]

In conclusion, KS-IRIS should be considered in HIV-infected patients with pre-existing KS who had clinical worsening of dermatologic and pulmonary lesions after initiation of cART.

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Journal of Microbiology, Immunology and Infection (2013) 46, 313–314

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LETTER TO THE EDITOR

A multidisciplinary team care bundle for reducing ventilator-associated pneumonia at a hospital in southern Taiwan

Sir,

We read with great interest the article in the *Journal of Microbiology, Immunology and Infection* by Wu et al,[1] reporting a decreasing incidence of catheter-related bloodstream infections (CRBSIs) after the introduction of standardization of the process of center venous catheter implantation in an intensive care unit (ICU) in a medical center in center Taiwan. In addition to CRBSIs, ventilator-associated pneumonia (VAP) is another common type of healthcare-associated infections, and is the leading cause of mortality for device-associated infections.[2,3] Therefore, we feel this issue needs to be addressed, in addition to CRBSI. However, study on the impact of bundle-care interventions on the development of VAP in Taiwan is lacking.

This project was carried out in a medical-surgical ICU with 63 beds at the Chi Mei Medical Center, Liouying branch, located in southern Taiwan. VAP was identified according to the Centers for Disease Control/National Healthcare Safety Network standard definitions.[4] The numbers of patient-days, device-days, and VAP cases have been collected monthly from the infection-control practitioner. We compared the rates of VAP, from April 2010 to October 2010, for a 7-month period prior to the initiation of the VAP prevention bundles, with the VAP rates after intervention from November 2010 to December 2011 (a 14-month period). The bundle-care interventions for prevention of VAP included: (1) maintenance of patients in a semi-recumbent position, 30–45° elevation of the head to the bed; (2) daily interruption of sedation and assessment for continuation; (3) daily spontaneous breathing trials; (4) performance of oral care three times a day with an antiseptic solution (0.2% chlorhexidine gluconate); (5) maintenance of endotracheal tube cuff pressure above 20 cm H_2O; and (6) assessment on the reduction of prophylactic use of histamine receptor 2-blocking agent or proton pump inhibitor for stress ulcers in high risk patients. Additionally, educational programs were arranged in November 2010 for the staff in all ICUs, including attending physicians, respiratory therapists, and nurse practitioners.

The implementation of the VAP prevention bundle resulted in the reduction of the VAP rate from a mean of 11.05 cases/1000 ventilator-days in the preintervention period to 2.81 cases/1000 ventilator-days in the post-intervention period ($p < 0.0001$). The surveillance showed a significant decreasing incidence of VAP after the introduction of intervention.

In the present work, we have one major finding. Similar to Wu et al's study,[1] which showed a decreasing incidence of CRBSI after the introduction of standardization of the process of center venous catheter implantation, we demonstrated that the introduction of bundle-care interventions with a multidisciplinary team approach can effectively prevent the development of VAP. It suggests that this effective preventive strategy should be implemented in the ICU to reduce the occurrence of VAP.

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