

## HIV-Negative Disseminated Cutaneous Kaposi's Sarcoma: Three Case Reports

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### Abstract

Kaposi's sarcoma (KS) is a malignant disease that originates from the vascular endothelium and has a very variable clinical course. Classic KS is usually limited the lower extremities and runs a relatively benign, indolent course for 10 to 15 years or more, with slow enlargement of the original tumors and the gradual development of additional lesion; whereas immunodeficiency-related diseases frequently disseminate and involve several organs. Here, we presented three HIV-negative disseminated cutaneous KS cases with different clinical presentations and coexistent diseases.

**Keywords:** Kaposi sarcoma; HIV/AIDS

### Introduction

KS is a vascular endothelial malignancy and the neoplastic cells are closely related to lymphatic endothelial cells. Although HHV-8 is found in the vast majority of all types of KS, there is no agreement on the exact mechanism of HHV-8 in KS. While immunosuppression of the host is commonly thought to promote replication of the HHV-8 virus, it is noteworthy that KS is much more strongly associated with HIV-1 infection than with immunosuppression in transplant recipients, suggesting a more complex process [1]. The four KS types (classic, HIV/AIDS-related, immunosuppression associated and African endemic) have somewhat different presentations and different clinical courses. Immunosuppression-associated KS can have a course with rapid progression and dissemination.

### Case Representations

#### Case 1

A 53-year-old man, seen for the first time in May 2005, had a one month history of asymptomatic erythematous to livid firm papules on his right arm and dorsal aspect of the right hand. There was a past history of chronic active hepatitis B infection for which the patient received lamivudine. The histopathologic examination of skin lesions showed features of Kaposi's sarcoma. Immuno-histochemical study of tumor showed immunoreactivity to CD31 and HHV-8, thus a diagnosis of Kaposi's sarcoma was confirmed. Skin lesions were healed and disappeared completely within 2 weeks without any treatment. In August 2014, his treatment with lamivudine changed to tenofovir with the suspicion of lamivudine-resistant HBV and finally in September 2014, involvement of the upper eyelid, lips, face, hands and feet was noticed. On physical examination, there were disseminated multiple purplish papules and nodules on his hands, arms and feet. Also, several violaceous papules and nodules ranged from 5 mm to 1.5 cm were observed on the face which had started gradually over the last month. Routine laboratory tests were all normal. The anti-HIV test (chemiluminescence) was negative. He had normal chest and abdominal computed tomography. Because of the aggressive course of KS, etoposide chemotherapy was started.

#### Case 2

A 53-year-old HIV-seronegative woman presented to our clinic with asymptomatic purple coloured skin lesions on her legs. Three years earlier, she had had been diagnosed with systemic sarcoidosis by histologically proven by lymph-node biopsy and treated with a methylprednisolone (32 mg/day for 60 days) with complete recovery from the disease. During the last 3 months, the patient's clinical status had been compromised by

malaise, weight loss, shortness of breath and she had been diagnosed with interstitial lung disease due to sarcoidosis and methylprednisolone 32 mg/day was started. On her physical examination, there were disseminated multiple violaceous macules and papules, ranged from 5 mm to 1 cm, on her arms and legs. The diagnosis of KS was confirmed by a histopathological examination. Biopsy specimen showed immuno-reactivity to CD-31 and HHV-8. Routine laboratory tests and abdominal ultrasonography was normal. Topical clobetasol propionate was prescribed with a twice daily application.

#### Case 3

A 83 year old woman seen for the first time in October 2009, had a two years history of asymptomatic, irregular red plaques of varying sizes on the trunk and hands. She was diagnosed with KS and topical clobetasol propionate treatment was started. She wasn't not show up for her scheduled follow-up visits and in July 2011 she applied with bluish-purple macules, papules and nodules with an atypical exophytic verrucous appearance on her feet which had started gradually over the last year. She was diagnosed with rheumatoid arthritis at the age of 29 years and chronically taking methylprednisolone 8 mg/day for 20 years. On her physical examination, multiple disseminated violaceous to dark-blue macules, plaques, nodules of varying sizes appeared on her legs and feet with a background of severely edematous skin on her legs and exophytic verrucous appearance on her feet were seen. 5 mm punch biopsy was performed both livid papules and verrucous areas of feet. The diagnosis of KS was confirmed histopathologically. Immuno-histochemical studies showed appropriate positive staining of CD-31 and HHV-8. Rheumatoid factor (RF) was 384 IU/mL (normal range 0-21 IU/mL), leukocyte count was 12.7 G/L (normal range 4.0-10.8 G/L), haemoglobin was 9.2 mmol/L (normal range 12-16 G/L), CRP was 14 mg/L (normal range<0.8). The patient tested negative for human immunodeficiency virus (HIV). She was complaining about severe joint and muscle pain all over body. Bone scintigraphy and computer

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tomography showed no evidence of metastatic disease. Accordingly, we considered as acute exacerbation of rheumatoid arthritis. Thus, with the diagnosis of classic Kaposi sarcoma, treatment was started with local radiation therapy (Figures 1-5).

## Discussion

Kaposi's sarcoma (KS) was first described in 1872 by Moritz Kaposi, a Hungarian dermatologist, as an "idiopathic multiple pigmented sarcoma of the skin" [2]. Kaposi's sarcoma-associated herpesvirus or human herpesvirus 8 (HHV-8) was detected for the first time in AIDS associated KS lesions in 1994 [3]. The four KS types (classic, HIV/AIDS related, immunosuppression associated and African endemic) have somewhat different presentations and different clinical courses.

Disseminated disease often associated with HIV infection but all of our patients were HIV negative and stated they were monogamous with marriages lasting more than 20 years, and disavowed both homosexuality and sexual relations with commercial sex workers.

Patient 1 had a chronic hepatitis B infection and rapid progression of the disease with involvement of labial mucosa prompted the use of systemic chemotherapy. It was reported Kaposi's Sarcoma-associated herpes virus infection rate in patients with chronic hepatitis B is significantly higher than in healthy people [4]. We assumed that predisposing factors in the occurrence of Kaposi's sarcoma is more likely than a coincidental association in this case. Skin lesions diminished significantly after chemotherapy.

Patients 2 and 3 had received oral steroids for the past years and patient 3 was still taking methylprednisolone 8 mg/day. Excessive use of immunosuppressive drugs in the second part of the 20th century has been associated with a higher prevalence of iatrogenic KS [5].



Figure 1: Erythematous to livid firm papules on his right arm and dorsal aspect of the right hand which are less than 1 cm in diameter.



Figure 2: Disseminated multiple purplish papules and nodules on his face, hands, arms and feet which ranged from 5 mm to 1,5 cm.



Figure 3: Disseminated multiple violaceous macules and papules, ranged from 5 mm to 1 cm, on her arms and legs.



Figure 4: In October 2009, had a two years history of asymptomatic, irregular red plaques of varying sizes on the trunk and hands.



Figure 5: In July 2011 she applied with bluish-purple macules, papules and nodules with an atypical exophytic verrucous appearance on her feet which had started gradually over the last year.

In the 39 non-AIDS and nontransplant recipients reported to have developed KS after treatment with corticosteroids, most of the primary diseases from which they suffered are of autoimmune pathogenesis including pemphigus vulgaris, bullous pemphigoid, dermatomyositis, polymyalgia rheumatica, rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, temporal arteritis, idiopathic thrombocytopenic purpura, biliary cirrhosis, autoimmune haemolytic anemia and allergic angitis [6]. CS de Chou et al. reported 4 patients who had affected concomitantly by sarcoidosis and KS [7]. In patient 2, we assumed sarcoidosis associated alteration of immune regulation and corticosteroid therapy may have promoted the development of disease. Accordingly, in patient 3 we assumed that occurrence of disseminated KS is both associated with corticosteroid therapy and rheumatoid arthritis but it is difficult to judge the significance of their role in facilitating the appearance of KS in these patients without knowing

the possible contribution of the autoimmune disorder because KS is reported to be associated with autoimmune disorders without prior steroid therapy.

Start of the disease, after administration of the triggering drug in previously reported studies, ranged from less than one month to more than 20 years. The dose of steroid ranged from 5 to 125 mg/day and there was no evident correlation between the development of KS and dose and duration of steroid therapy [6]. In fact, Tyros et al. reported a patient with generalized Kaposi's sarcoma after chronic and extensive topical corticosteroid use [8].

Both in patient 2 and 3, oral corticosteroid therapy couldn't be ceased because of their active systemic diseases. In patient 2, we started topical clobetasol propionate ointment and in patient 3, radiotherapy was initiated. Both patients didn't come for follow-up visits.

### Conclusion and Outcomes

The outcome in our series highlights the need for physicians to be aware that corticosteroid-induced immunosuppression, chronic infections and autoimmune diseases constitute a risk factor for the development of KS. If the activity of the underlying disease permits, an attempt should be made to reduce the corticosteroid dosage or discontinue its use. When the tumor does not regress or when the

underlying disease is not well controlled, additional anti-tumor treatment with radiation therapy, chemotherapy, and/or surgical excision can be added.

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