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Case Report

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The First Diagnosed Case of Steroid-induced Kaposi's Sarcoma in Mongolia

Khandsuren Byamba[1], Ariunaa Munkhbayar[2], Oyuntsatsral Batsaikhan[1], Undram Sainzaya[3]

[1]Department of Dermatology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [2]Department of Clinical Pathology, National Dermatology Center of Mongolia, Ulaanbaatar, Mongolia; [3] Department of Research and Training, National Dermatology Center of Mongolia, Ulaanbaatar, Mongolia

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Corresponding Author
Undram Sainzaya, MD, MMS
Department of Research and Training, National Dermatology Center of Mongolia, Sukhbaatar District, Police Street-11, Ulaanbaatar, Mongolia
Tel: +976-9903-5678
E-mail: undra.sz@gmail.com

Objectives: Kaposi's sarcoma (KS) is a vascular neoplasm with four main types. We report the first diagnosed case of steroid-induced KS in a non-HIV patient in Mongolia. **Methods:** A 57-year-old man presented hemorrhagic spots on his body after seven months of corticosteroid therapy due to the glomerulonephritis. Upon examination, the morphology, histopathology and immunohistochemistry indicated human herpes virus-8 (HHV-8) positive KS. **Results:** After the dose reduction of corticosteroids the lesions remarkably diminished in size and almost resolved as observed at the six-month follow-up. **Conclusion:** Medical professionals should be aware of the appearance of KS in patients receiving immunosuppressive therapies.

Keywords: Sarcoma; Adrenal Cortex Hormones; Herpesvirus 8, Human

Introduction

Kaposi's sarcoma (KS) is a vascular neoplasm, described for the first time in 1872 by Moritz Kaposi as multiple benign idiopathic pigmented hemorrhagic plaques and nodules [1, 2]. It has four main types: classical KS, HIV-related KS, African endemic KS and iatrogenic KS following immunosuppressive therapy [1, 3, 4]. In 1981, Leung et al. described the first case of steroid-induced KS [2]. Since then, many authors have described KS cases of patients with organ transplantation and long-term immunosuppressive therapy. Cases of KS after lengthy steroid

therapy in autoimmune diseases such as pemphigus vulgaris, pemphigoid, dermatomyositis and systemic lupus erythematosus have been reported in dermatology practice [1, 5, 6]. Here we report the first case of steroid-induced, human herpes virus-8 (HHV-8) positive KS in a non-HIV patient in Mongolia.

Case report

A 57-year-old man presented a hemorrhagic spot on his left foot arc from August 2014 which gradually increased in size and multiplied in number. The patient presented no other symptoms except tenderness at the site of the lesion. The patient's history included glomerulonephritis for which he had been receiving oral methylprednisolone (in a dose varying from 5-64 mg/day) since January 2014. Also, he had been hospitalized because of a left lung abscess in November 2014.

Physical examination revealed a 3 x 1 cm sized violaceous nodule on the left foot arc, which had a hard consistency and was tender upon palpation. Also, multiple brownish patches and nodules about 1 cm in size were found on the fourth and fifth digits of his right and left hands, respectively, left thigh, gluteus and right leg. They were soft and painless by palpation (Figure 1a-c). Mild edema was present around the left ankle. No changes were observed on the mucous membranes.

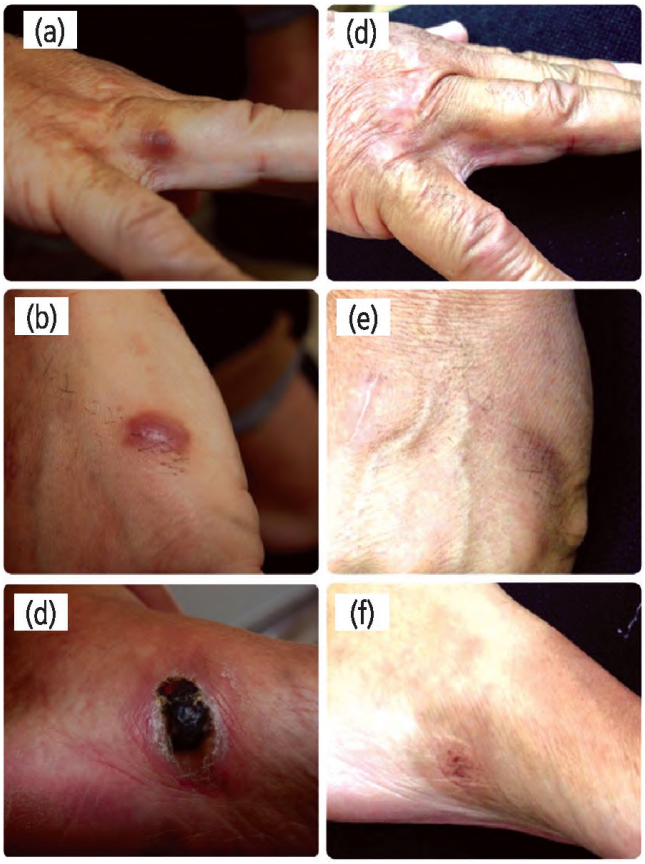

Figure 1. KS lesions on the hands and left foot arc at the time of diagnosis (a-c) and after the dose reduction of corticosteroids at the six-month follow-up (d-f).

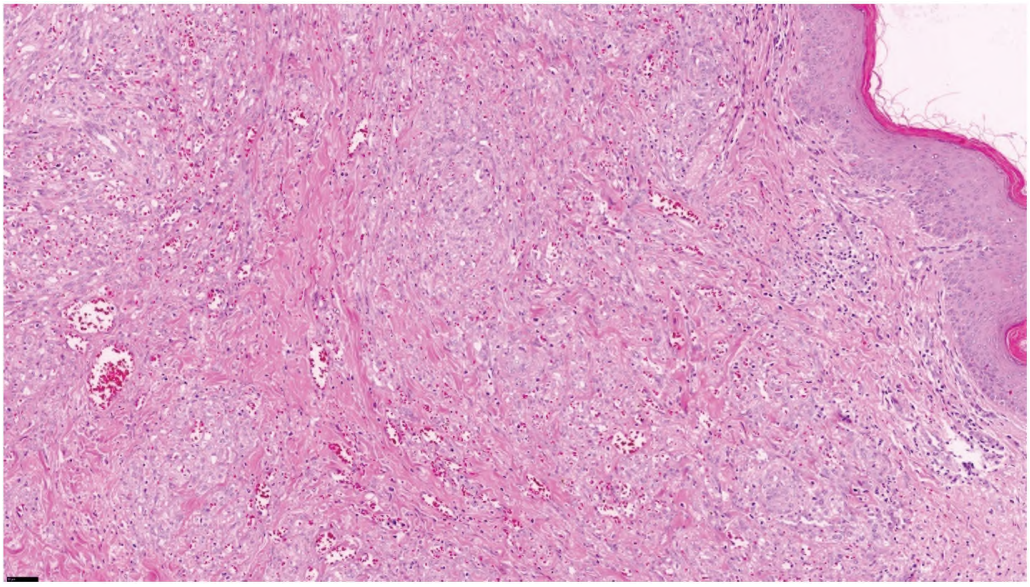

Figure 2. Histopathology image by hematoxylin and eosin staining at 10x. Neovascularization of the dermis with irregular slit-like vascular spaces containing extravasated red blood cells is seen. Eosinophilic spindle cells, plasma cells and lymphocytes with interweaving free red cells are observed.

Laboratory studies were within the normal ranges except for decreased levels of total protein, albumin, and a slightly-elevated level of cholesterol. Urinalysis revealed the presence of proteins. The serological test for HIV was negative or nonreactive.

Histopathologic examination of the skin biopsy from the left foot arc nodule showed neovascularization of the dermis with irregular slit-like vascular spaces, lacking endothelial lining and containing extravasated red blood cells. Presence of eosinophilic spindle cells around these vessels was noticeable. An admixture of plasma cells and lymphocytes with interweaving free red cells were observed. Some mitotic figures were identified (Figure 2).

On immunohistochemistry, the tumor cells were positive for CD31 and CD34. The vascular spaces were positive for D2-40. HHV-8 stain showed granular positivity (Figure 3).

Based on the clinical features, histopathology and immunohistochemistry results, the diagnosis of KS was confirmed.

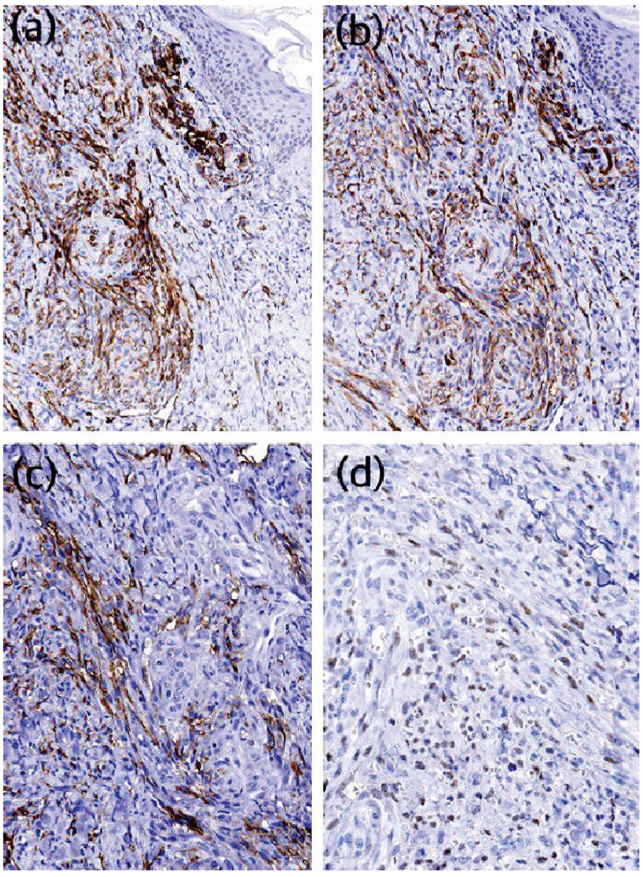

Figure 3. Immunohistochemistry images: (a) CD31+, (b) CD34+, (c) D2-40+, (d) HHV-8+ (each at 10x).

Discussion

KS is one of the malignancies mostly seen in HIV-positive individuals and/or patients treated with immunosuppressive medications. Recent in vitro studies suggest that glucocorticoids have a direct role in stimulating a tumor cell's growth and development. A study of KS tumor cells from HIV-positive individuals revealed that exogenous glucocorticoids stimulate their proliferation [4]. Also, it demonstrated that the glucocorticoid receptors are present at high levels on KS lesions and can be up-regulated by exogenous glucocorticoids and inflammatory cytokines [4].

In 1994, Chang et al. first reported an association between HHV-8 and KS [7]. The virus was isolated from all types of KS lesions, including corticosteroid-induced KS [7, 8]. It has been demonstrated that HHV-8 has an essential role in the pathogenesis of KS by promoting cell growth, angiogenesis and replication of spindle cells typical of KS. And at the same time, the activation of this virus is stimulated by glucocorticoids [9, 10].

There is no evident correlation between the appearance of KS and dose or duration of steroid therapy. Onset of the disease after administration of the triggering drug in previously reported studies ranged from 22 days to several years, while the dose of corticosteroid ranged from 5 to 125 mg/day [1-6].

Treatment modalities of KS include local therapy such as surgery, radiotherapy, chemotherapy with vinblastine and immune therapy by interferon, 9-cis retinoid acid or imiquimod. Patients with widespread disease may need systemic chemotherapeutic or immunologic medication such as pegylated liposomal doxorubicin, danaurubicin, paclitaxel and interferon-α. In the case of iatrogenic KS, cessation of immunosuppressive therapy is the most effective treatment. Patients on immunosuppressive therapy, specifically corticosteroids and cytotoxic drugs, experience partial or complete regression when therapy is discontinued. Thus, if possible, immunosuppressive medication doses should be reduced or discontinued before specific therapy for iatrogenic KS. In those cases when the immunosuppressive therapy is inevitable, for example in transplant recipients, immunosuppressive medication could be modified to sirolimus. Sirolimus has immunosuppressive, anti-angiogenic and anti-neoplastic potential [1-3, 10-12].

Our patient developed his first lesion after seven months of corticosteroid therapy due to the glomerulonephritis. After the dose reduction (from 64 to 16 mg/day) the lesions remarkably diminished in size and at the six-month follow-up were almost resolved (Figure 1d-f). The patient has not received specific treatment for KS, but we believe that suspending the corticosteroid therapy will fully resolve the problem. Unfortunately, due to his main illness the suspension of steroid therapy is being impeded.

KS is an unusual dermatologic disorder. This is the first case of steroid induced, HHV-8 positive KS in a non-HIV patient to be reported from Mongolia. Further, we should be aware of the appearance of KS in patients receiving immunosuppressive therapy.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgements

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