CASE REPORT

ISSN: 2456-8090 (online)
DOI: https://doi.org/10.26440/IHRJ/0611.02591

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Presence of Kaposi's Sarcoma and of Behcet's Disease Concomitantly in a Patient

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ABSTRACT

Iatrogenic Kaposi's sarcoma is a subtype of Kaposi's sarcoma (KS), which is a vascular malignant tumor and is seen in organ transplant recipients and in patients receiving immunosuppressive therapy due to other reasons. We describe a case of Behcet's disease associated with Kaposi's sarcoma occurring simultaneously in a 50-year-old male patient. Colchicine and steroids were administered for his mucocutaneous findings and polyarthritis. In few months on therapy, four symmetric, brown- red coloured, asymptomatic macules developed on the inner surface of his left foot. In histopathologic specimens; CD34 positive, atypical spindle cells with swollen nuclei formed bundles and vascular spaces filled with erythrocytes. The patient was diagnosed as KS clinically and histopathologically. HHV-8 DNA was positive with PCR. Regression was observed in the lesions after the cessation of corticosteroid treatment.

KEYWORDS: Behcet Disease, Iatrogenic Kaposi Sarcoma, Immunosuppressive Therapy

INTRODUCTION

Kaposi's Sarcoma (KS) is a vascular malignant tumor that has four sub-types, which have the same histological and clinical characteristics but affect different populations. Iatrogenic KS is a subtype of Kaposi's sarcoma seen in organ transplant recipients and patients receiving immunosuppressive therapy for other reasons. Iatrogenic KS can develop following the use of corticosteroids and/or immunosuppressive drugs in systemic lupus erythematosus, rheumatoid arthritis, polymyositis, dermatomyositis, polymyalgia rheumatica and Behcet's disease that is usually with ocular involvement. This case was presented in order to emphasize that iatrogenic KS may develop upon activation of Human Herpes Virus 8 (HHV-8) after frequently used corticosteroids and immunosuppressive treatments in the dermatology field and regression in clinical conditions may occur when these treatments are discontinued. In the literature, the comorbidity of Behcet's disease and KS has rarely been reported. Here, kaposi's sarcoma due to corticosteroid treatment in cases of Behçet disease with mucocutaneous and joint involvement was reviewed in the light of literature information.

CASE REPORT

Our case was a 50-year-old male patient and he first presented due to recurrent oral aphtha and joint pain. The patient was diagnosed with Behcet's disease according to the International Behcet's Disease Study Group diagnosis criteria due to the anamnesis of repeated oral aphtha, pathergy positivity, polyarthritis, multiple papulopustular rashes located in extremities and body, and erythema nodosum. During his routine follow-ups, the patient developed four symmetrical, brown-red, asymptomatic macules of 2x2 cm size on the inner surface of the left foot developed. The patient, who had previously been administered prednisolone at a dose of 15 mg/day for two months and 10 mg/day for 5 months due to arthritis attacks with severe pain, was started on colchicine 3x1 during our follow-ups. The patient's routine biochemical tests did not yield any abnormal findings either. Hepatitis markers and Anti-HIV were negative. Histopathological examination of the skin biopsy revealed spindle-shaped atypical cells stained with CD34, which formed bundles with enlarged nuclei and erythrocyte-filled channels in the tumoral tissue that developed nodular to the upper dermis, and diagnosis of KS was established histopathologically. The patient was considered to have KS clinically as well and his HHV-8 IgG test was negative. HHV-8 DNA was detected upon PCR examination. After the steroid treatment was stopped at a dose of 5mg/day, regression was observed in the lesions. The patient was started on interferon at 9 million units/week treatment.

Submitted on: 02-Sep-2022; **Accepted on:** 05-Feb-2023

DISCUSSION

There are four clinical types of Kaposi's sarcoma with defined epidemiological and clinical features; classic, endemic (African type), epidemic (associated with AIDS), iatrogenic (associated with organ transplantation) KS.[1,2] Iatrogenic KS is characterized by mostly asymptomatic brown-red, purple or black patches, plaques, and nodules that occur in organ transplant recipients and patients receiving immunosuppressive therapy for other reasons.[3] The clinical course of the disease is variable, it can be limited to the skin only, or it can have a progressive and widespread course as in endemic and epidemic KS. The incidence of KS has been reported as 0.52% in patients who have undergone kidney transplantation, and a 150-500-fold increased risk has been reported compared to the general population.[1,4] The second group consists of other diseases such as rheumatoid arthritis, systemic lupus erythematosus, polymyositis / dermatomyositis, vasculitides, polymyalgia rheumatica, Behcet's disease, leukemia, lymphoma, hemolytic anemia, asthma and ulcerative colitis, in cases of which, immunosuppressive therapy is administered.[5] The lesions may regress upon reduction or discontinuation of immunosuppressive therapy in iatrogenic KS. Among these four types, in epidemic and endemic types, visceral involvement and spread to lymph nodes are observed.

While epidemic-type lesions are found especially in the head, neck and upper parts of the trunk, lower extremity localization is more common in classical and iatrogenic KS. In studies conducted in the light of epidemiological data, viral pathogens have been blamed in the etiology, and the role of the virus, now known as HHV-8, in the pathogenesis has become clear with the isolation of the DNA sequences of the herpes virus from the Kaposi's sarcoma lesion of a patient with AIDS in 1994.[6] HHV-8 infection is not common and is usually asymptomatic. HHV-8 DNA can be detected in the blood of only 50% of infected patients, indicating the absence of significant viremia. The immune status of the host plays an important role in the course of HHV-8 infection. In healthy people, the immune system also helps to keep the infection under control, and in immunodeficiency cases such as AIDS and during immunosuppressive treatments, latent HHV-8 viral replication and reactivation occur. HHV-8 is located in tumor cells and lymphatic endothelial cells that cover the vascular areas. It is found in blood, especially in circulating B lymphocytes. Reactivation of the virus from the latent period in circulating lymphocytes is one of the mechanisms in the pathogenesis of the virus spreading along the dermal lymphatics.[7] Sex hormones, age, genetics, presence of HIV infection, post-inflammatory angiogenic cytokines and hypoxemia are the other factors that regulate the activation and development of HHV-8[7,8] In the literature, cases of iatrogenic KS observed during corticosteroid and immunosuppressive drug treatments at different doses and durations have been reported in rheumatological diseases.[5] Due to these cases, the most important factor in the development of KS in rheumatological diseases is considered to be corticosteroids. The number of glucocorticoid receptors in KS increases in both the cytoplasm and the nucleus. Furthermore, corticosteroids have the ability to trigger the replication and activation of the in vitro lytic cycle of HHV-8. These findings support the view that patients treated with corticosteroids activate HHV-8.[9] Many cases of iatrogenic KS have been seen only in the group of patients receiving corticosteroids, and partial or complete remission has been observed in KS lesions upon reduction or discontinuation of the dose of corticosteroids in several patients. Furthermore, despite the continued low-dose cyclophosphamide in some KS cases, it has been observed that the CS lesions regress upon discontinuation or dose reduction of the steroid.[10] In a case controlled study comparing classic KS cases with the general population, a small but significant increase in risk for KS was found with the use of any corticosteroid treatment, and in another study, there was a significant correlation between corticosteroid dose and the risk of developing iatrogenic KS.[11,12] In another study, it was demonstrated that exogenous glucocorticoid increased the reproduction of KS tumor cells in HIV+ patients.[13] Behcet's disease is a systemic disease that, in addition to the skin and mucous membrane symptoms, has the potential to involve numerous organs, especially the eyes and joints. This disease, the basic pathology of which is vasculitis, follows a chronic course with repetitive attacks. Corticosteroids, immunosuppressives, and colchicine, as well as analgesic, anti-inflammatory and, anti-aggregant drugs are used in the treatment depending on the symptoms. In our case, colchicine and corticosteroid (reduced 15-10-5 mg/day dose of prednisolone for a total of 7.5 months) was used due to mucocutaneous findings and polyarthritis, and histopathologically verified KS lesions developed on the inner surface of the left foot in the seventh month of steroid treatment.

After the corticosteroid treatment was discontinued, regression was observed in the lesions as stated in the literature. However, the majority of patients receiving

corticosteroid or immunosuppressive therapy do not develop KS, and KS is a very rare complication considering all rheumatic patients who need corticosteroid and/or immunosuppressive therapy. This suggests the presence of genetic or ethnic factors in the development of these neoplasms because majority of the patients with iatrogenic CS overlap with the population that is predisposed to classical CS[5,11] It should be considered that KS, the etiopathogenesis of which is still not well understood, may develop after corticosteroid treatment in Behcet's disease with mucocutaneous and joint involvement.

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Source of support: Nil, **Conflict of interest:** None declared

Cite this article as:
Murthy MS, Lawrence C, Brown T, Sharma S. Presence of Kaposi's Sarcoma and of Behcet's Disease Concomitantly in a Patient. Int Healthc Res J. 2023;6(11):RV1-RV3. https://doi.org/10.26440/IHRJ/0611.02591

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