

Iatrogenic Kaposi Sarcoma in an Immune Competent Woman

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Abstract

Kaposi's disease is a multifocal disease affecting the skin and viscera. Four clinical variants have been distinguished: classic KS, endemic KS, HIV-related KS and iatrogenic KS (iKS), the latter occurring in patients undergoing immunosuppressive treatments for organ transplant, malignant processes or immune-mediated diseases. We report a case of KS associated with glucocorticoids therapy for chronic arthralgia. Clinical manifestations generally resolve after immunosuppressive drugs are reduced or discontinued, whereas maintaining immunosuppression frequently leads to further disease progression. Prognosis also depends on the severity at presentation. All dermatologists dealing with immune suppressors must be aware and have a high index of suspicion when a patient present with rapidly progressive violaceous papules.

Keywords: Kaposi's sarcoma; Human herpes virus 8; Glucocorticoids

Abbreviations: KS: Kaposi's Sarcoma; AIDS: Acquired Immunodeficiency Syndrome

Introduction

Kaposi's sarcoma (KS) is a rare lymph angioproliferative disease associated with human herpes virus 8 (HHV8) [1]. Although HHV-8 infection appears to be necessary, it may not be sufficient for the development of KS without other cofactors. A potentially important cofactor is immunosuppression of the host. Iatrogenic KS (iKS) in particular is associated with immuno-suppressive therapy [2]. We describe a case of KS occurred after the administration of glucocorticoids, in order to highlight the importance to keep in mind this form of Kaposi's sarcoma in patients under chronic immunosuppressant's.

Case Presentation

A 54-year-old woman with 15 years' history of arthralgia treated with corticotherapy, prednisone at the dose of 60 mg daily, by self-medication. The patient was also operated one year ago for cataract. She consulted for multiple painless cutaneous nodules on the left lower limb. Clinical examination revealed papules and nodules, which conclude into a large warty cupboard of the feet and legs (Figure 1). As well as bluish-violaceous plaques of the upper limbs, the thorax, the left cheek and the thighs (Figure 2). Dermoscopy showed a rainbow pattern with yellowish crusts (Figure 3), erythematous background with linear vessels (Figure 4). No mucous lesion or palpable lymph nodes were noted, neither any reported hemorrhage nor gastrointestinal or pulmonary complaints. The skin biopsy revealed Kaposi's disease by

showing a vascular proliferation of fusiform cells (Figure 5) with immunohistochemical staining positive to Anti-CD34 anti body (Figure 6). Biological assessment revealed adrenal insufficiency and CT scan of vertebral compression of osteoporosis. Given the isolated cutaneous involvement, Therapeutic abstention with progressive stopping of corticotherapy was decided. At follow-up visits, the patient reports a collapse of the lesions after stopping corticosteroid therapy. The current decline is 4 months.



Figure 1: Multiples confluent papules and nodules into a large warty cupboard of the feet and legs.



Figure 2: Bluish-lilaceous plaques of the upper limbs and the thorax.

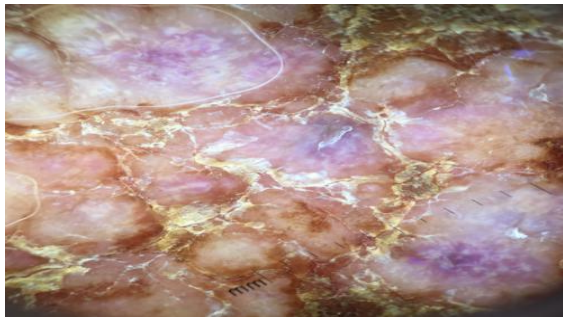


Figure 3: Dermoscopy showing a rainbow pattern with yellowish crusts.

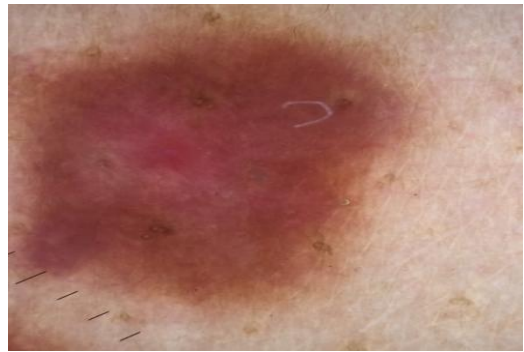


Figure 4: Dermoscopy showing an erythematous background with linear vessels.

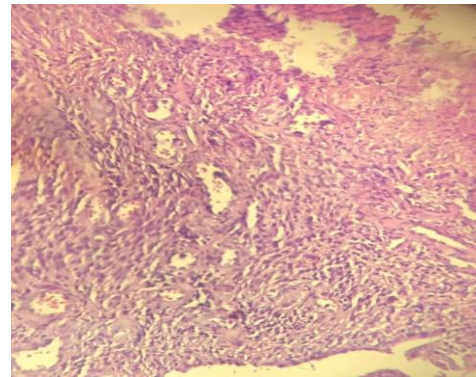


Figure 5: Microphotography showing proliferation of spindle-shaped tumor cells with formation of slit-like spaces containing red blood cells (HE, 200X).

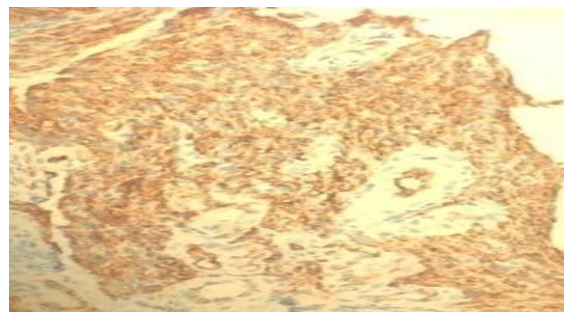


Figure 6: Immunohistochemical stain positive to Anti-CD34 anti body.

Discussion

Kaposi's sarcoma (KS) is a malignant neoplasm of endothelial cells with low proliferation, described by Moritz Kaposi in 1872 [3]. It is widely assumed that KS is

caused by human herpes virus 8 (HHV-8) infections in association with immunosuppression. KS is commonly seen in patients with acquired immunodeficiency syndrome (AIDS) and in organ transplant recipients, and has been reported in patients receiving chronic immunosuppressive therapy [2]. The prevalence of iKS has grown in the last few years among patients undergoing immunosuppressive therapy [1]. KS in immunosuppressed patients was first reported in transplant recipients under cyclosporine [4]. Prednisone and azathioprine were the most implicated medications. Our case is a strong example of this unusual complication of corticosteroid therapy. Corticosteroids seem to be implicated in activation of HHV-8 replication [5]. Although several hypotheses have been proposed, the currently most accepted is that immunosuppressant's lead to iKS by weakening the immunological surveillance system, reactivating a pre-existent HHV8 infection and giving rise to the proliferative transformation of the infected endothelial cells [6]. Corticosteroids directly induce iKS by up regulating KS cell proliferation through the blockage of transforming growth factor beta, a protein that inhibits endothelial cell growth. Nevertheless, corticosteroids increase expression of glucocorticoid receptors on KS cells [1]. In the reviewed literature, the KS may appear between one month and 20 years after the immunosuppressive drug is introduced [7]. However, it is unknown about the differences in the frequency of KS according to type of glucocorticoids and a clear time- or dose-dependent relationship between glucocorticoids treatment and development of KS [2].

Clinical presentations are similar as all types of Kaposi, affecting more commonly men and localized preferentially to distal extremities [5]. KS clinical lesions may vary from brownish macules and plaques to violaceous exophytic tumors. Some lesions may ulcerate or invade surrounding tissues, such as the bones. Different stages may coexist, as seen in this case report, but adjacent tissues and inner organs remain intact [3]. Exclusive cutaneous and/or mucosal involvement is usually seen, even though widespread disseminated forms with visceral involvement may be found. The management of iKS consisted of a reduction in doses and/or withdrawal of immunosuppressive agents upon diagnosis, frequently leading to complete remission or partial response [1], which was illustrated with our case. iKS commonly recurs when immunosuppressive therapy is reintroduced or after a second transplantation; thus, a balance between therapeutic and adverse effects of the immunosuppressant's should be maintained. In the same way, shifting from corticosteroid monotherapy to other immunosuppressant's, such as methotrexate, mycophenolate mofetil or azathioprine, may induce partial response or complete remission [8].

When regression of iKS is not obtained or when the underlying disease is not well controlled, local therapies may be associated such as silver nitrate cauterisation, surgical excision, radiotherapy, compressive therapy with elastic stockings and intralesional chemotherapy [9]. Local therapies alone should be considered for localized disease. Systemic chemotherapy or IFN α should be reserved for more advanced stages not responding to immunosuppressant reduction and/or withdrawal associated with local therapies. Vinblastine and bleomycin are first-line chemotherapeutic agents, whereas gemcitabine, etoposide, liposomal anthracyclines, paclitaxel and docetaxel are second- and third-line treatments [1]. In our case, the therapeutic abstention with withdrawal of the inducing drug, which is the corticotherapy, has ensured a favorable evolution of the disease with a regression of the lesions.

Conclusion

KS is a HHV-8-associated tumor that must be taken into account and should screen as the case for skin cancers, for all cases of patients undergoing immunosuppressive therapy, regardless of the drug used. Providing clear and exhausting information on the necessity to avoid immunosuppressive drugs, particularly corticosteroids, represents the most useful tool in order to prevent not only iKS relapses, but also an iatrogenically induced progression of classic KS.

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