BULLOUS PEMPHIGOID ASSOCIATED WITH IATROGENIC KAPOSI'S DISEASE - CASE PRESENTATION

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Summary

Kaposi's disease represents a multifocal endothelial proliferation which may involve several organs, but most frequently it is associated with skin lesions. There have been described four different clinical variations of this disease, each with its own symptoms, epidemiology and evolution. One of these forms develops in immunosuppressed patients who undergo systemic therapies, such as Prednisone, calcineurin inhibitors or chemotherapy. It is unanimously accepted that HHV-8 infection is the main etiologic factor for Kaposi's disease. Kaposi's disease due to iatrogenic immunosuppression is characterized by violaceous skin lesions which appear during systemic immunosuppressive therapy (such as oral corticosteroids). The disease usually progresses at a slow rate and it may resolve itself spontaneously in early stages or by removing the immunosuppressive therapy.

We present the case of a patient with Kaposi's disease due to corticosteroid treatment administered for bullous pemphigoid.

Key words: *Kaposi's disease, bullous pemphigoid, HHV-8, Dapsone in Kaposi's disease treatment.*

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Introduction

Kaposi's disease, described for the first time in 1872, represents a multifocal vascular proliferative process associated with HHV-8 infection [1,2]. The pathogenic pathway of this disease, triggered by the HHV-8 virus identified in all lesions, regardless of the clinical form, remains uncertain: first of all, it is unclear whether the lesions are caused by a reactive vascular proliferation or by a neoplastic proliferation; secondly, it is still under debate which type of endothelia – vascular or lymphatic – plays a more important role in pathogenesis [1,2,3]. *In vitro* studies have shown that HHV-8 can infect both the vascular and the lymphatic endothelia, thus explaining the development of inferior limb lymphedema which may be significant in some patients [2]. There are four principal clinical variants of Kaposi's disease: chronic; African endemic; epidemic, associated with HIV infection; iatrogenic, due to acquired immunosuppression (including systemic corticotherapy) [4,5].

We present a case of iatrogenic Kaposi's disease, secondary to immunosuppressive therapy administered for bullous pemphigoid.

Clinical case

A 77-year-old female patient, previously diagnosed with bullous pemphigoid, for which she was administered systemic corticosteroids 0.5 mg/kg body weight/day with progressive tapering over the course of several months, was admitted into our clinic for exacerbated bullous lesions and the development of erithemato-violaceous nodules, 0.5 to 5 cm in diameter, with

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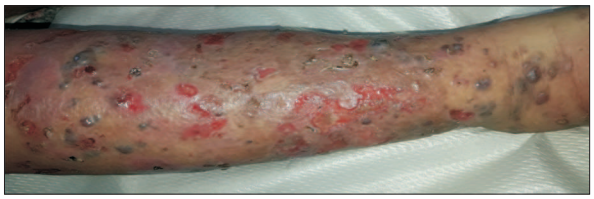

Fig. 1. Erithemato-violaceous nodules, 0.5 to 2.5 cm in diameter, with well-defined margins, spread across the limbs; disseminated bullous lesions, in tension, with clear contents, erosions and crusts

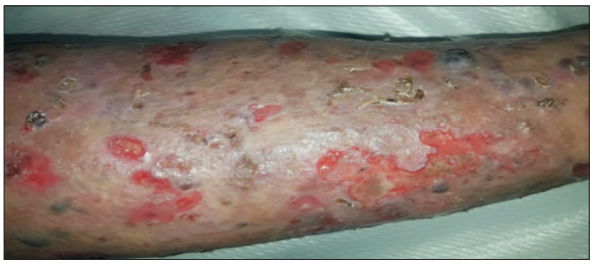

Fig. 2. Exacerbation of bullous lesions and appearance of erithemato-violaceous nodules

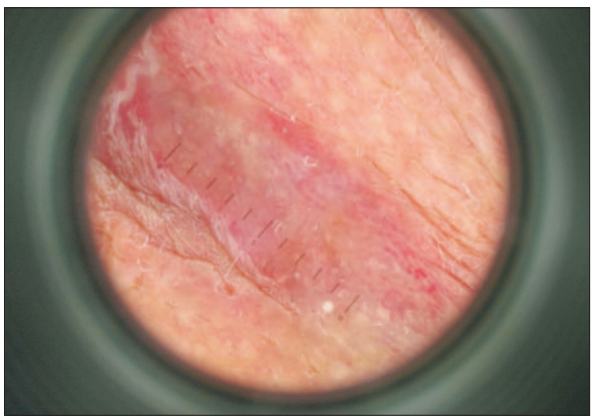

Fig. 3. Differently colored areas - blue, red, described as the "rainbow pattern", due to its resemblance to the rainbow color specter

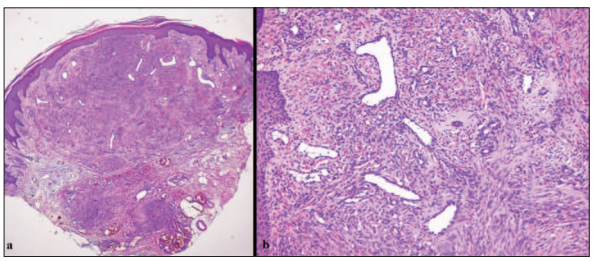

Fig. 4. Spindle cells, arranged in fascicles, forming micronodules, with frequent extravasated erythrocytes and fine inlays of collagen strips; protrusive tumor cells in pre-existing vascular spaces; some blood vessels lacked their own walls (HE stain, 4X - a; HE, 10X - b)

well-defined margins, very itchy, spread across the trunk and limbs. In addition, the patient also presented with right inferior limb lymphedema, several months old. (Fig. 1,2)

Dermoscopy of the violaceous nodules revealed different colored areas – blue, red, described as the "rainbow pattern", due to its resemblance to the rainbow color specter [6,7]. (Fig. 3)

We performed a punch-biopsy from the left forearm which was described by the pathology laboratory as: tumor fragment located in the dermis, composed of spindle cells, arranged in fascicles, forming micronodules, with frequent extravasated erythrocytes and fine inlays of collagen fibers; protrusive tumor cells in pre-existing vascular spaces; some blood vessels lacked their own walls. Therefore, the result was conclusive for the diagnosis of Kaposi's disease [5]. (Fig. 4)

In order to rule out the epidemic variant of Kaposi's disease, we also tested the patient for HIV markers, which turned out negative.

Based on the patient's history, the clinical examination, the para-clinical investigations and the histopathology examination, we established the diagnosis of Kaposi's disease associated with bullous pemphigoid.

The patient was initially administered Prednisone 0.8 mg/kg body weight/day, with a gradual decrease in dosage, up to 0.6 mg/kg body weight/day. In addition, we prescribed gastric protective agents and Dapsone 50 mg/day. Topical treatment consisted of silver sulfadiazine. During the admission the patient's condition greatly improved. Therefore, we decided to continue lowering the Prednisone dose by 0.15 mg/kg body weight/week until cessation and replacement with Dapsone 50mg/day.

Discussions and conclusions

Patients undergoing systemic corticotherapy, chemotherapy or calcineurin inhibitor treatment, may develop Kaposi's disease. Of the immunosuppressive drugs, ciclosporin is most commonly involved, and a more rapid onset of the disease is described. [2,3]

Managing patients with Kaposi's disease associated with bullous pemphigoid may prove to be challenging due to the fact that immunosuppressive therapy is indicated in the treatment of bullous pemphigoid, exacerbating Kaposi's disease.

Therefore, in our case, we decided to progressively reduce the dose of corticosteroid until cessation and replace it with Dapsone 50 mg/day.

According to literature citations, administering Dapsone is indicated in both pathologies. For example, in Kaposi's disease, the histopathological examination describes a reduction of spindle cells and an increase of mature vessels – using the endothelial cellular marker (F VIII R-Ag) in immunohistochemical stains [8]. On the other hand, multiple clinical trials researched prescribing Dapsone for bullous pemphigoid and concluded that it was safe to be used and it had very few side effects [9,10]. Sticherling et al. compared the efficiency of methylprednisolone associated with azathioprine to that of methylprednisolone associated to Dapsone. The results were that Dapsone can potentially increase the effect of methyl-prednisolone, more than azathioprine. The one-year mortality rate in patients treated with these drug combinations was relatively low [11].

There have been described several cases of Kaposi's disease triggered by systemic corticotherapy, especially prescribed for bullous pemphigoid. Therefore, even though it is a relatively rare complication, every dermatologist must take into consideration Kaposi's disease when a patient undergoing immunosuppressive therapy develops violaceous papules. Although this variant of Kaposi's disease progresses hastily, rapid diagnosis and cessation of corticosteroids may lead to the resolution of these lesions. In addition, since HHV-8 plays an important role in the physiopathology of Kaposi's disease, improving the patient's immune status may help control the disease manifestations [12].

There is a multitude of treatment options for Kaposi's disease. For example, if a small area is involved, excision or superficial radiotherapy is recommended. The latter represents the treatment of choice for patients with nodular disease of the extremities. Cryotherapy may be an option for treating nodular lesions.

Extensive clinical variants of Kaposi's disease may benefit from intralesional injections of cytotoxic drugs, such as: Vinblastine, Vincristine, Bleomycin.

As far as the iatrogenic variant of Kaposi's disease is concerned, lowering the doses of immunosuppressive therapy and replacing calcineurin inhibitors with rapamycine are the main objectives [1,5].

In our case, we successfully managed to completely cease corticotherapy and replace it with Dapsone, thus significantly improving both Kaposi's disease and bullous pemphigoid.

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Conflict of interest
NONE DECLARED

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