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Kaposi Sarcoma after Kidney Transplant: A Clinical Case Report

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Abstract

Kaposi sarcoma is a neoplasm caused by human herpesvirus 8 (HHV8) that most commonly affects immunosuppressed patients. The skin is the most affected area, but other sites can be involved such as the lung, digestive tract and lymph nodes. The classical presentation involves a violaceous skin lesion that can be small or hidden, leading to a delay in diagnosis. We report a clinical case of a kidney transplant patient, who presented, 14 months after kidney transplant, with unilateral edema of the inferior member and cutaneous rash misdiagnosed and taken initially for erysipelas. The diagnosis of Kaposi's sarcoma was retained, on a lymph node biopsy of an inguinal adenopathy. The evolution was marked by a local and general improvement after systemic chemotherapy, reducing Tacrolimus and discontinuation of *Mycophenolate mofetil*. Graft function remained stable during the follow-up.

Keywords

Kaposi, Kidney Transplant, HHV8, Immunosuppression

1. Introduction

De novo malignancy after organ transplant rank as the third leading cause of morbidity and mortality in solid organ transplantation, following infectious and cardiovascular complications.

Immunosuppressive drugs as Tacrolimus and Ciclosporin [1], genetic predisposition and oncogenic viruses like Ebstein Bar Virus (EBV), Cytomegalovirus (CMV), Hepatitis B and C viruses (HVB and HVC) and Human Herpesvirus (HHV8) [2], appear to be significant risk factors for neoplasm development.

Post-transplant Kaposi sarcoma is often attributed to HHV8 reactivation (due

to immunosuppressive therapy), and less frequently to virus transmission from the graft donor [3] [4].

Prevalence varies by region [5], with the highest incidence observed in Mediterranean countries and Africa. This data aligns with HHV8 seroprevalence, which is also high in Mediterranean countries and in sub-Saharan Africa (30% in Southern Italy, 51% in Uganda), less common in South America America (10% - 20%), and low (1% - 5%) in the western regions of Northern Europe and North America [4] [6].

The use of mammalian target of rapamycin inhibitor has shown promise in improving Kaposi sarcoma prognosis and incidence [7] [8].

We present a clinical case of post-renal transplantation Kaposi sarcoma, initially identified by unilateral lower limb lymphoedema.

2. Case Report

A 59-year-old woman diagnosed with IgA nephropathy received her first kidney transplant from her sister related donor in 2019.

Immunosuppression consisted of thymoglobulin induction, tacrolimus, mycophenolate, and prednisone. Baseline serum creatinine was 1.5 mg/dl with normal urinalysis.

Both kidney donor and recipient were CMV and EBV seropositive (D+/R+) but HHV8 serological status were not assessed, due to a reagent shortage.

Fourteen months post-transplant, she developed a cytomegalovirus disease, with severe leukopenia. No other organ symptoms related to CMV infection were observed despite extensive work-up.

Following this diagnosis, the patient was administered Ganciclovir, resulting in negative antigenemia within 3 weeks.

However, she experienced intermittent, unilateral, erythematous lymphedema of the left lower limb (**Figure 1**), along with ipsilateral inguinal adenopathy, accompanied by fever, elevated CRP levels (160 mg/l), procalcitonin (1.05 ng/ml), and a positive blood culture for *Staphylococcus haemolyticus*.

She underwent intravenous antibiotic therapy for her erysipelas.

After one week of treatment, there was clinical deterioration of the cutaneous lesions (**Figure 2**) with no biological improvement.

A CT-screening revealed profound latero-aortic adenopathy's, and a PET-scan demonstrated active under diaphragmatic, lombo-aortic and left inguinal lymph nodes with a pathological left lower limb metabolism. (**Figure 3**)

The patient underwent an excisional biopsy of her inguinal adenopathy.

CMV and *Mycobacterium tuberculosis* were tested on the samples, yielding negative results.

Histological study employing light microscopy and immunohistochemistry (IHC) led to the diagnosis of Kaposi's sarcoma. (**Figure 4** and **Figure 5**)

Skin biopsy of the left leg also revealed Kaposi's sarcoma. (**Figure 6**)

Extension work up, based on a MRI (**Figure 7**), didn't find any profound infiltrate.

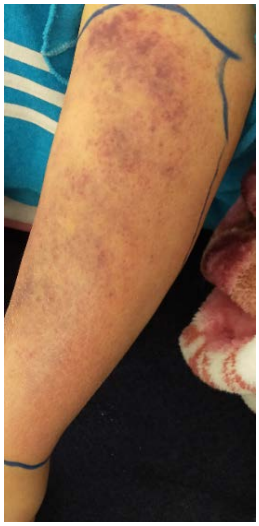

Figure 1. Erythematous lymphedema of the left lower limb.

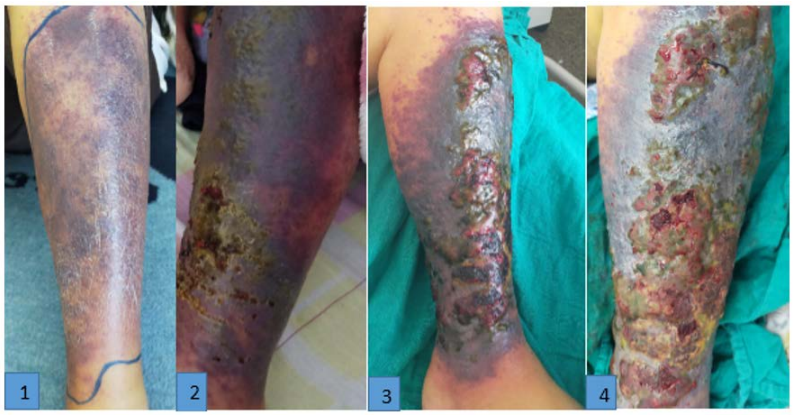

Figure 2. Fast deterioration of the cutaneous lesions.

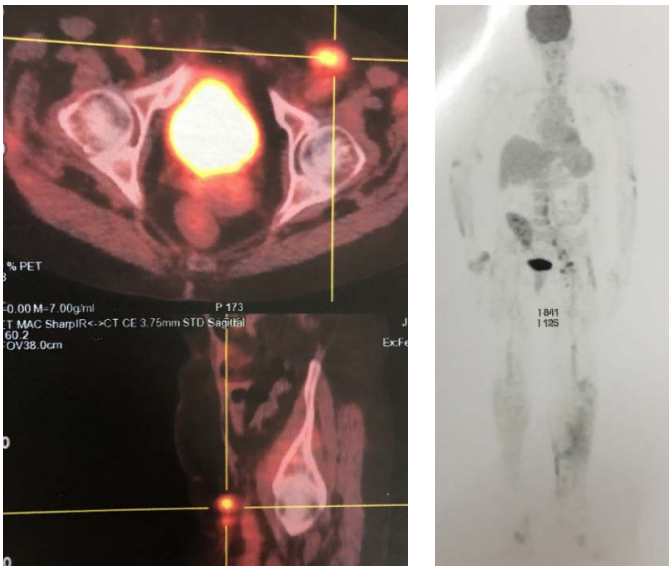

Figure 3. PET-scan, active under diaphragmatic, lombo-aortic and left inguinal lymph nodes with a pathological left lower limb metabolism.

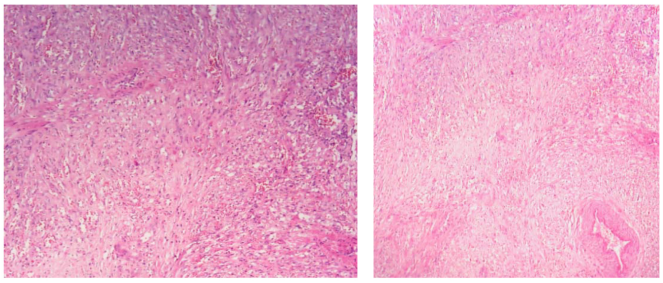

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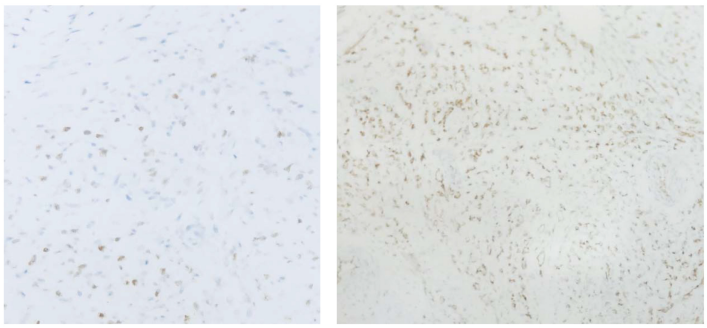
Figure 4. Lymph node biopsy showing a proliferation made of spindle cells arranged in short bundles, surrounding often narrow vascular slits containing red blood cells.



IHC: AC anti-HHV8 IHC Ac anti-CD34

Figure 5. Immunohistochemical study of lymph node biopsy showing positivity for anti-HHV8 and anti-CD34 antibodies.

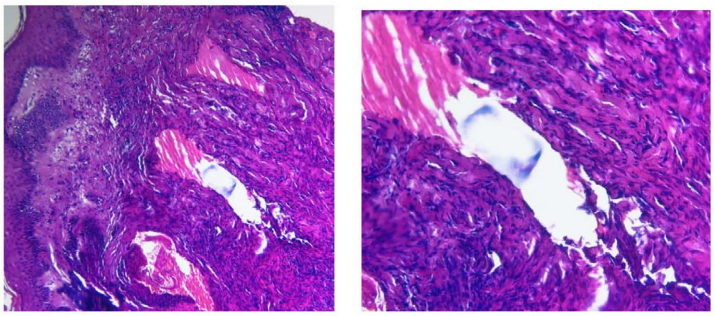


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Figure 6. Skin biopsy showing in the superficial and deep dermis a proliferation made of spindle cells arranged in short bundles surrounding vascular slits containing red blood cells.

Our therapeutic approach was based on systemic chemotherapy with Paclitaxel infusions every 21 days for 6 cycles. We proceeded to a *Mycophenolate mofetil* discontinuation and a reduction in Tacrolimus doses to achieve a residual level of 4 ng/ml. We also ensured an anti-infectious prophylaxis by combining valaciclovir with trimethoprim-sulfamethoxazole.

After 14 months, the evolution was marked by a local clinical improvement (**Figure 8**) and general improvement, with disappearance of the latero-aotic and inguinal lymph nodes on the thoraco-abdomino-pelvic CT scan (**Figure 9**).

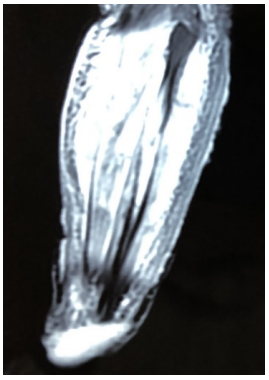

Figure 7. Normal MRI with no profound infiltrate.

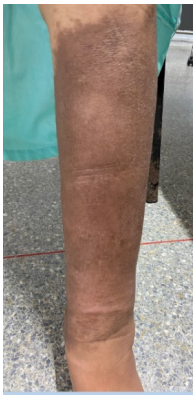

Figure 8. Local clinical improvement after 14 months.

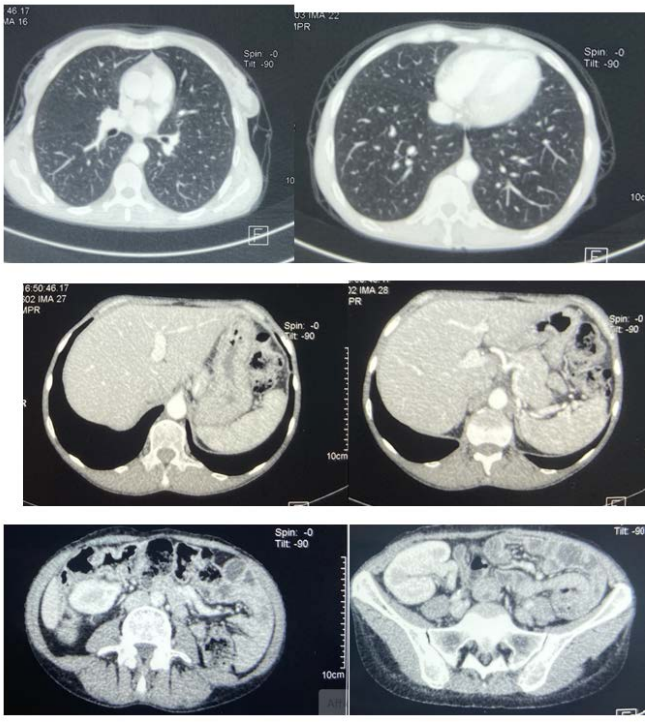

Figure 9. Normal thoraco-abdomino-pelvic CT scan, 14 months after Chemotherapy and reduction of immunosuppression.

3. Discussion

Kaposi's disease (KD) is due to a lymphatic endothelium-derived cells proliferation that is infected with the HHV-8 virus. In solid organ transplantation, the risk of developing it is approximatively 25% in HIV-positive recipients, compared to 0.7% in HIV-negative recipients. Moreover, 80% of patients with post-transplant Kaposi's disease are HHV-8 seropositive prior to transplantation. HHV-8 is usually quiescent in endothelial cells and CD19+ B lymphocytes.

The pathogenesis of Kaposi's disease is based on the experimental model of Montaner *et al.*, who described the transformation of HHV-8-infected endothelial cells into spindle cells [9].

Additionally, HHV8 encodes a number of genes that can deregulate the cell cycle angiogenesis and inhibit apoptosis, that are potentially implicated in the pathophysiology of KD [4].

The first case of post-renal transplant KD was documented in 1969. It generally occurs early after transplantation, with an average onset time of 20 months (ranging from 12 months to 39 months) [10] [11].

According to a recent American study by Cahoon *et al.* reported that in 84.7% of post-organ transplant KD cases were diagnosed within the first three years. [12].

The incidence of Kaposi's disease in renal transplantation varies from team to team, ranging from 4.5% in a Tunisian series series [13], to only 0.4% in a French study [14]. In our series, out of 166 renal transplants between 1998 and 2022, we report one case of KD.

Reactivation of other viruses may act as a cofactor for HHV8 [9], as in our case report, where CMV disease preceding the onset of MK, could be one of those viruses. A similar case has been reported in the literature [14].

The lesions observed in transplant patients lack specific characteristics. The elementary lesions are macules, erythematous and purplish patches that progressively infiltrate. These lesions do not disappear with vitro pressure, and frequently take on an ecchymotic, hemorrhagic or pigmented appearance. Angiomatous nodules or, more rarely, soft lymphangiectatic nodules, may be present either in association or isolated from the previously described lesions. Lymphoedema may be present, but very rarely [4], as described in our case.

Lesions occur preferentially on the trunk and extremities, or less frequently on the face. The ear, nose, conjunctivae and oral mucosa, may also be involved. Involvement of the oral mucosa is frequent [5].

KD in the immunocompromised individuals is often more aggressive than classical MK, with more widespread cutaneous lesions, and more frequent mucosal and visceral involvement, estimated at 25% in cases of renal transplantation and over 50% in liver or heart transplants [15].

Visceral involvement mainly concerns lymphatic organs, gastrointestinal tract (lesions most frequently observed endoscopically), and lungs. Extension workup (X-ray and/or CT scan bronchial and gastrointestinal endoscopy) is essential in identifying any possible location.

The diagnosis of certainty is histological, with evidence of spindle cells grouped in bundles, associated with vascular endothelial cells and an inflammatory infiltrate of mononuclear cells. On immunohistochemistry, HHV-8 is always present in Kaposi's disease lesions, and occasionally in healthy tissue [5].

Therapeutic management is mainly based on reducing or even discontinuing immunosuppressive therapy [16], which is the main cofactor in HHV8 expression. In cases of isolated cutaneous signs, this strategy can lead to remission in 30% to 50% of cases [17], but with a risk of rejection estimated at 50% [18].

Replacing calcineurin inhibitors with sirolimus has demonstrated efficacy.

Indeed, M-Tor inhibitors have both an immunosuppressive and antineoplastic effect [19]. In a recent Italian study, Picelli *et al.* demonstrated a significant decrease in the incidence of post-transplant KD in patients taking m-Tor inhibitors [8].

In visceral and lymph node forms, chemotherapy based on vinblastine, bleomycin or Taxanes is indicated.

For our patient, discontinuation of Mycophenolate Mofetil combined with Paclitaxel chemotherapy resulted in clinical and radiological remission within 14 months.

No antiviral treatment has been proved effective. Foscarnet appears to reduce the occurrence of new lesions, as well as the treatment of febrile cytopenias associated with HHV8 primary infections [20]. Some publications have also demonstrated the value of Ganciclovir in preventing the onset of KD, and in achieving partial remissions [21].

4. Conclusion

Post-renal transplantation KD is a virus-induced neoplastic pathology secondary to reactivation of HHV8, most often due to an immunosuppression state, or can rarely be transmitted a contaminated graft donor. Cutaneous involvement is ubiquitous, but an extension work-up involving a thoraco-abdomino-pelvic CT scan, bronchial and digestive endoscopy is essential to detect extra-cutaneous localization, which is often asymptomatic. Treatment begins with a reduction in immunosuppression, and the use of m-Tor inhibitors, followed by systemic chemotherapy in visceral forms. Graft loss is the major consequence.

Consent

We had the patient's consent to publish this clinical case.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

- HHV8: Human herpesvirus 8
- EBV: Ebstein Bar Virus
- CMV: Cytomegalovirus
- HVB: Hepatitis B Virus
- HVC: Hepatitis C virus
- D/R: Donor and Recipient status
- CRP: C reactive protein
- KD: Kaposi's disease
- IHC: Immunohistochemistry