TREATMENT OF POST TRANSPLANTATION KAPOSI'S SARCOMA WITH INTERFERON ALFA

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ABSTRACT

Kidney transplanted patients under the immunosuppressive therapy are at risk of acquiring Kaposi's sarcoma (KS). A 26 years old Somali male patient developed KS (10 months after renal transplantation) whilst on cyclosporin A, azathioprine and prednisolone. The clinical diagnosis of KS was confirmed by the biopsy. There was no lymphadenopathy nor visceral involvement. The patient received recombinant alpha 2a interferon in an subcutaneous injection of 6 million units three times weekly for three months (36 injections). The KS regressed gradually and disappeared completely with brownish pigmented skin. Now, after more than 20 months, the patient is well with a well functioning graft and there is no recurrence of the KS inspite of the patient is still on the same immunosuppressive therapy.

Introduction

Kaposi's sarcoma (KS) is a rare cutaneous neoplasm. Since the 1960s an increasing frequency has been recognized in patients who have been receiving immunosuppressive treatment[1]. KS showed a four hundred to five hundred fold increase in it's incidence in kidney transplant recipients compared with patients of the same ethnic origin in a control population[2]. In Qatar the estimated incidence of KS in kidney transplant patients is 4.09%[3].

It is proposed that the etiology of KS is multifactorial and that a combination of immunosuppression and/or immunologic stimulation combined with a hereditary predisposition to the disease are responsible for the major increase in its incidence[4].

In the classical KS, there are several lines of treatment as surgical excision, diathermocoagulation, radiotherapy and systemic chemotherapy[5]. But, there is little information in the literatures about the management of KS in kidney transplant patients. Now, interferon (in high dose) is used successfully in the epidemic KS[6,7].

We are describing a unique trial of using low dose interferon alpha 2a for treatment of KS in kidney transplanted patient.

Case Report

A 26 years old Somali male patient working as a soldier presented by recurrent fever and vomiting, generalized weakness, burning low amount of urine, constipation and dry mouth. He had markedly abnormal renal functions, creatinine was 2700 umol/l and BUN was 270 mmol/l. In October 1991, he was diagnosed as having end-stage renal failure "congenital bilateral small kidneys". He was maintained on regular hemodialysis for more than one year. In December 1992, he had a living unrelated kidney transplantation. The transplantation procedure and the post operative course were uneventful. Immunosuppressive regimen consisted of maintenance daily therapy of cyclosporin A 5 mg/kg, azathioprine 2 mg/kg and prednisolone 0.2 mg/kg. There were two episodes of rejection with deterioration of the renal functions which were controlled by high dosage steroid therapy. In October 1993 (10 months after transplantation), the patient noticed multiple brownish-violaceous nodules increased gradually and limited to both legs and feet (Fig 1,2). There were no mucous membrane involvement nor lymph node enlargement. A skin biopsy was performed.

On histological examination, there were normal epidermis and replacement of the dermis with numerous vascular spaces. The vascular structures were lined by rows of bulging endothelial cells.

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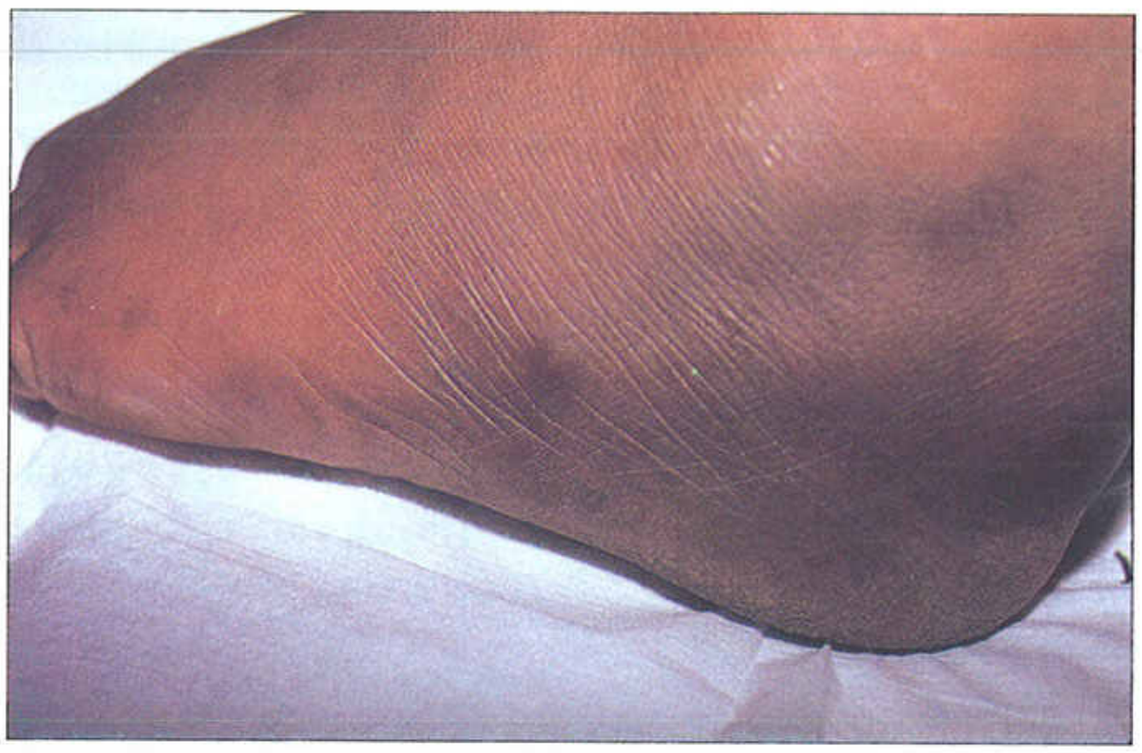

Fig 1: Kaposi's Sarcoma in the left foot before treatment

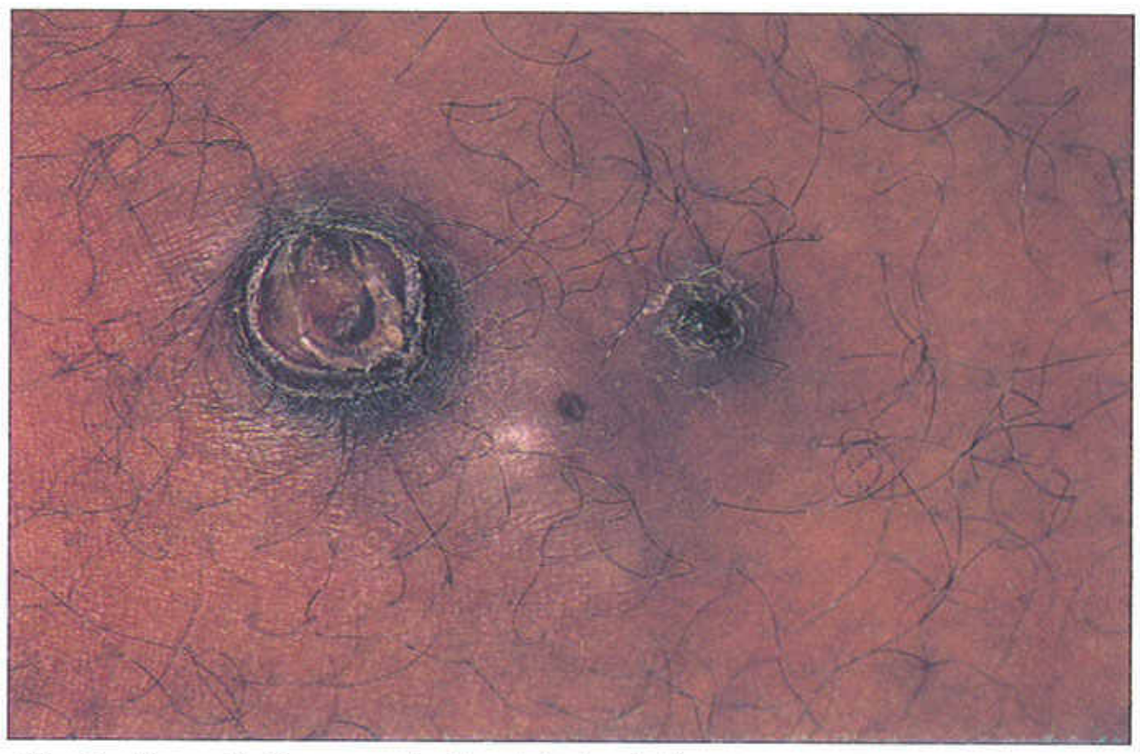

Fig 2: Kaposi's Sarcoma in the right leg before treatment

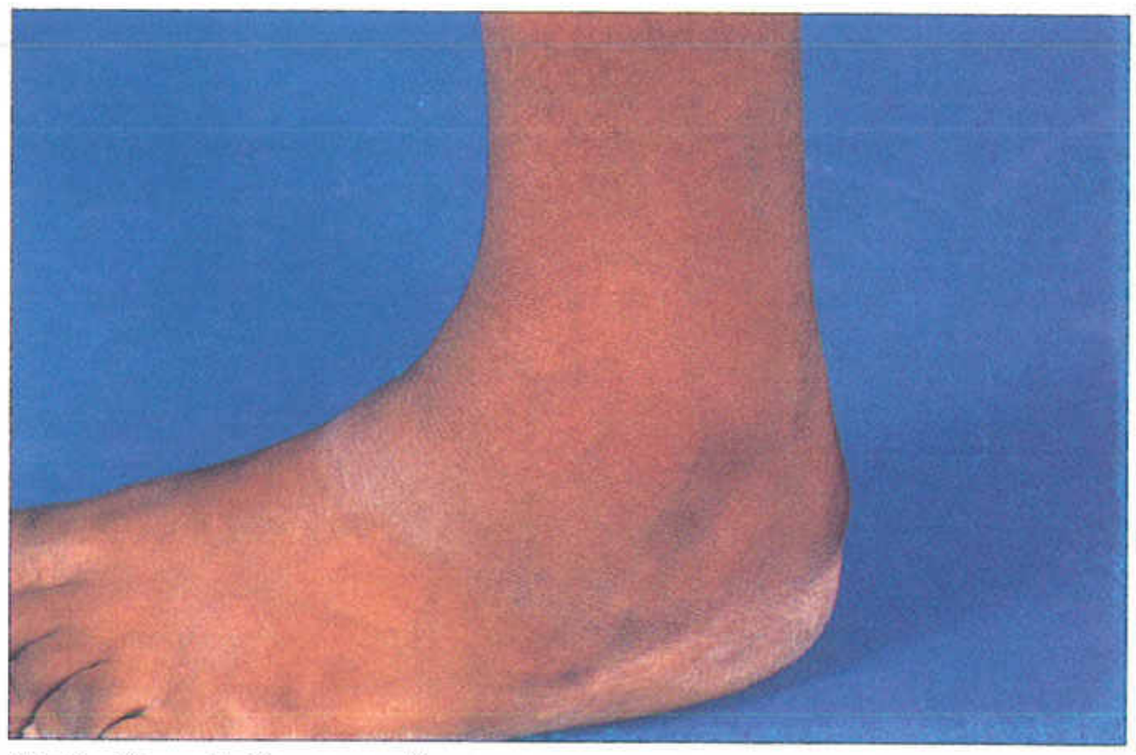

Fig 3: Kaposi's Sarcoma after treatment

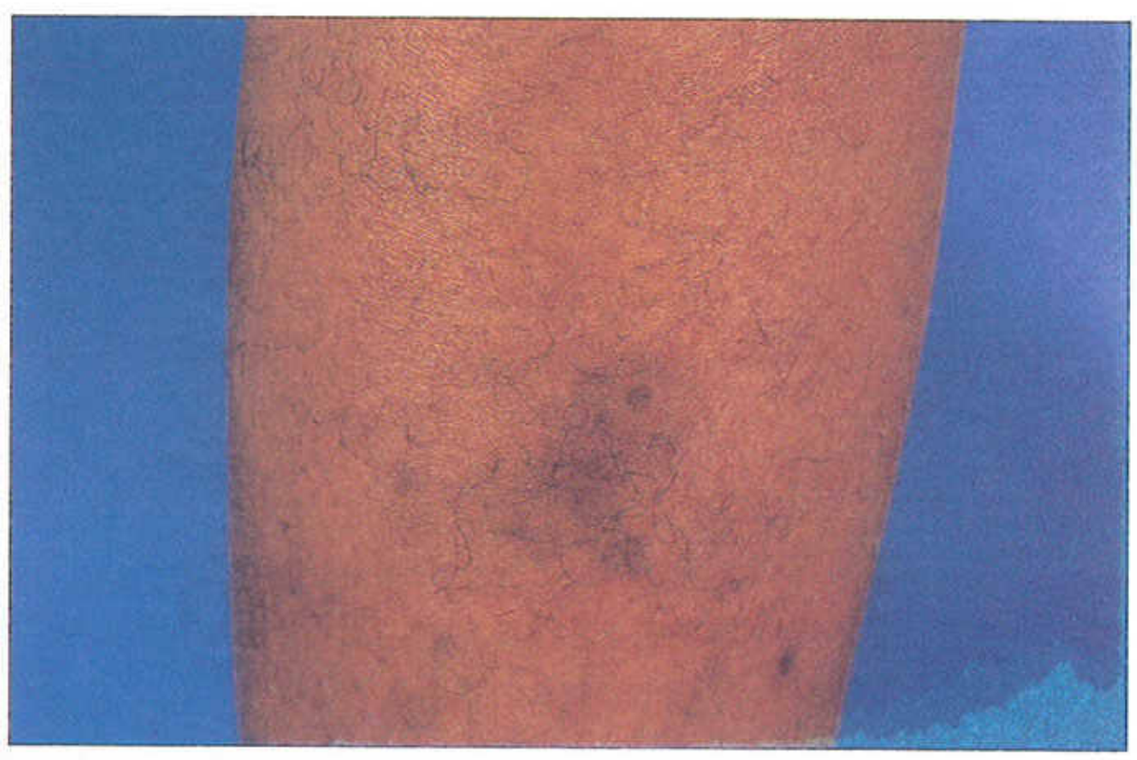

Fig 4: Kaposi's Sarcoma after treatment

Vascular slits were present, interspersed with a proliferation of spindle cells. A diffuse cellular infiltration, which was composed of lymphocytes, plasma cells and histiocytes were present. A modest amount of hemosiderin pigments and extravasation of erythrocytes were seen.

A clinical diagnosis of KS was confirmed by histopathological picture. There was no visceral involvement by upper and lower gastrointestinal tract endoscopies and CT scan of the abdomen and chest. Laboratory findings included complete blood counts, hemoglobin, electrolytes, liver and kidney functions were all within normal limits. The serology for human immunodeficiency virus (HIV), cytomegalovirus (CMV) and herpes simplex virus (HSV) were negative. CD4/CD8 ratio was slightly low 1.1 (normal 1.8 ± 0.6), CD4 (45.5%) was within normal limits (31-55%) and CD8 (40.4%) was elevated (normal 17-38%).

Patient received recombinant alpha 2a interferon (Hoffman La Roche). The drug was administrated in an subcutaneous injections of 6 million units three times weekly for three months (36 injections). There was no side effect except mild pain at the site of injection, fatigue, joint and muscle aches in the first week. These side effects were mild and disppear with subsequent injections. For monitoring the therapy, there were no significant changes in the laboratory findings as complete blood counts, electrolytes, liver and kidney functions and CD4, CD8 and CD4/CD8 ratio (all were within normal limits).

The lesions of Kaposi's sarcoma regressed gradually and disappeared completely leaving brownish pigmented skin (Fig 3,4) at the end of the treatment. Now, after more than 20 months, the patient re-

mained with a well functioning graft and there is no recurrence of the KS inspite of the patient is still on the same immunosuppressive therapy cyclosporin A, azathioprine and prednisolone.

Discussion

Kaposi's sarcoma is a rare malignant tumor. Since the 1960s an increasing frequency of KS has been recognized in patients who are receiving immunosuppressive treatment and since 1979 the epidemic form has emerged in patient with the acquired immunodeficiency syndrome[1]. The potential risk of malignant tumors as KS to the graft recipient may be due to one of the three major mechanisms: (1) chronic antigenic stimulation by the graft tissue, (2) loss of surveillance mechanisms against proliferating malignant cells resulting form the depression of immune responsiveness by immunosuppressive agents and (3) virus induced oncogenesis[8].

For multiple KS lesions radiotherapy, chemotehrapy and immunotherapy have been used with varying degree of success and side effects[5]. Because, of the antiviral, immuno-modulatory and anti-proliferative properties of interferon, the commencement trials with this drug in KS have started[10]. Now, interferon alpha 2a is an effective treatment for a subset of patients with KS[8,9,11]. High doses (>20 million units per day) of interferon are partially efficacious in acquired immunodeficiency syndrome (AIDS) related Kaposi's sarcoma, whereas low doses are not[12]. However, low doses (3 million units per day, 5 days a week) recombinant alpha interferon are used successfully for classic KS[13].

It is well known that reduction or stop in the immunosuppressive therapy may be sufficient for disappearance of KS in kidney transplant recipients (KTR). But, because as there were episodes of graft rejection, we carefully managed our patient in order to maintain the function of the grafted kidney. Up to our knowledge, there are no published trials to use interferon alpha in KS after kidney transplantation. However, for our patient we used low dose recombinant interferon alpha 2a successfully. There was a complete disappearance of the KS lesions.

There were no significant changes in the laboratory findings of the patient during the treatment, such as complete blood count, kidney and liver functions tests CD4, CD8 and CD4/CD8 ratio. As the interferon dose was low, the adverse effects were mild in the initial period and disappeared with the subsequent injections.

There is no recurrent of KS after 20 months, with normal graft function, inspite of the patient still on the same immunosuppressive therapy. Our result has demonstrated a positive antitumoral effect of the interferon alpha 2a in KS supporting the results of other investigations[6,9,11,13].

In summary, low-dose interferon alpha 2a treatment for KS in KTR is effective, well tolerated and easily done on an outpatient basis. So, it has a place in the treatment of these patients specially if there are multiple lesions and when there are episodes of graft rejection.

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