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CASE REPORT

A Novel Immunosuppressive Agent, Sirolimus, in the Treatment of Kaposi's Sarcoma in a Renal Transplant Recipient

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Renal transplant recipients are susceptible to Kaposi's sarcoma (KS) because of treatment with immunosuppressive drugs. Sirolimus, a new immunosuppressive agent, has been successfully used for immune-suppression in kidney transplant recipients. Several studies have shown the potential role of sirolimus to inhibit progression of KS in kidney-transplant recipients. This report details a kidney-transplant recipient with cutaneous KS who had a complete remission in response to sirolimus therapy.

Keywords transplant, complications, immunosupression, malignancy, treatment

INTRODUCTION

Kaposi's Sarcoma (KS) is a rare (0.02–0.07%) neoplasm among the general population; however, the incidence in immunosuppressed renal transplant recipients is as high as 400- to 500-fold.[1,2] KS accounts for 3–4% of the malignancies associated with immunosuppression for renal transplantation in the United States,[3] and the ratio varies from 1.5–3% in Turkish renal transplant recipients.[4–6] KS patients benefit from the reduction or cessation of immunosuppressive therapy, which may evoke a high risk of graft rejection. Approximately 50% of cutaneous KS patients respond to the withdrawal of immunosuppressive therapy.[7] Conventional chemotherapy has a minor role in the treatment, even in the case of visceral organ involvement.

Sirolimus, a new immunosuppressive agent, has been successfully used for immunosuppression in renal transplantation. Several studies have shown a potential role of sirolimus to inhibit progression of KS in kidney-transplant recipients.[8,9] This study reports on a kidney-transplant recipient with cutaneous KS who had a complete remission in response to sirolimus therapy.

CASE

A 29-year-old female patient with a primary disease of focal segmental glomerulosclerosis underwent renal transplantation in 2003. She was on triple immune-suppressive treatment consisting of prednisolone, cyclosporine, and

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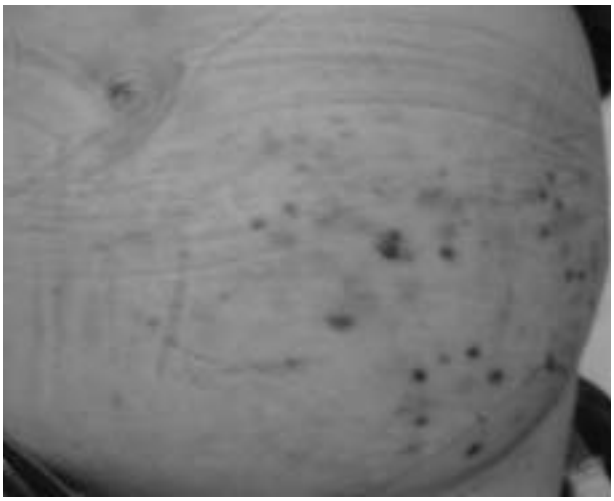

Figure 1. Multiple purple nodules on the overlying skin of the left lower quadrant where graft located.

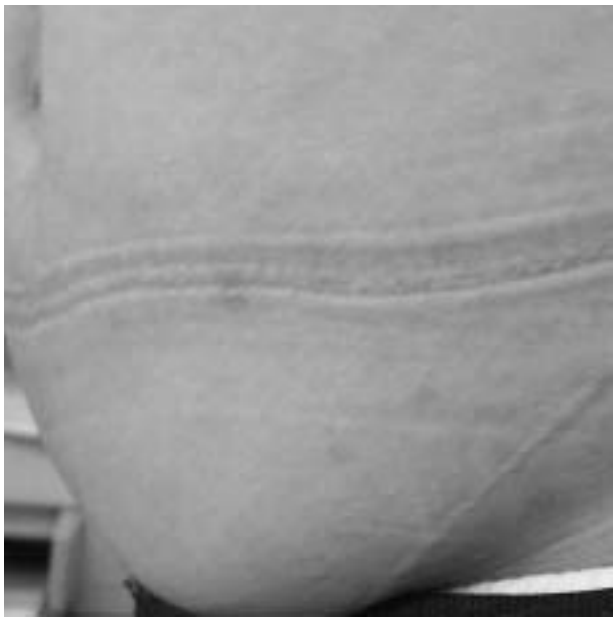

Figure 2. The lesions resolved completely after five months of sirolimus therapy.

mycophenolate mofetil. Twenty months after transplantation, itchy, purple nodules appeared on the overlying skin of her left lower quadrant where graft located (see Figure 1). The patient underwent a skin biopsy and had a diagnosis of Kaposi's sarcoma. No visceral involvement was detected. Serum creatinine was in the normal ranges at the time of diagnosis. Because the kidney transplant recipient had biopsy-proven Kaposi's sarcoma, cyclosporine was switched to sirolimus and the dosage was subsequently adjusted in accordance with serum levels. The patient did not have any other alternative treatment modalities. Within a month, the lesions started to become pale, and they resolved completely after five months of sirolimus therapy (see Figure 2). There was no acute rejection or change in kidney-graft function while the patient showed complete regression of Kaposi's sarcoma.

DISCUSSION

The incidence of KS has been increasingly reported in renal transplant patients. The average interval between renal transplantation and the onset of KS is approximately 20 months. KS in kidney-transplant recipients may be limited to one cutaneous site or more, disseminated to multiple cutaneous regions, or involves viscera. Mucocutaneous KS has a better prognosis than visceral disease.

Cutaneous KS responds to the withdrawal of immunosuppressive therapy, which may contribute to the disappearance of the KS lesions. Surgical excision, radiotherapy, cryosurgery, intralesional, and systemic chemotherapy are alternative treatment modalities for cutaneous neoplasm. Persistent disseminated cutaneous disease or visceral KS requires systemic therapy.

Sirolimus, a mammalian target of rapamycin inhibitor (mTOR), is a natural antibiotic produced by *S. hygroscopics*. It was approved by the Food and Drug Administration (FDA) as an immunosuppressive agent used in renal transplantation in 1999 and it is currently used alone or in combination with cyclosporine to prevent renal graft rejection. The drug is a potent inhibitor of T cell activation and can also inhibit proliferative responses induced by cytokines, including interleukin 1, 2, 3, 4, and 6; insulin-like growth factor (IGF); platelet-derived growth factor (PDGF); and colony-stimulating factors (CSFs).[10] The agent is currently undergoing clinical investigations for anti-tumor therapy. Antineoplastic effects of sirolimus appear to be mediated by several different mechanisms. Sirolimus blocks the cell cycle progression from G1 to S phase due to mTOR inhibition.[11,12] Thus, the growth of cell arrests in the G1 phase of the cell cycle.[13] The inhibition of tumor angiogenesis through the downregulation of vascular endothelial growth factor (VEGF),[11,14] the induction of apoptosis, and the inhibition of IL-10 production[12] are the other antitumor effects of sirolimus.

In one study, authors suggest that sirolimus inhibits the progression of KS in two kidney-transplant recipients preserving the renal graft functions.[11]. Similarly, Stallone et al. used sirolimus to treat fifteen renal transplant patients who had diagnosed cutaneous KS.[8] Three

months after the initiation of sirolimus, cutaneous lesions of KS regressed. The results were confirmed by skin biopsies. They provided effective immunosuppression and regression of the cutaneous lesions in all 15 recipients.

In the present case, the patient had a diagnosis of KS twenty months after renal transplantation. Immunosuppressive treatment had consisted of prednisone, cyclosporine, and mycophenolate mofetil at the time of diagnosis. Immediately, cyclosporine was switched to sirolimus in combination with prednisone and mycophenolate mofetil. The patient did not have any other treatment modalities. The cutaneous lesions of KS regressed within five months after the therapy without any change in kidney-graft function.

In conclusion, sirolimus may be an efficient therapy for Kaposi's sarcoma in kidney transplant recipients while preserving renal graft functions.

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