Kidney Transplantation

Kaposi Sarcoma in Kidney Transplanted Patients

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ABSTRACT

Purpose: Newly developed malignancies in kidney transplanted patients are one of the complications attributed to immunosuppression. Kaposi sarcoma is an unusual malignancy in general population, but may develop in kidney transplanted patients with highly varying prevalence. Our aim is to evaluate the prevalence, clinical manifestations, and outcome of Kaposi sarcoma in kidney transplanted patients.

Materials and Method: Five hundred and eighty cases (330 male, 250 female) with a mean age of 39.2 were followed for 36 months (range 9 months to 10 years), visiting every two months. History taking and physical examination with emphasis on skin and mucousa were taken. Biopsy of suspicious skin, mucosal, and visceral lesions assigned by other paraclinical methods was performed. Except 7 cases which were HLA identical to donors, all patients were managed with ciclosporine, Azathioprine and Prednisolone.

Results: Fourteen patients (2.3%) developed Kaposi sarcoma (biopsy documented) which constituted 60% of all post-transplantation malignancies. They were 11 males and 3 females with a mean age of 41 years. Sarcoma developed 8 to 31 months after transplantation with an average age of 18 months. Of these patients, 3 had skin involvement that one of them had pulmonary involvement too. Another patient had only abdominal involvement. Azathioprine was discontinued in all patients, and ciclosporine was reduced in skin affected patients. In patients with visceral involvement ciclosporine was discontinued and then chemotherapy was initiated. All 3 patients with visceral involvement didn’t respond to chemotherapy and expired after 6 months. Of 11 patients with skin involvement, one had completed and 2 had incomplete remission of whom, one expired due to acute rejection. Renal function in 8 patients was acceptable, but 2 had impaired renal function, yet didn’t need dialysis.

Conclusion: Prevalence of Kaposi sarcoma in our patients is more than western countries. Visceral involvement is uncommon, but has poor prognosis. Reducing immunosuppression with discontinuation of Azathioprine and significant reducing ciclosporine dosage can cease skin evolvement, with preserving renal function in most of the patients.

KEY WORDS: Kaposi sarcoma, malignancy, kidney transplantation

Introduction

New onset malignancies as the subsequent complication of immunosuppressive therapy in kidney transplant recipients are now well known and the overall incidence of malignancies is 100 folds more than general population. A series of mechanisms play a role in increasing the risk, each have its own importance in different types of cancers. These include compromised immune system, direct carcinogenic effects of drugs, carcinogenic effects of drugs, carcinogenic effects of drugs, carcinogenic effects of drugs.
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Kaposi sarcoma in kidney transplanted patients

Algeric virus, chronic antigen stimulation, uremia, genetic susceptibility, recipient-donor interactions, and environmental factors. Some studies show a 2.8% incidence of non-cuteous tumors in kidney recipients, made the researchers believe in a low risk of post-transplant malignancies. The sampling method of transplant patients underestimates the risk, because in such samples there are always a considerable number of recently transplanted patients. Latest reports indicate that 30-50% incidence 28 years after transplantation. Common cancers in general population (pulmonary, breast, prostate,...) don't have any increase in transplant patients. Following non-melanoma skin malignancies and cervix carcinoma in situ, which are the most common ones, a series of cancers uncommon in general population are more prevalent in this group of patients consisting of psoriasis (22% vs. 6%), lip malignancy (6.2% vs. 0.3%), Kaposi sarcoma (5.6% vs. non-significant incidence), renal stenosis (0.5% vs. 2.4%), etc. Kaposi sarcoma has a 400 to 500 times more risk of developing in transplant recipients than in general population. However, it is an uncommon cancer which constitutes a varying proportion of new onset malignancies after transplantation. Kidney recipients of African, Arabian, Italian, Jewish, Greek, and Turkish ethnicity are more susceptible to Kaposi sarcoma, as an association exists between its incidence and the ratio of Mediterranean people living in a community. Kaposi sarcoma develops in 0.25% of organ recipients in western countries, that is 2-3% of the whole malignancies in this group of patients. Whereas, 5% of the recipients will have Kaposi sarcoma in Saudi Arabia, which constitutes 40-50% of the tumors. On the other hand, it is rare in Japan. Male to female ratio of the disease is 3:1. Interactions of the risk factors such as Herpes Simplex virus and compromised immune system is apparent. Complete improvement is seen in some cases by discontinuing immunosuppressants. Kaposi sarcoma is defined as tumors with endothelium covered vascular areas, spindle shaped cells, extrusion of red blood cells, and groups of inflammatory cells. Sixty percent of patients suffer from skin or oropharyngeal mucous involvement presents as lesions such as purple macules with defined margins or refractory granuloma. The rest of patients have visceral involvement, particularly of gastrointestinal and respiratory systems and lymph nodes. Although visceral involvement may cause resistance to treatment, complete or relative remission can be achieved by decreasing or ceasing immunosuppressive drugs in 40% of patients with non-visceral lesions. In addition, drug discontinuation causes graft rejection. The aim of this study was to depict the incidence, clinical manifestations, and outcome of Kaposi sarcoma in kidney transplant recipients at Golistan hospital, Ahvaz.

Materials and Methods

A total of 580 patients who had undergone kidney transplantation at Golistan hospital were followed for a mean duration of 36 months (range 9 months to 10 years). Three hundred and twenty of whom were males and 250 were females. Mean age of the patients was 38.2 (range 6 to 68) years. Outpatient visits were performed every two months and physical examination with special focus on skin and mucosa were done. Paraneclinically taken specimens of identified lesions would be sent to pathology. All except 7 patients with complete HLA matching had been under triple drug treatment of Cyclosporine (4.5 mg/kg/day), Azithroline (2.5 mg/kg/day), and Prednisolone (10-12.5 mg/kg/day). Complete HLA matched patients would have undergone the treatment with Azathioprine and Prednisolone only.

Results

An overall of 14 patients (2.2%) had biopsy confirmed Kaposi sarcoma, 11 men and 3 women (male to female ratio of 4:1). Mean age of them was 11 (range 27 to 59 years) and the mean interval between transplantation and diagnosis was 18 (range 8 to 31) months. All the cases had received triple immunosupressant therapy and none of them were HLA identical (p=0.003). Two patients had developed acute rejection and subsequently treated with Methyl Prednisolone pulse therapy (3 g) of whom one had not responded and underwent ATG (Anti-thymocyte Globulin) therapy. Skin involvement was observed in 13 cases of Kaposi sarcoma of which one had simultaneous widespread bilateral pulmonary involvement and one had simultaneous gastric and intestinal involvement. None of the patients had oral, pharyngeal, or laryngeal lesion of mucosa. Gastrointestinal involvement was presented most-
Discussion

Kaposi sarcoma has a higher prevalence in our country than the western countries, in which Kaposi sarcoma affects 0.25% of kidney recipients and comprises 2 to 3% of post-transplant malignancies.\(^{10}\) In this study, Kaposi sarcoma was observed in 2.2% of the patients and comprised approximately 60% of all post-transplant malignancies (3.4%). The most prevalent malignancies of kidney recipients in western countries are skin tumors and lymphoma, respectively, and Kaposi sarcoma takes the third place (12%) whereas, it is the most common one according to our study, followed by skin tumors and lymphoma. Thus, the prevalence of Kaposi sarcoma in our country seems to be similar to the one in Mediterranean and Arabian countries.\(^{10,15}\) So that, environmental and genetic factors should be taken into account. Solar radiation, ultraviolet radiation, some viral infections, and a series of drugs are the examples of environmental factors.\(^{11}\)

Kaposi sarcoma had a male to female ratio of 4:1, almost the same as the results in other studies.\(^{14}\) Skin and visceral involvement was observed in 78% and 22% of the cases, respectively, compared to 58-60% and 40-42% in other studies.\(^{15}\) The difference may be due to our small sample.

The mean interval between transplantation and developing of malignancies is 61 months and it is 21 months for Kaposi sarcoma which is the earlier.\(^{20}\) This interval was 18 months in our patients.

Skin lesions were recovered in 9 out of 11 patients and relatively improved in 1. Renal graft function was normal in 8 live patients and moderately impaired in 2. It can be concluded that lowering immunosuppression by Azathioprine cessation and aggressive reduction of cyclosporine dose is effective in the improvement of Kaposi sarcoma and renal function will remain normal.\(^{13}\) All the three patients with visceral involvement died in 6 months; although other studies have shown improvement is 29% of such cases, 57% of whom improved merely by dose alteration of immunosuppressants.\(^{13}\) Our study showed a poor prognosis for this uncommon complication.

Conclusion

Prevalence of Kaposi sarcoma in our patients is more than western countries. Visceral involvements are uncommon but have poor prognosis. Reducing immunosuppression with discontinuation of Azathioprine and significant reducing cyclosporine dosage can cease skin involvement, with preserving renal function in most of the patients. It is recommended that Kaposi sarcoma should be considered if refractory infectious granuloma, blue to red macule or plaques in the skin, or oropharyngeal mucosa is observed and subject to confirmed diagnosis, visceral involvement is necessary to be fully evaluated.

References

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