Saudi J Kidney Dis Transpl 2009;20(5):775-778

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Kaposi's Sarcoma after Renal Transplantation

Shahin Abbaszadeh[1,2], Saeed Taheri[1]

[1]Dr. Taheri Medical Research Group, [2]Baqiyatallah University of Medical Sciences, Tehran, Iran

ABSTRACT. In this study, we aimed to evaluate the incidence, features and outcome of post transplant KS among Iranian recipients of living kidney allograft. We studied 2211 kidney allograft recipients who underwent living renal transplantation at our center between January 1984 and August 2007. All patients in our study received cyclosporine based immunosuppressive agents. The diagnosis of KS was confirmed with pathological evaluations of tissue biopsy specimens. There were 10 of 2211 (0.45%) incident cases of KS kidney transplant population at our center during a mean follow up of 57 ± 38 months. Of the 10 KS patients, 8 were males and two were females with a median age of 52 years. The median time from transplantation to the development of KS was 8 months. Overall, two (20%) patients developed visceral involvement (one eye, one bladder), and eight patients manifested only KS restricted to the skin. Immunosuppression was reduced in 5 patients and thoroughly withdrawn in the remainder (including two cases of visceral involvement); KS did not abate in the patient with bladder involvement. All the KS patients remained alive after a mean of 35.6 ± 39.3 months of follow up; two patients lost their allograft and underwent dialysis (one after 3 months and one another after 4 months of KS diagnosis). The KS patients were significantly older at their transplantation time (*P*= 0.008; table 1). Survival analysis using Kaplan Meier method and log-rank test revealed no difference in graft and patient survival between both groups. In conclusion, we found low incidence of KS in our living renal transplant recipients. The outcome of the KS patients was excellent with low morbidity and mortality. The incidence of KS was significantly associated with an older age at transplantation time for the allograft recipients. Further studies with larger patient population are warranted to confirm our results.

Correspondence to:

Dr. Saeed Taheri
Dr. Taheri Medical Research Group;
Baqiyatallah Research Center for
Gastroenterology and Liver Disease
Baqiyatallah Hospital, Mullasadra St,
P.O. Box 14155-6437, Postal Code 1435915371
Tehran, Iran
E-mail: taherimd@gmail.com

Introduction

Kaposi's sarcoma (KS) is a soft tissue cancer that is related to several intrinsic and environmental factors.[1] In the general population, KS is an extremely rare tumor; however, the risk of its development is substantially increased in immunecompromised patients including patients with acquired immune deficiency syndrome (AIDS) and solid organ recipients.[1,2] Genetic

predisposition,[3,4] seropositivity for human herpes virus type 8 (HHV-8),[5,6] and increased HHV-8 prevalence in the general population[1,7] are some proposed factors for the development of KS.

Middle East is reported as a highly prevalent region for the incidence of post transplant KS;[1] reports from Saudi Arabia,[8] Egypt[9] and Turkey[10] indicate a high incidence of this disease.

In this study, we aimed to evaluate the incidence, features and outcome of post transplant KS among Iranian recipients of living kidney allograft.

Methods and Materials

We studied 2211 kidney allograft recipients who underwent living renal transplantation at our center between January 1984 and August 2007. Almost all the transplanted patients were under observation monthly at our outpatient clinic within the first year after transplantation and at least every 2-3 months thereafter.

We usually suspect KS when a kidney recipient presents with multiple hyperpigmented cutaneous nodules that may be associated with gastrointestinal discomfort and pulmonary symptoms resistant to conventional therapies. Then a battery of endoscopic, broncoscopic, radiologic, and pathologic tests are used to diagnose KS.

All patients in our study received cyclosporine based immunosuppressive agents. There were two main distinct periods of immunosuppressive regimen: the first period was from 1984-2001 azathioprine (1.5 mg/kg), cyclosporine (6 mg/kg) and prednisolone (50 mg/d), and the second period was from 2001 onwards during which the patients received triple immunosuppressive therapy consisting of Cellcept (2 gr/day), cyclosporine, and prednisolone at the same dosages mentioned above. Induction therapy using antithymocyte globulin (ATG) or antilymphocyte globulin (ALG) was preserved to the high risk patients in the early phase of transplantation or for treatment of acute rejection; OKT-3 was not used in any of the studied populations.

The doses of the immunosuppressive agents were reduced, or the agents were withdrawn upon diagnosis of KS. The method of reduction of immunosuppression and decision on which the agent to be reduced or withdrawn were dependent on the individual patient's health condition, response to treatment, and his/her physician's judgment.

Statistical Analysis

Software SPSS v.13.0 was used for data analyses. Statistical differences between patients' groups were performed by using $\chi 2$ and Fishers' exact tests for proportions and the non-parametric Mann-Whitney U test for continuous data. Survival analysis was performed using Kaplan-Meier method and log rank test. All statistical tests were considered significant at the level of $P< 0.05$.

Results

The diagnosis of KS was confirmed with pathological evaluations of tissue biopsy specimens. There were 10 of 2211 (0.45%) incident cases of KS kidney transplant population at our center during a mean follow up of 57 ± 38 months.

Of the 10 KS patients, 8 were males and two were females with a median age of 52 years. The median time from transplantation to the development of KS was 8 months. Overall, two (20%) patients developed visceral involvement (one eye, one bladder), and eight patients manifested only KS restricted to the skin.

Immunosuppression was reduced in 5 patients and thoroughly withdrawn in the remainder (including two cases of visceral involvement); KS did not abate in the patient with bladder involvement. All the KS patients remained alive after a mean of 35.6 ± 39.3 months of follow up; two patients lost their allograft and underwent dialysis (one after 3 months and one another after 4 months of KS diagnosis).

Table 1 shows the characteristics of the study patients with and without KS. The KS patients matched with the non-KS patients in their gender, donor gender, age of donor, immunosuppression type, and receiving induction therapy; however, the KS patients were significantly older

Table 1. The characteristics of the study patients

Variables	KS group (n=10)	Non-KS group (n=2201)	*P* value
Age of recipients	53 ± 13	40 ± 13	0.008
Age of donor	28 ± 6	28 ± 5	0.713
Gender of recipients (male)	80%	68%	0.516
Gender of donors	90%	86%	0.932
Immunosuppression; MMF based (vs. AZA based)	70%	61%	0.749
Induction (ALG, ATG)	20%	10%	0.587

MMF: Mycophenolate Mofetil, AZA: Azathioprine, ALG: Antilymphocyte Globulin, ATG: Antithymocyte Globulin, KS: Kaposi's Sarcoma

at their transplantation time (*P*= 0.008; table 1). Survival analysis using Kaplan Meier method and log-rank test revealed no difference in graft and patient survival between both groups.

Discussion

The results of this study showed lower incidence of KS (0.45%) in our transplant population than that reported from other regional countries.[1,8-10]

The KS incidence peaks during the first year post transplantation. In our study, 70% of all KS cases were diagnosed in the first 2 years after receiving a renal allograft, which is compatible with previous studies.[11-14] Several factors have been proposed as explanations for the higher incidence of KS in the early periods post transplantation such as a higher prevalence of HHV-8 seroprevalence among the general population. A South African study demonstrated that the prevalence of anti-HHV-8 antibodies in white individuals is substantially lower than that in non-white general population,[15] with a considerably higher incidence of KS in the non-white than the white patients. Unfortunately we have no data on the prevalence of HHV-8 infection among our transplant population or the general population, which calls for more studies in our population.

The potency of immunosuppression is a highly relevant factor in the development of KS after transplantation.[16] Patients receiving more intense immunosuppressive protocols are at a significantly high risk of developing post transplantation KS.[16] Iranian renal transplant recipients reveal serum levels of cyclosporine substantially lower than recommended (unpublished observations), which may explain the low incidence of KS in our population.

In our study, we found that patients who developed post transplant KS were significantly older at the time of transplantation. This finding contrasts previous reports about high incidence of KS among younger organ recipients.[17] Moreover, most previous studies have reported a male preponderance in the incidence of post transplant KS.[18-20] In our study, although males constituted 80% of the KS population, the gender compareson with the non-KS patients showed no significant difference. This suggests that observations indicating a male predominance in the development of post transplant KS might be related to an overall high proportion of males in the transplant population.

Only 20% of our patients manifested a visceral involvement and just one of them did not experience a complete remission. None of our patients died, while two lost their allograft. However, the graft and patients' survival were equivalent in KS and non KS patients. This finding can corroborate arguments suggesting KS as a benign hyperplasia rather than a malignancy.[21]

The treatment strategy for our patients was to taper the immunosuppressive drugs. In five cases, we discontinued the immunosuppressive agents in order to achieve remission. One case with a bladder involvement did not respond to treatment, although he remained alive with a functioning graft for 18 months of follow-up.

The limitations of our study include its retrospective nature and the use of registry data, which may be incomplete.

In conclusion, we found low incidence of KS

in our living renal transplant recipients. The outcome of the KS patients was excellent with low morbidity and mortality. The incidence of KS was significantly associated with an older age at transplantation time for the allograft recipients. Further studies with larger patient population are warranted to confirm our results.

References

1. Einollahi B. Kaposi sarcoma after kidney transplantation. Iran J Kidney Dis 2007;1(1):2-11.
2. Winters Z, Mannell A. Kaposi's sarcoma of the oral cavity. A case report. S Afr Med J 1985; 68(5):330-1.
3. Harwood AR, Osaba D, Hofstader X, et al. Kaposi's sarcoma in recipients of renal transplants. Am J Med 1979;67:759-65.
4. Brunson ME, Balakrishnan K, Penn I. HLA and Kaposi's sarcoma in solid organ transplantation. Hum Immunol 1990;29:56.
5. Cattani P, Capuano M, Graffeo R, et al. Kaposi's sarcoma associated with previous human herpes virus 8 infection in kidney transplant recipients. J Clin Microbiol 2001;39:506-8.
6. Moore PS. The emergence of Kaposi's sarcoma-associated herpes virus (human herpes virus 8). N Engl J Med 2000;343:1411-3.
7. Francès C. Kaposi's sarcoma after renal transplantation. Nephrol Dial Transplant 1998;13 (11):2768-73.
8. Qunibi W, Akhtar M, Sheth K, et al. Kaposi's sarcoma: the most common tumor after renal transplantation in Saudi Arabia. Am J Med 1988;84(2):225-32.
9. El-Agroudy AE, El-Baz MA, Ismail AM, Ali-El-Dein B, Ghoneim MA. Clinical features and course of Kaposi's sarcoma in Egyptian kidney transplant recipients. Am J Transplant 2003;3 (12):1595-9.
10. Duman S, Töz H, Aşçi G, et al. Successful treatment of posttransplant Kaposi's sarcoma by reduction of immunosuppression. Nephrol Dial Transplant 2002;17(5):892-6.
11. Bouwes-Bavinck JN, Hardie DR, Green A, et al. The risk of skin cancer in renal transplant recipients in Queensland, Australia: a follow-up study. Transplantation 1996;61:715-21.
12. Mbulaiteye SM, Engels EA. Kaposi's sarcoma risk among transplant recipients in the United States (1993-2003). Int J Cancer 2006;119(11): 2685-91.
13. Serraino D, Piselli P, Angeletti C, et al. Risk of Kaposi's sarcoma and of other cancers in Italian renal transplant patients. Br J Cancer 2005;92: 572-5.
14. Serraino D, Angeletti C, Carrieri MP, et al. Kaposi's sarcoma in transplant and HIV-infected patients: an epidemiologic study in Italy and France. Transplantation 2005;80:1699-704.
15. Moosa MR. Kaposi's sarcoma in kidney transplant recipients: a 23-year experience. Q J Med 2005;98(3):205-14.
16. Penn I. The changing pattern of post transplant malignancies. Transplant Proc 1991;23(1 Pt 2): 1101-3.
17. Penn I. Kaposi's sarcoma in organ transplant recipients: report of 20 cases. Transplantation 1979;27(1):8-11.
18. Moosa MR, Walele AA, Daar AS. Renal transplantation in developing countries. In: Kidney Transplantation: Principles and Practice, 5th edn. Philadelphia, WB Saunders, 2001:659-92.
19. Shepherd FA, Maher E, Cardella C, et al. Treatment of Kaposi's sarcoma after solid organ transplantation. J Clin Oncol 1997;15(6):2371-7.
20. Webb MC, Compton F, Andrews PA, Koffman CG. Skin tumors post transplantation: a retrospective analysis of 28 years' experience at a single centre. Transplant Proc 1997;29(1-2): 828-30.
21. Schwartz RA. Kaposi's sarcoma. Ann Transplant 1998;3(1):5-12.