Treatment of an Early Kaposi's Sarcoma Case Post Kidney Transplantation by Sirolimus: A Case Report

Farzaneh Najafi[1], Parichehr Kafaie[2], and Hossein Neamatzadeh[3]

[1] *Department of Internal Medicine, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

[2] *Department of Dermatology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

[3] *Mother and Newborn Health Research Center, Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

Received: 17 Nov. 2015; Accepted: 16 Feb. 2016

Abstract- Kaposi′s sarcoma (KS) can develop in 0.06% to 4.1% of kidney transplant recipients. Here we describe a case of 50-year-old man who developed KS a few months after kidney transplantation**.** After transplantation, he had delayed graft function and was managed by anti-thymocyte globulin (ATG) for five days. At the discharge, his immunosuppressive therapy was prednisolone 20 mg/day, tTacrolimus (Pprograf®) 4 mg/day, and mycophenolate mofetil (MMF) 2 gr/day, while he also took Vvalcyte and diltiazem. Once diagnosed with KS, the Prograf® (tacrolimus) was replaced by prednisolone (5 mg/day) and sirolimus (2 mg/day). Gradually the skin nodule on the patient arm disappeared, and the others nodule on the right his leg was decreased. It seems that the examination of skin should be a part of regular follow-up and dermatologist examination is recommended every 6 months.

Acta Med Iran 2017;55(2):139-141.

Keywords: Kaposi's sarcoma; End stage renal disease; Kidney; Transplantation

Introduction

Long-term immunosuppression in kidney transplant recipient increases the risk of malignancy approximately 100 times as high as in the general population (1). Kaposi′s sarcoma (KS) is one of these tumors with 500 fold more frequently in renal transplant recipients than the general population (2,3). The first case of post-kidney transplantation KS was reported in 1969, and since then a number of reports have confirmed the high incidence of this among kidney transplant recipients (4). Kaposi′s sarcoma can develop in 0.06% to 4.1% of kidney transplant recipients and was 3% to 70% of all post-transplantation tumors (2). The differences in incidence are mainly dependent on geographic and ethnic variation, the immunosuppressive regimen, genetic predisposition, environmental factors and exposure to carcinogenic agents (4). Renal allograft recipients with Jewish, Mediterranean, Black or Arabic ancestry have been reported to be at increased risk of developing KS (2,4).

An increased risk of post-transplant KS may be related to HHV-8 infection, and pre-transplantation HHV-8 seropositivity is a risk factor (5,6). KS has been reported to occur from a few months to 18 years post-transplant (4). The mean interval that reported in international series was about 12.2 months (2). The ratio of male to female in post-transplant KS is 3.3:1 to 1:1 and the mean age at the time of diagnosis are 43 years, which is younger than among patients with classic KS (4,5).

Case Report

Here we describe a case of 50-year-old man who developed KS a few months after kidney transplantation. The cause of end-stage renal disease (ESRD) in the patient was primary crescentic glomerulonephritis and was managed with hemodialysis for two years before transplantation. He gets kidney transplant from non-related living donor. After transplantation, he had delayed graft function and was managed by anti-thymocyte globulin (ATG) for five days. At the discharge, his immunosuppressive therapy was prednisolone 20 mg/day, tacrolimus (Prograf®) 4 mg/day, and mycophenolate mofetil (MMF) 2 gr/day, while he also took Valcyte and diltiazem. His serum creatinine at discharge was 1.2 mg/day. After then he

Corresponding Author: F. Najafi
Department of Internal Medicine, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
Tel: +989133512673, Fax: +983536241146, E-mail address: dr.f_najafi@yahoo.com

was visited regularly and according to lab tests, his immunosuppressive regimen especially prednisolone gradually tapered, and blood level of tacrolimus was hold between 9.3-10.6 ng/ml. Eight months after kidney transplantation he consulted his nephrologists about nodules on his skin. On examination, he had three purple-red-brown nodules on the right leg (front) and one nodule on the left leg and one nodule on the left arm. He explained that about 3 months ago: First, (almost 5 months after kidney transplantation) this nodule appeared on right leg, and after 2 months on the left leg and later after about 20 days again one nodule appeared on upper left arm, respectively. As soon as, he was referred to the dermatologist (second author) and skin biopsy was determined that he had Kaposi′s syndrome. Again he was referred to hematologist and was considered for visceral KS, for example, chest X-ray and abdominal and pelvic computed tomography scanning and fortunately, was showed that he had only cutaneous KS.

During this time, the immunosuppressive therapy was reduced, and MMF prescribed 1 gr/day and Prograf® 3 mg/day respectively. Parallel that; we evaluated him for some viruses and lab testes .The patient and his donor weren't screened for HHV-8 before transplantation, and therefore, he was firstly screened for HHV-8 after transplantation, and it was negative, but his donor didn't cooperate to do screen test. The pre-transplant serology showed negative tests for hepatitis B surface antigen, anti-HCV, and HIV. High plasma levels of specific immunoglobulin G were found indicating previous infections by cytomegalovirus, herpes simplex, varicella-zoster, and Epstein-Barr (EBV). This serology remained intact after transplantation.

Therefore, he had transplant-related (acquired) KS and as soon as, we withdrew the Prograf® and MMF but continued prednisolone 5 mg/day and started sirolimus 2mg/day. When sirolimus was started, the patient serum creatinine was 1/3 mg/dl, and urine protein was 400 mg/day. Gradually the skin nodule on his arm disappeared, and the others nodule on right leg was decreased and had considered recovery (Figures 1,2,3).

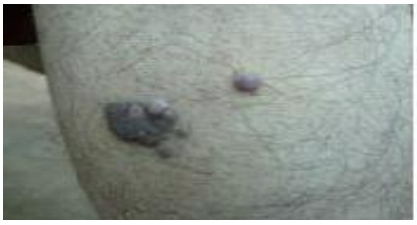

Figure 1. At first: purple blue nodules

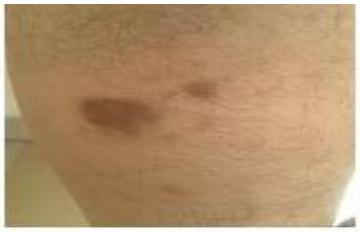

Figure 2. Six months later: purple brown plaques

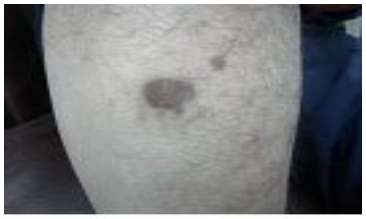

Figure 3. One year later: brown macula

The immunosuppressive regimen conversion to sirolimus nearly conserved the allograft function and until serum creatinine is 1.3 mg/dl but the urine protein increased (Table 1).

Table 1. The patient serum creatinine and 24 h urine protein variations

	At first	6 months later	1 year later
Serum creatinine	1.3 mg/dl	1.2 mg/dl	1.3 mg/dl
24h urine protein	400 mg	900 mg	2400 mg

Discussion

Kaposi´s sarcoma is one of the most common malignancies occur in kidney transplant recipient, especially in developing countries. Its prevalence in Iran is relatively high, more than 35% and in Egypt was diagnosed in 46.2% (2,4). There are 4 different subtypes of KS including (4,7).:

a. Classic KS variant that affects elderly means (ages of 50 and 70) of the Eastern European and Mediterranean origin.
b. The endemic or African form that develops in young people living in equatorial Africa.
c. Epidemic or AIDS-related KS, and this is the most frequent cause of KS due to the spreading of AIDS.
d. Immunosuppression associated or Transplant-related (acquired) KS that is increasingly encountered as a consequence of long-lasting suppression of the immune system.

The risk of KS is increased with cyclosporine treatment compared with azathioprine-based treatment,

and in patient on cyclosporine, the latency period for the development of KS is shorter than for azathioprine (8). Therapy with polyclonal antilymphocyte sera may also be responsible for the development of KS. Genetic factors may play a pathologic role because the prevalence of KS is higher in Mediterranean, Caribean and black African patient. The presence of anti-human herpes virus type-8 serology is another contributory factor (9,10). The average time between transplantation to diagnosis of KS is 20 months with the shortest interval in cyclosporine-treated recipients. Patients mostly presented with cutaneous involvement, more than 90% of KS, and less frequent is the involvement of viscera (2,3). The purely visceral disease occurs in 10% of patients (4). In cutaneous form, the legs are affected twice as commonly as the arms. The course of skin disease is generally benign except the aggressive cutaneous form of post-transplant KS seems to be confined to Saudia Arabia (2,4). The case of KS described here, presents some peculiarities such as the early onset, 5 months after transplantation and rapidly progressive spreading course and that withdrawn the tacrolimus and MMF and conversion to sirolimus caused a very good remission of this cancer and seemed to be relatively safe for kidney allograft function. The patient underwent the immunosuppressive regimen that included ATG and tacrolimus that both of them are accounted for the increased prevalence of KS in transplanted patients. Also, may be tacrolimus as same as cyclosporine reduces the latency period for the development of KS, and was showed in this case.

Summary

First: malignancy is an important cause of mortality and morbidity after kidney transplantation, and since skin cancer is the most common tumor associated with transplantation, and skin lesions are encountered in more than 90% of KS, it seems that the examination of skin should be a part of regular follow-up and dermatologist examination is recommended every 6 months. Second: for surveillance of transplant patients, anti HHV-8 serology should be checked. Third: cutaneous KS could have complete remission in response to sirolimus therapy.

References

1. Raeisi D, Payandeh M, Madani SH, Zare ME, Kansestani AN, et al. Kaposi's Sarcoma after Kidney Transplantation: a 21-Years Experience. Int J Hematol Oncol Stem Cell Res 2013;7:29-33.
2. El-Agroudy AE, El-Baz MA, Ismail AM, Ali-El-Dein B, El-Dein AB, Ghoneim MA. Clinical features and course of Kaposi's sarcoma in Egyptian kidney transplant recipients. Am J Transplant 2003;3:1595-9.
3. Yildirim Y, Ozyilkan O, Emiroglu R, Demirhan B, Karakayali H, Haberal M. Early diagnosis of cancer in renal transplant patients: a single center experience. Asian Pac J Cancer Prev 2006;7:336-9.
4. Einollahi B. Unusual site of kaposi sarcoma after kidney transplantation. Iran J Kidney Dis 2012;6:164-5.
5. Cattani P, Capuano M, Graffeo R, Ricci R, Cerimele F, Cerimele D, et al. Kaposi's sarcoma associated with previous human herpesvirus 8 infection in kidney transplant recipients. J Clin Microbiol 2001;39:506-8.
6. Lahlaoui H, Niija H, Ben Moussa M. Seroprevalence of human herpesvirus 8 in kidney transplant recipients in a single-center study from Tunisia. Iran J Kidney Dis 2012;6:14-6.
7. De Blasio A, Palmiero G, Russo D. Kaposi's sarcoma occurring in a young black man after kidney transplantation. Nephrol Dial Transplant 2005;20:2839-41.
8. Moosa MR. Kaposi's sarcoma in kidney transplant recipients: a 23-year experience. QJM 2005;98:205-14.
9. Dow DE, Cunningham CK, Buchanan AM. A Review of Human Herpesvirus 8, the Kaposi's Sarcoma-Associated Herpesvirus, in the Pediatric Population. J Pediatric Infect Dis Soc 2014;3:66-76.
10. Euvrard S, Kanitakis J, Claud A. Skin Cancers after Organ Transplantation Medical Progress: N Engl J Med 2003;348:1681-91.