Asymptomatic Pulmonary Allograft Kaposi Sarcoma: A Case Report

Nazarena Nannini,1 Alessandro Rebusso,2 Francesca Lunardi,1 Monica Loy,2 Francesca Calabrese,2 Lucia Battistella,2 Marco Schiavon,2 Federico Rea,2 Fiorella Calabrese1

Abstract

Solid-organ transplant recipients are at high risk of developing malignancies. A greater risk of Kaposi sarcoma has been reported in lung recipients in our country, particularly in those from Southern Italy, probably due to the high prevalence of Human herpes virus 8 infection. Kaposi sarcoma affecting only the lung allograft is extremely rare. We describe a case of a lung recipient who developed Kaposi sarcoma only in the graft, 22 months after transplant. The patient, a 65-year-old man from Southern Italy, underwent bilateral lung transplant for idiopathic pulmonary fibrosis in January 2009. He developed mild/moderate acute cellular rejection (≥ A2) in 4 of 6 scheduled transbronchial biopsies thus was treated with increased immunosuppressive therapy, shifting from cyclosporine to tacrolimus and mycophenolate mofetil. In July 2010, a high-resolution computed tomography scan showed small bilateral lung nodules, despite a generally good condition. After 2 months, his condition worsened with a severe weight loss. A positron emission tomography scan showed mild metabolic activity in the lesions with no other localizations. In October 2010, a lung biopsy was performed, with results showing typical histologic and immunohistochemical features of Kaposi sarcoma. Molecular tissue evaluations and serologic analyses were positive for Human herpes virus 8. The patient’s immunosuppressive therapy was suspended, and he started liposomal doxorubicin treatment; however, after the first cycle, he developed severe respiratory dysfunction. The patient died 27 months after lung transplant for neoplasm. Our report highlights the importance of considering Kaposi sarcoma in the differential diagnosis for lung nodules in lung transplant recipients, even in the absence of any initial specific symptom or cutaneous lesion.

Key words: Human herpesvirus 8, Lung transplant, Neoplasms

Introduction

Solid-organ transplant recipients are at an increased risk of developing malignancies compared with the general population. Kaposi sarcoma accounts for 5.7% of these malignancies, with the skin being the most commonly affected organ.1 Here, we report a case of a lung transplant recipient with Kaposi sarcoma affecting the lung allograft without any skin or other organ lesions and without any initial specific symptoms.

Case Report

A 65-year-old white man underwent bilateral lung transplant in January 2009 for idiopathic pulmonary fibrosis. The donor was a 10-year-old boy who had deadly meningitis but who fulfilled the criteria for lung donor status (OTO score of 0).2 The patient was not treated with an immunosuppression induction regimen and was followed by maintenance therapy with cyclosporine, azathioprine (2 mg/kg/d), and prednisone. The cyclosporine dose was adjusted according to target therapeutic ranges for trough level of 200 to 400 ng/mL (months 1-3), 100 to 250 ng/mL (months 4-6), and 60 to 200 ng/mL (months 7-12). Target whole blood levels of cyclosporine 2 hours after a dose were 1200 and 800 μg/L at the same time points. Methylprednisolone administration was started intravenously in the operating room.
(10 mg/kg before reperfusion) and then maintained at diminishing doses and switched to oral deltacortene (1 tablet/d at 25 mg). Because of cytomegalovirus immunoglobulin G seropositivity, the patient received the prophylactic ganciclovir for 1 month.

The patient developed acute cellular rejection > A2 in 4 of 6 scheduled transbronchial biopsies. For this, he was treated with pulse-dose steroid therapy, shifting at the fourth biopsy (8 mo after lung transplant) from cyclosporine to tacrolimus and mycophenolate mofetil. In July 2010 (18 mo after transplant), a high-resolution computed tomography scan showed small bilateral lung nodules (all up to 1 cm in diameter), despite a generally good condition.

Bronchoalveolar lavage culture was positive for Aspergillus fumigatus, and the patient was started on voriconazole treatment. After 2 months, the patient’s general condition worsened with a severe weight loss. A whole-body positron emission tomography-computed tomography scan showed mild metabolic activity in the lung nodules without any other organ localization. A lung biopsy was done by minithoracotomy, and pathology showed spindle cells with mild to moderate atypia and numerous mitoses. The tumor cells stained positive for CD34, vimentin, factor VIII, and Human herpesvirus 8 antigen. Moreover, polymerase chain reaction assay performed in lung tissue confirmed the presence of DNA sequences of Human herpes virus 8. All of these findings were consistent with a final diagnosis of Kaposi sarcoma. A careful skin evaluation, cerebral magnetic resonance, and other principal instrumental and biohumoral tests excluded other organ involvement. Serum human immunodeficiency virus testing was negative, and serum immunoglobulin G results against Human herpes virus 8 were positive. Retrospective testing of the patient’s lung donor serum for Human herpes virus 8 was negative. The patient’s immunosuppressive therapy was suspended, and he was started on liposomal doxorubicin treatment. After the first cycle, however, he developed severe respiratory dysfunction. The patient died 27 months after lung transplant due to diffuse neoplastic involvement of the graft.

**Figure 1.** Morphological and Molecular Findings in Our Patient

(A) Emblematic field showing lung parenchymal infiltration of Kaposi sarcoma (hematoxylin and eosin staining, original magnification ×25). (B) Spindle cells with moderate atypia are well seen (hematoxylin and eosin staining, original magnification ×200). (C) Immunohistochemistry for CD34 showing a strong positivity in the spindle cells (original magnification ×200). (D) Agarose gel electrophoresis of polymerase chain reaction products (lane 1: molecular weight marker VIII; lane 2: Human herpesvirus 8 amplicon of lung biopsy; lane 3: polymerase chain reaction negative control; lane 4: polymerase chain reaction positive control).
Discussion

Kaposi sarcoma was first described by Moritz Kaposi in 1872. It is a low-grade mesenchymal tumor that involves blood and lymphatic vessels. It primarily affects the skin and can cause disseminated diseases in different organs. Human herpesvirus 8 and other cofactors (eg, cytokine-induced growth factors) play an important role in the development of the disease. Presently, variants of the disease with different clinical courses are recognized: classic or sporadic, African or endemic, organ transplant-related or iatrogenic, and acquired immunodeficiency syndrome-related or epidemic. The seroprevalence of Human herpes virus 8 and the incidence of Kaposi sarcoma are significantly higher in parts of Asia, South America, and Mediterranean countries. Kaposi sarcoma in transplant patients can be due to reactivation of latent virus during immunosuppression; however, the virus can also be transmitted from donor to recipient. Because the donor serum in our patient was Human herpesvirus 8 negative and our recipient was from Southern Italy, the development of Kaposi sarcoma was most likely due to viral reactivation after transplant.

A multicenter longitudinal Italian study performed in a 4,767 recipients demonstrated that the primary predictors of increased risk of Kaposi sarcoma were male sex, older age, and lung transplant. A 5-fold reduction was observed after 18 months post-transplant. Recipients born in Southern Italy compared with Northern Italy demonstrated a significant 2.2-fold increased risk.

Medical history, physical examination, and radiologic imaging are the first steps in the diagnosis of Kaposi sarcoma. Computed tomography and positron emission tomography scans have shown that the nodule usually exceeds 1 cm diameter. Although other causes of bilateral lung nodules may commonly develop after lung transplant (eg, infections such as mycobacteria and fungi or post-transplant lymphoproliferative disorders), Kaposi sarcoma should be included within that differential diagnosis even in the absence of classic skin lesions as was in our case. To the best of our knowledge, there are a few cases of Kaposi sarcoma with only graft involvement and only 1 previous report with lung allograft involvement without any related symptoms.

The succession of this unfortunate case underlines the potential morbidity of transplant-related Kaposi sarcoma and the need to maintain a high level of suspicion for Kaposi sarcoma in this population, even in the absence of cutaneous involvement and significant initial respiratory distress.

References