

Pulmonary haemorrhage following renal transplantation

Ghazali A Khan, Philip Klapper

Abstract

The case history is presented of a 32 year old black man who developed haemoptysis leading to pulmonary haemorrhage and bilateral pulmonary infiltrates. He was found to have Kaposi's sarcoma of the lung with no evidence of skin or endobronchial lesions.

(Thorax 1995;50:98-99)

Keywords: pulmonary haemorrhage, Kaposi's sarcoma, renal transplantation.

Kaposi's sarcoma has been reported in patients receiving immunosuppressive treatment, together with other myeloproliferative malignancies. The diagnosis of pulmonary Kaposi's sarcoma can be difficult when cutaneous or endobronchial lesions are not present. We describe a patient who presented after renal transplantation with bilateral pulmonary infiltrates and haemoptysis leading to fatal pulmonary haemorrhage secondary to Kaposi's sarcoma.

Case report

A 32 year old black man with end stage renal disease secondary to hypertension was on maintenance hemodialysis until he received his first cadaveric renal transplant in November 1992. He was HIV and PPD negative before his renal transplantation and was subsequently maintained on immunosuppressive treatment with azathioprine, prednisone, and cyclosporin. His baseline serum creatinine level was 176.8 µmol/l. In June 1993 he presented with a three day history of an influenza-like illness with chills and a cough productive of yellow sputum and subsequently of blood. His systolic blood pressure was 60 mm Hg, pulse 120/min, respiratory rate 28/min, and oxygen saturation 74% breathing air. His rectal temperature was 38.1°C. The neck veins were not distended and small cervical lymphadenopathy was noted. Bilateral crackles were present, more on the left side than on the right. The heart sounds were normal and the abdomen was soft with no organomegaly; there was no peripheral oedema. No focal abnormal neurological signs were seen.

Laboratory data on admission were white blood cell count of 9000 with normal differential count, haemoglobin 13.2 g/l, platelet count 31 000/mm³, prothrombin time 11 sec-

onds (control 12 seconds), partial thromboplastin time 40 seconds (control 36 seconds), D-dimer >2, fibrinogen 4.8 g/l, electrolytes normal, blood urea nitrogen 22.84 mmol/l, creatinine 353.6 µmol/l and glucose 6.6 mmol/l. Arterial blood tensions breathing 50% oxygen via a ventimask were pH 7.34, PCO₂ 3.19 kPa, PO₂ 11.30 kPa. The electrocardiogram showed left ventricular hypertrophy with non-specific ST segment depression in the anterolateral chest leads. Chest radiography showed extensive bilateral alveolar infiltrates on the left more than the right. He was given a rapid infusion of two litres of saline and his blood pressure improved to 100/60. Broad spectrum antibiotics (vancomycin, erythromycin, and ticarcillin) were started. Over the next few days his clinical state, platelet count, and renal function improved, but he continued to have episodes of haemoptysis and worsening hypoxaemia. Other investigations including sputum culture, blood culture, and sputum *Legionella* direct fluorescent antibody (DFA) were all negative. In view of his fluctuating pulmonary infiltrates bronchoscopy was performed and revealed normal vocal cords, trachea, carina, and bronchi. There was haemorrhagic fluid in several airways which was easily aspirated and no endobronchial lesions were noted. A transbronchial biopsy sample and bronchoalveolar lavage (BAL) fluid from the left lower lobe revealed negative DFA for *Legionella*, smears for acid fast bacilli, and fungi. The BAL fluid tested positive for cytomegalovirus by monoclonal antibody studies, but no viral inclusions were noted. Gancyclovir nevertheless was added to the treatment. Histological examination of the transbronchial biopsy specimen revealed an exuberant collection of spindle-shaped cells which were probably of endothelial origin and were von Willebrand antigen positive, compatible with Kaposi's sarcoma. Stains for cytokeratin and muscle specific antigen were negative in these tumour cells. Gallium scanning did not reveal any abnormal uptake but thallium scanning showed an increased diffuse uptake in both lungs. A cervical lymph node biopsy was performed which confirmed Kaposi's sarcoma. Repeat HIV testing proved to be negative. His immunosuppressive treatment was discontinued, and adriamycin, bleomycin, and vincristine were given, despite a platelet count that was low normal. There was no clinical improvement and he continued to have hypoxaemia, haemoptysis, and fluctuating infiltrates. His clinical status deteriorated, requiring intubation, and he died a short time later. Post mortem examination showed only limited involvement of the lungs and lymph nodes with Kaposi's sarcoma. His gastrointestinal tract, liver, spleen, and bone marrow were not involved.

Discussion

Kaposi's sarcoma is a well recognised complication of renal transplantation and immunosuppression which is known to involve the lungs. Its presentation with diffuse bilateral

Division of Nephrology and Pulmonary Medicine, Montefiore Medical Center of the Albert Einstein College of Medicine, 111 East 210 Street, Bronx, New York 10467, USA
G A Khan
P Klapper

Reprint requests to:
Dr G A Khan.

Received 24 January 1994
Returned to authors
10 March 1994
Revised version received
8 April 1994
Accepted for publication
18 April 1994

pulmonary shadowing may mimic diffuse opportunistic infection and intra-alveolar haemorrhage. It is a rare malignancy believed to arise from precursor endothelial cells in a multicentric fashion leading to tumour of mixed vascular and fibroblastic origin.¹ The histological patterns of Kaposi's sarcoma are a continuum characterised by early angiomatous, and later sarcomatous, change.² Immunosuppressed patients are at increased risk for development of malignancies such as lymphoma and Kaposi's sarcoma.³ In western countries, Kaposi's sarcoma occurs in 0.4% of transplant recipients and represents 3–4% of all cancers occurring in that context.⁴ Its incidence in renal transplant recipients has increased to 400–500 times to that seen in a control population of the same ethnic group. This complication is more common in Mediterranean, African, Jewish, and Arabic patients, and occurs in 5.3% of transplant patients in Saudi Arabia.⁵

The high incidence of Kaposi's sarcoma in renal transplant recipients suggests that immunosuppressive therapy may be responsible. Its frequency is influenced by the type of immunosuppression, increasing up to 500-fold in those treated with azathioprine and methylprednisone, and 1000-fold in cyclosporin-treated patients.⁶ Corticosteroids affect the immune system in several ways, but their role in the development of Kaposi's sarcoma is unclear.⁵ Cyclosporin is an effective immunosuppressant with known inhibitory effects on T helper cells. It is also associated with other malignancies such as skin cancer, lymphoma, and other lymphoproliferative malignancies. These tumours usually appear within a few months after commencing immunotherapy and usually regress after discontinuation of treatment.¹

Ostlere *et al* have postulated that the imbalance in the immune system seen during post-transplant immunosuppression may be responsible for the increased circulation of factors with angiogenic properties, or alternatively the loss of molecules with an inhibitory effect on

angiogenesis.⁵ This may contribute to the increased frequency of Kaposi's sarcoma seen in renal transplant patients.

Bencini *et al* reported Kaposi's sarcoma in 11 of 820 kidney transplant recipients (1.3%), mainly in the skin with very few patients having widespread mucocutaneous, visceral, and lymphatic lesions. They also point out that Kaposi's sarcoma developed after a relatively short period of immunosuppression (6–40 months) in the patients treated with cyclosporin, suggesting that immunosuppression in the immediate post-transplant period may be an accelerating factor for the development of Kaposi's sarcoma in a population predisposed.⁶ Shmueli *et al* have also reported an increased incidence of Kaposi's sarcoma among patients treated with cyclosporin compared with azathioprine.⁷

Although the diagnosis was made before death in our patient, discontinuing the immunosuppressant treatment and initiating aggressive combination chemotherapy made no difference, although the duration of both these interventions was short. In some patients there have been reports of regression of Kaposi's sarcoma lesions when their immunosuppressive therapy was altered or discontinued.¹

Whilst Kaposi's sarcoma is increasingly described in the renal transplant population, it is not usually associated with fatal pulmonary haemorrhage and must be considered in this clinical setting.

- 1 Hanid MA, Suleiman M, Haleem A, Al Karawi M, Al Khader A. Gastrointestinal Kaposi's sarcoma in renal transplant patients. *Q J Med* 1989;73:1143–9.
- 2 Martin RW, Hood AF, Farmer ER. Kaposi sarcoma. *Medicine* 1993;72:245–61.
- 3 Chang P, Fernandez V. Kaposi sarcoma in a kidney transplant patient. *Int J Derm* 1991;30:134–5.
- 4 Butkis DE, Kirchner KA, Neill J, Raju S. Kaposi's sarcoma in a transplanted kidney. *Transplantation* 1989;48:146–9.
- 5 Ostlere LS, Harris D, Sweny P, Rustin MHA. Kaposi's sarcoma following renal transplantation. *Int J Derm* 1992;31:439–40.
- 6 Bencini PL, Montagnino G, Tarantino A, Alessi E, Ponticelli C, Caputo R. Kaposi's sarcoma in kidney transplant recipients. *Arch Dermatol* 1993;129:248–50.
- 7 Shmueli D, Shapira Z, Yussim A, Nakache Z, Shaharabani E. The incidence of Kaposi sarcoma in renal transplant patients and its relation to immunosuppression. *Transplant Proc* 1989;21:3209–10.