Kaposi's Sarcoma in an Immunosuppressed Renal Allograft Recipient

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SUMMARY

A 47-year-old White man developed a buccal Kaposi's sarcoma 15 months after receiving a renal allograft. Atypical clinical and histological features were noted. A previous viral infection might have played a role in the occurrence of this patient's tumour but other possibilities of tumour induction in the immunosuppressed host are discussed. Although the condition is lethal when diagnosed after renal transplantation, this case report demonstrates that prompt diagnosis and radiotherapy may result in permanent cure.


Burnet, and Thomas predicted that a high incidence of tumours would be seen among patients with immune deficiency diseases. Starzl warned that tumours may arise and Thomas' predicted that a high incidence of neoplasms which occurred after transplantation have formed. Histology of the kidney suggested advanced chronic glomerulonephritis. In October 1971 the patient underwent a renal transplant. The transplanted kidney, which was obtained from a cadaver, functioned immediately. The urine volume dropped precipitously and an accelerated diuresis was obtained. Two further rejection episodes, which occurred after transplantation have been reported. We wish to report an unusual case of Kaposi's sarcoma which involved the buccal cavity in a recipient of a renal allograft obtained from a cadaver.

CASE REPORT

A 43-year-old Portuguese man referred from Mozambique was admitted to hospital in May 1971, with severe hypertension, cardiac failure and end-stage renal failure. After preliminary haemodialysis, bilateral nephrectomy was performed. Histology of the kidney suggested advanced chronic glomerulonephritis. In October 1971 the patient underwent a renal transplant. The transplanted kidney, which was obtained from a cadaver, functioned immediately. The HL-A typing was donor 2.3, W15; patient 2.11, W5 14. There was a negative cytotoxic cross-match with the donor, but the patient was mildly presensitised to some members of a randomly selected 24-patient lymphocyte donor panel. After 20 hours of satisfactory diuresis, the urine volume dropped precipitously and an accelerated form of rejection was diagnosed. This was treated with high doses of prednisolone and actinomycin C, while azathioprine treatment (150 mg daily) was maintained. The early rejection settled without the patient requiring haemodialysis. Two further rejection episodes, which occurred 38 and 80 days postoperatively, required intensification of prednisolone treatment. By the end of the eighth month the serum creatinine was stable at an average of 1.4 mg/100 ml and the patient was maintained on 15 mg of prednisolone and 150 mg of azathioprine daily.

He remained well until July 1972, when he was re-admitted with Herpesvirus hominis type II infection which involved the penis and perineal area. The lesions were extensive and became ulcerated and secondarily infected. The patient was treated with antibiotics and iodoxyuridine ointment and was discharged well 1 month later.

In October 1972 he was admitted with a flail chest sustained in a motor vehicle accident. He had no facial injuries. He responded well to conservative treatment and was discharged in December. One month later, that is 14 months after transplantation, he presented with an elevated, necrotic, granuloma-like lesion in the mouth. This covered an area in the gum (2 x 1 cm) originally occupied by the lower right molar teeth which had previously been extracted. Most of his other teeth were carious and many had been extracted. Three further lesions, two in the upper and one in the lower jaw, appeared rapidly over a 2-week period. In each case they appeared to be related to carious teeth. There was no regional lymphadenopathy and the rest of the physical examination revealed no abnormality.

The results of biochemical, haematological and radiological studies (including X-ray examinations of the jaw and skeletal survey) were essentially normal. A notable exception was an elevated serum alkaline phosphatase (18 King-Armstrong units), 25% of which consisted of the placental or 'Regan' type iso-enzyme. The pathological features of the initial biopsy specimen were considered to indicate a non-malignant process resembling an atypical infective granuloma. For this reason, extraction of all the teeth and excision of the lesions were undertaken, but at operation the original mass was noted to extend well posteriorly into the pharynx, and total excision was therefore not possible. Histological sections of the excised tissue showed features of Kaposi's sarcoma with many more mitotic figures than the original biopsy specimen. On electron microscopy, a viral-like 'C' particle was noted but tissue culture of the lesion failed to grow any organism.

It was decided to modify rather than to withdraw immunosuppression. The dose of prednisolone was altered from 15 mg daily to 40 mg on alternate days; azathioprine was discontinued and replaced with a daily dose of 125 mg cyclophosphamide. A total of 2 500 rad deep X-ray therapy was given to the affected areas and rapid re-
progression of the lesions was noted. Three months after the completion of antitumour therapy there were no clinical signs of recurrence and daily prednisolone was reinstated because of a deterioration in the patient's renal function (serum creatinine 1.9 mg/100 ml). He remained well for a further 4 months, but then became acutely ill and died of a Gram-negative sepsicaemia. At autopsy, 7 months after completion of antitumour therapy, there was no evidence of tumour recurrence or spread.

**DISCUSSION**

An association between organ transplantation, immunosuppressive therapy and malignancies is widely accepted. The reported incidence of malignancies in patients who survive their operations for at least 4 months is 6%. Hypotheses to explain this relationship include a breakdown of immunological surveillance, proliferation of oncogenic viruses, direct induction of neoplastic change by immunosuppressive drugs and the presence of foreign grafted tissue in the immunosuppressed host. This may influence host immune responses owing to continuous antigenic stimulation or via a graft-versus-host mechanism. No mention has been made in the literature of the theoretical role of interferon. This substance has been shown to have antitumour properties and it is well known that corticosteroids inhibit the normal action of interferon. Of 75 post-transplant malignancies reported, 43 have been of epithelial and 32 of mesenchymal origin. The average time after transplantation at which mesenchymal tumours have first been noted is 19 months (our patient presented 15 months postoperatively). Mesenchymal tumours are associated with a particularly high mortality rate, only 3 reported patients having survived. Of the mesenchymal neoplasms, 3 were Kaposi's sarcomas.

The first of these, which involved many viscera, was reported by Siegel et al. The disease ran a fulminant course, and ended in death 3 months after initial presentation. The 2 other patients were both recorded in Israel; one had an associated lymphosarcoma and died, while the other presented with skin and buccal lesions and survived.

Several unusual features in our patient require emphasising. Characteristically, Kaposi's sarcoma occurs in children or young adults. It is a rare tumour in White patients and in Africa it occurs with diminishing frequency to the north and south of the Congo Basin. In our patient, his age, racial characteristics and geographical location make the spontaneous development of this tumour a rarity.

Difficulty is frequently experienced in differentiating some Kaposi's tumours from infected granulomas. In this patient, the rapid growth and spread of the mass in an area of local dental sepsis, which on the original biopsy showed few mitotic figures, suggested an infective origin rather than a tumour. However, the histology of the tissue removed at operation was diagnostic of Kaposi's sarcoma. The histological similarity between *Toxoplasma* granulomas and various sarcomas was also considered, but excluded.

Recently, both herpes-type viral particles and cytomegaloviral particles have been grown in tissue culture from Kaposi's sarcoma in patients from Central Africa. The possibility of a viral aetiology in the development of our patient's neoplasm is suggested by the history of a preceding *Herpesvirus hominis* type II infection, and this hypothesis is further strengthened by the demonstration of a virus particle in the tumour on electron microscopy. The occurrence of trauma in this patient may have been a precipitating event, but this seems unlikely.

The decision whether or not to withdraw immunosuppressive therapy in a potentially fatal condition is a difficult one. Starzl pointed out that in the case of epithelial tumours of the skin, lip and cervix, standard methods of therapy could be successfully carried out without cessation of immunosuppression. In the treatment of mesenchymal tumours and epithelial neoplasms which involve visceral structures, withdrawal or modification of immunosuppressive drugs must be seriously considered.

In view of the localised nature of this patient's neoplasm and its known sensitivity to radiotherapy, immunosuppression was continued but in a modified form. Azathioprine was discontinued, and cyclophosphamide, which has been successfully used in the therapy of Kaposi's sarcoma, was substituted. The rapid regression of the lesions after deep X-ray therapy was striking, and there was no evidence of recurrence after 7 months.

An additional interesting feature in this case was the high concentration of serum placental alkaline phosphatase. This iso-enzyme was originally found in the serum of a patient with carcinoma of the lung and has since been described as being produced by many malignant neoplasms. To our knowledge its occurrence in Kaposi's sarcoma has not been described yet. Measurement of the iso-enzyme might be of value in the assessment of the response of the tumour to treatment.

**REFERENCES**