

## CASE REPORT

# Hodgkin's disease after cardiac transplant: a report of two cases

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**Summary** Non-Hodgkin's lymphoma is a well recognized sequela of transplant related immunosuppression. Hodgkin's disease has only rarely been described in this context. We describe two cases of Hodgkin's disease after heart and heart/lung transplants respectively. Both patients continued to receive immunosuppressive therapy with cyclosporin and prednisolone, and received combination chemotherapy. One died of *Aspergillus* infection following the second course of chemotherapy. The other patient completed his chemotherapy and remains in remission. We discuss the possible aetiology and management of post-transplant Hodgkin's disease.

**Keywords** Hodgkin's disease, cardiac transplant

### Case report 1

In 1986 a 31-year-old man had a heart/lung transplant for histiocytosis X. Post-operatively he was commenced on cyclosporin A, blood levels were maintained at 200–300 µg/l. In mid 1992 he developed cervical lymphadenopathy accompanied by a rise in Epstein–Barr viral (EBV) antibody titres. Six months later he complained of night sweats and left upper quadrant abdominal pain. Examination revealed cervical lymphadenopathy and splenomegaly. Results of investigations were: Hb 7.9 g/dl (normochromic, normocytic), WBC  $2.4 \times 10^9/l$  (neutrophils  $2.04 \times 10^9/l$ ), platelets  $53 \times 10^9/l$ , albumin 24 g/l, bilirubin 47 mmol/l, alkaline phosphatase 227 U/l. A lymph node biopsy confirmed the diagnosis of nodular sclerosing Hodgkin's disease. A CT scan showed splenomegaly, retroperitoneal lymphadenopathy and a mass at the portahepatis. A bone marrow trephine was normal. He was diagnosed as having stage IIIB Hodgkin's disease and was initially treated with prednisolone for 2 weeks to which he had a good haematological response.

In April 1993 he received combination chemotherapy with ChlVPP (chlorambucil, procarbazine, prednisolone, vinblastine). Fourteen days after his first course of chemotherapy he was admitted with fever and breathlessness. Bronchioalveolar lavage confirmed the diagnosis of pul-

monary aspergillosis for which he received 2 weeks amphotericin at a dose of 1 mg/kg.

Seven days following his second course of chemotherapy he was admitted with neutropenic fever associated with oral mucositis, abdominal pain and increasing breathlessness. On repeat bronchioalveolar lavage he had evidence of aspergillosis. CT scan of his abdomen was suggestive of colitis in the ascending colon. Despite broad spectrum antibiotics and intravenous amphotericin therapy he developed multiorgan failure requiring ventilation, haemofiltration and inotropic support. He continued to deteriorate and died in June 1994. A post-mortem was refused by his relatives.

### Case report 2

In January 1994, a 54-year-old man, who had a heart transplant for viral cardiomyopathy in 1985, presented with a 3-month history of weight loss, night sweats, fever and dry cough. He was receiving cyclosporin A as immunosuppressive therapy and the blood level of this was maintained at 200–300 µg/l. Examination revealed right supraclavicular lymph nodes and chest X-ray showed superior mediastinal widening. A CT scan confirmed a mediastinal mass, but there was no disease below the diaphragm. Laboratory results were as follows: Hb 10.8 g/dl, WBC  $6.7 \times 10^9/l$  (lymphocytes  $1.69 \times 10^9/l$ ), platelets  $372 \times 10^9/l$ , ESR 100 and albumin 33 g/l, LDH 322 U/l. Immunoglobulin electrophoresis revealed a polyclonal

increase in immunoglobulins. A lymph node biopsy confirmed the diagnosis of nodular sclerosing Hodgkin's disease.

He was diagnosed as having stage IIB disease and was commenced on ChlVPP chemotherapy. He completed six courses of chemotherapy in June 1994. A CT scan after his final course confirmed a good partial remission. He remains well 12 months later.

## Discussion

Immunosuppressed allograft recipients run a higher than normal risk of developing malignancy (Penn 1977). Since the introduction of cyclosporin immunosuppression, lymphomas are becoming the predominant tumour in such patients (Penn 1987). However, in most instances the histological appearances tend towards that of non-Hodgkin's lymphoma, usually large cell or immunoblastic type. Hodgkin's disease has been reported only rarely in organ transplant recipients (Sterling 1974; Cerilli, Rynosiewicz & Rothermel 1977; Doyle *et al.* 1983; Oldafer *et al.* 1989; Nalesnik *et al.* 1993). Penn (1992) cites only 24 out of 5386 organ recipients in his Transplant Tumour Registry.

We report the occurrence of two cases of Hodgkin's disease after cardiac transplant and to date there is only one other documented case after cardiac transplant (Chen *et al.* 1993). Patient 1 had serological evidence of acute EBV infection and we postulate that this may have been an aetiological factor. Post-transplant lymphomas are frequently tumours of EBV. The EBV immortalizes B cells which proliferate unchecked due to the absence of T cell suppression. The incidence of EBV positive lymphomas is about 2% after renal and hepatic transplants, 5% after cardiac transplants, 10% after heart and lung transplants and less than 1% in bone marrow transplant recipients (Cohen 1991). Hodgkin's disease is not considered to be part of this spectrum and is rarely seen in the post-transplant population.

There is, however, increasing evidence that EBV is involved in the aetiology of Hodgkin's disease. Between 1991 and 1993, there was an average 50% positivity for EBV in the Reed–Sternberg cells of 1000 patients tested using techniques such as *in situ* hybridization, immuno-

histochemistry, and PCR (Joske & Knecht 1993). Hodgkin's disease may therefore be part of the spectrum of post-transplant EBV associated lymphoproliferative disorders. The therapeutic implications of this might include antiviral therapy and a reduction in immunosuppressive therapy prior to chemotherapy. But as the cells of Hodgkin's disease do not express viral proteins to act as targets for cytotoxic T lymphocytes it appears unlikely that a reduction in immunosuppression will have a significant effect. Antiviral therapy with acyclovir has had a modest impact in treatment of post-transplant lymphoma, this may be due to the absence of viral replication (Joske & Knecht 1993).

In conclusion, post-transplant Hodgkin's disease should be treated with conventional chemotherapy, but precautions taken to minimize the increased risk of infection associated with immunosuppression.

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