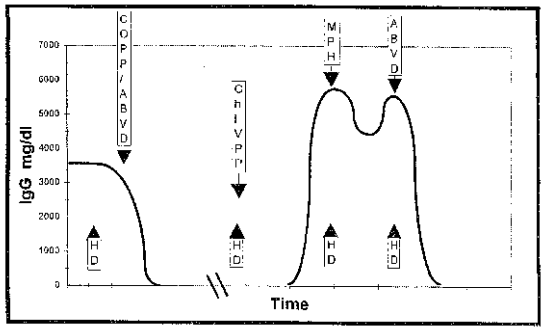

Figure 1. Association of the monoclonal component (IgG) concentration with the recurrences of Hodgkin's disease (HD) and its response to various therapeutic regimens.

lary lymphadenopathy. Biopsy revealed a mixed cellularity HD (Stage IIB). He attained a complete remission (CR) of both malignancies after six courses of COPP/ABVD and involved-field radiotherapy. One year later, his HD relapsed (stage IIIB). A 4-month CR was achieved with ChlVPP but both diseases relapsed. Two courses of intermediate dose melphalan failed to control either of them. Bone marrow biopsies showed infiltration with Hodgkin and plasma cells. Cytogenetic and FISH analysis on marrow samples demonstrated cells with a gain or loss of Y chromosome, findings which are more compatible with constitutional mosaicism. A third CR of both diseases was achieved with three ABVD courses but the patient succumbed to overwhelming acute hepatitis B and hepatic failure.

Patients with HD who also presented monoclonal gammopathy without overt MM,[1] or who developed MM after radio- or chemotherapy[2] have been reported, but the simultaneous occurrence of MM and HD has also occasionally been reported.[3-6] One wonders whether any pathogenetic association between the two diseases exists. Both are believed to have lymphoid, probably B-cell, origin,[7] and similar karyotypic abnormalities have been detected in them,[8] while the same cytokines, such as IL-6, could play a major role in both cases. IL-6 acts as a factor for growth and apoptosis for plasma cells,[9] while Reed-Sternberg cells (infiltrating the marrow) express IL-6 mRNA and high IL-6 levels are found in patients with advanced HD.[10] Although this stimulus does not seem enough to promote monoclonality, it is possible that the excess IL-6 in the marrow microenvironment might directly stimulate the long-livings plasma cells there. Although MM criteria were fulfilled in our patient, the course of this disease was not autonomous, it did not cause bone lytic disease and was always associated with the progression of HD (Figure 1). Consequently, these two distinct malignancies may not be irrelevant to each other. Questions remain to be answered in the future when the pathogenetic mechanisms of malignancy are better understood.

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Key words
Multiple myeloma, Hodgkin's disease.

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Demonstration of Epstein-Barr virus in a case of multiple myeloma after renal transplantation

Immunosuppresed organ transplant recipients have an increased risk of developing lymphoproliferative disorders that are often associated with Epstein-Barr virus (EBV) infection. We report a pacient who developed multiple myeloma after renal transplantation. EBV-RNA was demonstrated in the neoplastic cells suggesting the implication of this virus genome in the pathogenesis of this posttransplantation lymphoproliferative disorder.

Sir,

Multiple myeloma (MM) represents no more than 4% of all post-transplantation lymphoproliferative disorders (PTLDs)[1] and is associated with a poor response to discontinuation of immunosuppression and conventional therapy and a short median survival.

In March 1997 a 47-year old man was admitted to our hospital with a 6-week history of fatigue, anorexia, left eye progressive blindness and left thoracic pain. He had required a cadaveric renal transplantation in 1988 because of idiopathic chronic glome-

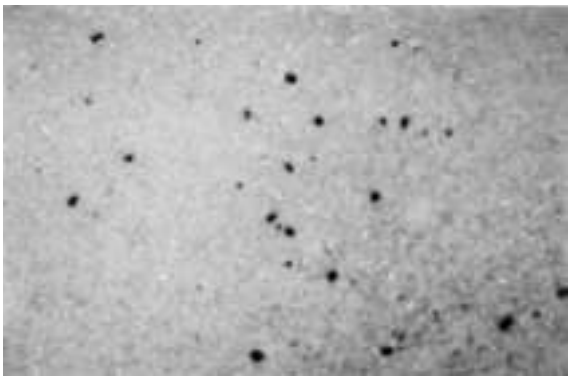

Figure 1. Black dots in the section demonstrate EBV-RNA in the neoplastic cells (plasma cells). Technique performed by *in situ* hybridization of EBERs (PNA ISH detection kit-DAKOR).

rulonephritis. One year later he suffered chronic rejection. In April 1995, he received a second renal allograft. Since then and until the time of admission, he had been maintained on therapy with cyclosporine and prednisone.

Physical examination discovered a 5-6 cm mass in the hard palate and another 5×4 cm mass in the left anterior thoracic wall. The skeletal survey showed multiple lytic lesions. A cranial computed tomography scan showed multiple masses in the left cavernous sinus, left optic foramen, and at the posterior limits of the superior maxillary bone

The patient's analytic parameters were all normal except: urea nitrogen 20.3 μmol/L, creatinine 324 μmol/l, and protein 101 g/L. Serum protein electrophoresis and immunofixation revealed a monoclonal paraprotein of the IgGκ type. The IgG level was 5,500 mg/dL with low levels of IgA and IgM. A 24-hour urine collection revealed 1.83 g of protein identified as free κ chains. He was Epstein-Barr virus (EBV) seropositive (IgG anti-VCA, not IgM).

A biopsy of the maxillary mass showed a diffuse proliferation of large plasma cells with round, vesicular nuclei and basophilic cytoplasm, negative for LCA (CD45), and T-or B-cell lineage antigens. Bright cytoplasmic κ light chain was found. By in situ hybridization of EBERs, EBV-RNA could be demonstrated in approximately 50% of neoplastic cells (Figure 1). The bone marrow aspiration and biopsy showed massive infiltration of immature and atypical plasma cells. The immunophenotype of plasma cells was positive for CD38 (96%), CD138 (85%), CD44 (74%), CD56 (22%), and negative for CD19 and HLA-DR.

The administration of cyclosporine was discontinued, and the patient was started on CNOP (cyclophosphamide, mitoxantrone, vincristine and prednisone) chemotherapy for 6 courses. He also received external local radiotherapy to the involved cranial area, with a total dose of 40 Gy. Six months after diagnosis a complete clinical, analytical and radiological remission was achieved.

Immunosuppresed organ transplant recipients have an increased risk of developing cancer[2] such as Kaposi's sarcoma and post-transplantation lymphoproliferative disorders. Although PTLDs may have plasmacytoid differentiation, terminal differentiation to plasma cells secreting immunoglobulines is very rare. After organ transplantation, immunosuppressed patients have a 30% incidence of monoclonal gammopathy of unknown significance. The M-proteins are usually IgM and are detected 1-25 weeks after transplantation.[3] Whether persistence of M protein predicts development of PTLDs is not known.

PTLDs are associated with EBV infection in more than 80% of patients[4] but the role of this virus in the pathogenesis of MM is not well understood. EBV DNA has been demonstrated in some cases of post-transplantation extramedullary plasmacytoma[5] (EMP) and has only been reported in two cases of post-transplant MM, both demonstrated by Southern blot.[6]

Our patient developed MM eight and three years after two consecutive renal transplants. The demonstration of EBV RNA in the neoplastic cells suggests that this virus genome was implicated in the pathogenesis of this post-transplantation myeloma in a chronically immunosuppressed patient.

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