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*Case Report*

# 'Transient multiple myeloma' after intense immunosuppression in a renal transplant patient

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## Introduction

B-cell lymphoproliferative disease, especially large cell lymphoma, is a well-recognized complication of immunosuppression early after organ transplantation, whereas the incidence of multiple myeloma does not appear to be increased [1]. We wish to report a patient who was diagnosed as having multiple myeloma during intense immunosuppression after renal transplantation. All abnormalities, however, later disappeared after reduction of immunosuppression.

## Subjects and methods

The patient, a 51-year-old woman, had suffered from chronic glomerulonephritis since 1958. End-stage renal failure had been reached in 1976 and maintenance haemodialysis was begun. A first cadaveric renal transplant was rejected under conventional immunosuppression with azathioprine and prednisone within 6 weeks in 1978. Since she developed high titres of panel-reactive antibodies, she could not be retransplanted for several years thereafter.

In October 1990 she finally received a second cadaveric kidney graft. Immunoelectrophoresis before transplantation was normal. Because of her history of rejection and lymphocytotoxic antibodies, an intensified immunosuppressive regimen was administered, consisting of 5 mg OKT3 for 14 days, cyclosporin 400 mg daily from day zero, azathioprine 2 mg/kg and methylprednisolone pulses for 3 days followed by 0.5 mg/kg of oral prednisone thereafter (Figure 1).

Although the graft functioned well from the first day, biopsy-proven vascular rejection on day 23 required therapy with seven daily doses of 5 mg OKT3, and seven pulses of methylprednisolone. The retreatement was well tolerated except for diarrhoea and slight pancytopenia. The patient had to be readmitted on day 40 because of an increase in serum creatinine, and subfebrile temperature, dyspnoea, and cough.

Admission serum protein electrophoresis revealed biclonal gammopathy, IgG kappa and lambda. Bronchoscopy specimens stained positive for *Pneumocystis carinii*, which prompted a therapy with co-trimoxazole. She was treated for suspected rejection with four additional steroid pulses and 7 days of rabbit anti-thymocyte globulin (ATG Fresenius) 2 mg/kg body weight. Serum IgG increased from 8.1 g/l at transplantation to 33.1 g/l by day 57. Urine electrophoresis was trace positive for the IgG kappa monoclonal component. Bone marrow examination revealed plasma cell infiltrates of 30% (focally up to over 50%). These cells were polymorphic with atypical nuclei, some with blastic nuclear structure (Figure 2). A radiological work-up for osteolysis or organ infiltration was negative.

A diagnosis of multiple myeloma was made and removal of the renal transplant was therefore considered. However, since graft function improved in response to the rejection

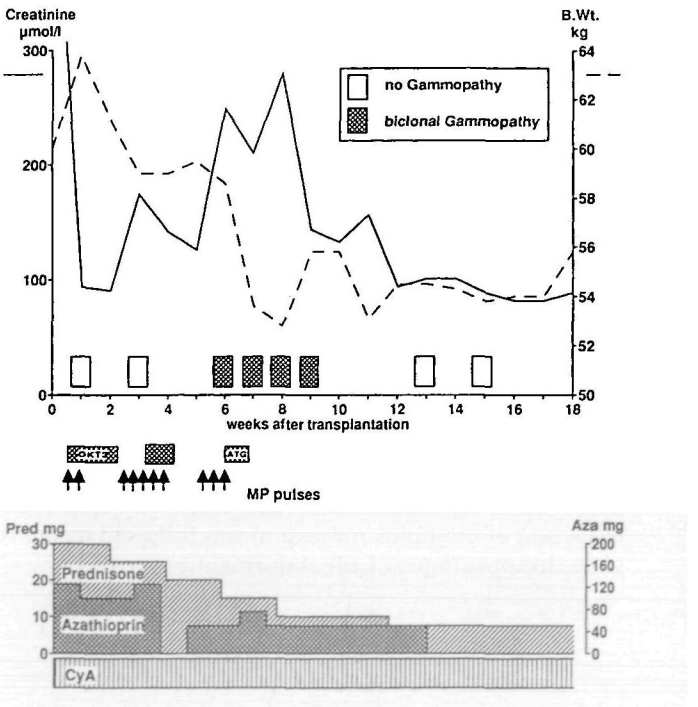


**Fig. 1.** Course of the patient's disease (top) and administered immunosuppression (bottom). B.Wt. = body weight.

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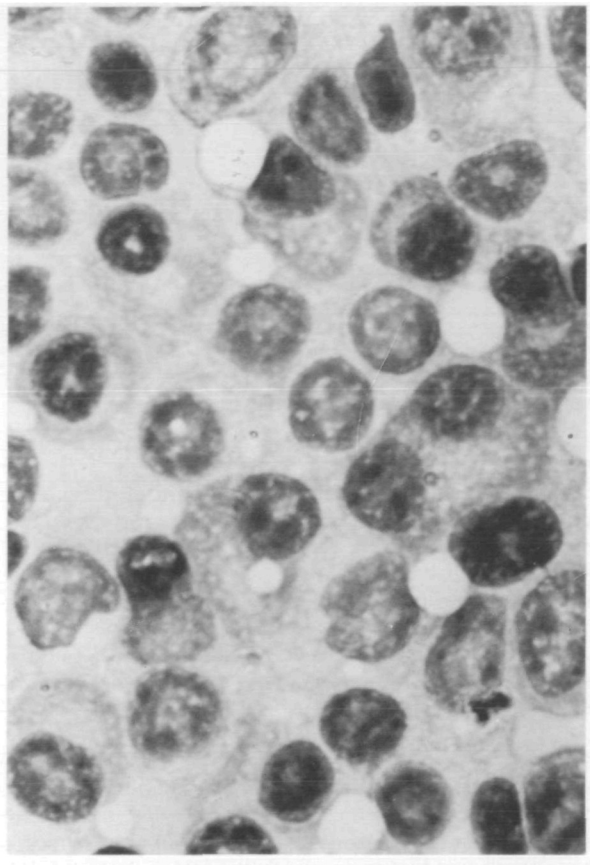

**Fig. 2.** Bone marrow smear with dense infiltrate of plasma cells.

treatment, immunosuppression could be reduced (see Figure 1) at week 13. At day 90 the clonal gammopathy had disappeared. A repeat bone marrow at that time showed less than 5% plasma cells. Today, 18 months after transplantation, her graft functions satisfactorily with a serum creatinine of 109 μmol/l. Immunosuppression is maintained with 300 mg cyclosporin and 7.5 mg prednisone daily. Serum protein electrophoresis still shows no sign of clonal gammopathy.

## Discussion

In summary, this patient developed clonal gammopathy after intense immunosuppression with OKT3 (total dose 105 mg) and MP pulses in addition to the baseline medication with prednisone, azathioprine and cyclosporin. Bone marrow examination disclosed polymorphic infiltrates of plasma cells. By commonly recognized criteria the combination of $>10\%$ plasma cell infiltrate and clonal gammopathy in serum or urine allows the diagnosis of multiple myeloma [2]. However, reduction of immunosuppression was followed by complete disappearance of all abnormalities.

Multiple myeloma has only rarely been reported after renal transplantation [3], but clonal gammopathies are frequently encountered in transplant patients [4]. Their reported incidence ranges between 4 and 68%, depending on the organ transplantated, the timing of sampling, and the sensitivity of the methods used to detect clonality [5]. Not unexpectedly the incidence appears to be greatest after bone marrow transplantation [6] and may be least after renal transplantation [7]. Clonal gammopathy after transplantation is often transient, and the quantity of clonal immunoglobulin is generally small [4]. The cause of pathological clonal expansion is believed to be impaired control of B-cell clones by suppressor T cells, most probably due to immunosuppression [8].

Spontaneous remissions have to our knowledge not been reported in multiple myeloma. Since there is no sharp distinction between monoclonal gammopathy and multiple myeloma, there may be a zone of diagnostic overlap. B-cell lymphomas after organ transplantation are well known and their disappearance after dose reduction of immunosuppressives has been reported.

The lesson to be learned from the present case is that a transient plasma cell dyscrasia may present like multiple myeloma in the setting of heavy immunosuppression after organ transplantation. The alarming findings suggesting myeloma after OKT3 therapy may completely resolve simply by reducing immunosuppression without sacrificing the transplant.

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