A rare cause of fever associated with leukopenia in a renal transplant patient

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Introduction

The occurrence of fever in association with leukopenia in renal transplanted patients is related to viral infection in the majority of cases.

We report a rare cause of such an association in a renal transplant woman.

Case

A 24-year-old woman was referred to our unit for end-stage renal failure secondary to reflux nephropathy. She had mild proteinuria (0.45 g/24 h) without haematuria. Routine immunology tests performed before the diagnosis of reflux nephropathy showed the absence of antinuclear antibodies (ANA). She required haemodialysis for 1 year before receiving a live-related renal transplant from her sister with total HLA identities in 1998. The post-operative course was uneventful and the patient recovered renal function in a satisfactory manner. She was maintained on an immunosuppressive regimen with corticosteroids at a dose of 5 mg/day and azathioprine at a dose of 2 mg/kg/day. Two months later, she developed hypertension, which was treated by amlopidin and acebutalol.

In September 2002, she presented with fever associated with arthralgias and watery diarrhoea. Clinical work-up showed a fever of 39.5°C, weight loss of 8 kg over a period of 4 months, a fixed erythematous and papulous rash located in extended areas of the elbows and knees, arthritis of the left knee, and absence of proteinuria or haematuria on STET. Laboratory tests also revealed the following: serum creatinine 72 μmol/l, haemoglobin 12 g/dl, blood leukocytes 3300/mm³, platelets 210 000/mm³, erythrocyte sedimentation rate 26 mm/h and C-reactive protein 10 mg/dl. Liver function tests were normal.

Viral and bacterial serologies were normal. Cytomegalovirus (CMV) serology was as follows IgG 64 mg/l, IgM 8 mg/l, with an increase in the concentration of IgG 15 days later to 128 mg/l and a high replication of CMV, with viraemia at 24 000 copies/ml (by PCR method) suggesting a recent CMV infection. The patient then received ganciclovir at a dose of 700 mg/day over 21 days. This treatment was associated with the disappearance of diarrhoea, arthralgias, fever and CMV replication, but not of leukopenia and skin lesions.

One month later, she was admitted for recurrence of the fever and arthralgias, extension of the skin lesions to the rest of the arms, the feet and the face (over the cheeks), associated with hair loss, pulpitis affecting all the fingers bilaterally and oral ulcers. A lupus band test in the cutaneous lesion area revealed deposits of C3. Immunologic tests showed the presence of ANA with a titre of 1/1600 (by indirect immunofluorescence), and of anti-DNA antibodies with a low concentration of CH50, but a normal concentration of C3 and C4. Histone antibodies and anti-RNP antibodies were not detected.

The association of these symptoms and the positive immunologic tests confirmed the diagnosis of systemic lupus erythematosus (SLE). Therefore, the corticosteroid dosage was increased to 1 mg/kg/day for 2 months, with progressive tapering and azathioprine was replaced by mycophenolate mofetil at a dose of 2 g/day. After a follow-up of 10 months, the outcome was favourable.
with apyrexia, weight gain and improvement of skin
lesions, normalization of white blood cell count,
negative serum ANA and normalization of the serum
CH50 level.

Discussion

The occurrence of SLE after renal transplantation is
extremely rare. In fact only one case of de novo lupus
nephritis appears to have been reported, which
occurred 9 years after cadaveric renal transplantation
in a patient with initial diabetic nephropathy. The
authors found only three ARA criteria of SLE, namely
nephritis, ANA antibodies and DNA antibodies [1].
The diagnosis of SLE in our patient is certain as she
exhibited five ARA criteria: arthritis, oral ulcers,
leukopenia and positivity of ANA and anti-DNA
antibodies [2]. We believe that she had de novo SLE,
as at first presentation with end-stage renal failure,
clinical features were absent and immunologic tests
negative. Furthermore, improvement of clinical and
serologic signs after treatment was observed.
Acebutalol-induced SLE was ruled out in our patient,
as anti-histone antibodies were absent [3]. We sup-
pose that our patient could have had polyclonal B-cell
or helper T-cell activation despite immunosuppressive
therapy secondary to environmental or genetic factors
explaining de novo SLE.

We replaced azathioprine with mycophenolate
mofetil because the latter is a T-cell directed immuno-
suppressive therapy responsible for the inhibition
of helper T-cell proliferation and subsequently a decrease
in pathogenic DNA antibody production [4].

Conflict of interest statement. None declared.

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