deteriorating renal function were 211, 318, 329, 332 and 404 ng/ml. In addition, in another four cases (three patients) a renal biopsy was performed because of worsening renal function which showed evidence of cyclosporin A exposure (cytoplasmic vacuolation in tubular cells) and in one instance, nephrotoxicity with vascular hyalination. Trough concentrations at biopsy were 170, 258, 272 and 273 ng/ml. On three of these occasions, Neoral dose reduction led to improving renal function and in the other case, where vascular abnormalities were observed, dose reduction in combination with intravenous methylprednisolone (for moderate cellular rejection) was successful. In the 45 patients who received renal allografts prior to our change to Neoral and followed for the first 4 weeks, there were no cases of deteriorating renal function which responded to Sandimmun dose reduction, and changes attributable to cyclosporin A exposure or nephrotoxicity were observed in only one case on renal biopsy, with a blood cyclosporin level of 545 ng/ml.

Achievement of a therapeutic plasma cyclosporin A in the immediate post-transplant period is essential to reduce the risk of acute rejection. Our clinical experience with Neoral is that nephrotoxicity can occur with lower trough plasma concentrations than we have observed previously with Sandimmun. Thus, our immunosuppression policy has now changed so that all patients are commenced on Neoral 5 mg/kg in two divided doses and the dose adjusted to maintain trough concentrations of 200–300 ng/ml. We feel that our clinical observations are of relevance to physicians managing renal allograft recipients and patients with glomerulonephritis receiving cyclosporin A.

Department of Medicine P. A. Rutherford  
Transplantation Surgery and Histopathology A. Kumar  
Royal Victoria Infirmary A. Davison  
Newcastle upon Tyne A. R. Morley  
NE1 4LP M. Thick  
T. H. J. Goodship UK


OKT3 monoclonal antibody therapy and visual loss

Sir,

In their report on visual loss complicating acute renal allograft rejection in a 30-year-old female Dr Jin et al. (Nephrol Dial Transplant 1995; 10: 2144–2146) suggest this severe side effect to be related to OKT3 monoclonal antibody therapy. Although some reports on ophthalmological problems following OKT3 administration have been published recently, we believe that the presented data do not allow this conclusion [1,2].

The authors fail to exclude acute cytomegalovirus (CMV) infection which is well known to cause chorioretinitis with perivascular infiltrates, exudates, and haemorrhage, and a permanent reduction in visual acuity [3,4]. The classical lesions are due to vasculitis and often involve both macula and papilla. We base our argument on personal experience with a renal transplant recipient who developed severe neuritis of both optic nerves, necrotizing retinitis and permanent visual loss during an episode of otherwise subclinical CMV infection. This happened 10 days post-operatively when the patient was on high-dose steroids and cyclosporin, but had not received OKT3.

The ophthalmological findings reported by Dr Jin et al. are compatible with those resulting from CMV infection which is most common with potent immunosuppression. In their patient, accelerated rejection on the second post-operative day was unsuccessfully treated by a 6-day course of pulse methylprednisolone, before OKT3 was started on the 8th post-operative day. CMV infection, for example, by transmission from the donated organ, may well have occurred after more than a week of high-dose steroid therapy. It is not mentioned whether the donor was tested for anti-CMV antibodies. Regrettably, the onset of visual disturbances was not noticed by the transplant physicians and the exact time course is thus not known. Their patient retrospectively reported a 10-day period of slowly progressing ophthalmological problems 12 days after start of antibody therapy (7 days after stopping OKT3). At no time was acute CMV infection ruled out as the underlying cause of the ophthalmological problems by investigation of direct CMV-antigen in peripheral blood leukocytes, viral DNA by polymerase chain reaction, or CMV-specific IgM [5].

We conclude that the occurrence of ophthalmological problems in this particular patient cannot be clearly related to OKT3 monoclonal antibody therapy. The underlying cause of visual loss could as well have been an ophthalmological manifestation of acute CMV infection.

Department of Medicine Jörg H. Horina  
Sabina Horn  
Herwig Holzer
Department of Ophthalmology Karl Franzens University  
Gerald Langmann  
A-8036 Graz, Austria.


Reply by authors

Sir,

CMV infection usually develops 4–6 months after transplantation, probably reactivation due to prolonged immunosuppression. The patient preoperatively was IgG anti-CMV antibody positive as usual transplant recipients in our centre. We have not seen chorioretinitis in over 1000 patients including over 200 treated with pulse solumedrol therapy.

Recently we studied CMV reactivation, and the results were presented at the 4th Congress of Asian Society of Transplantation (Dr Wie et al., August 1995). Using an immunohistochemical assay for CMV antigenaemia in peripheral blood, we found positive results in about 60% of transplant recipients, but no chorioretinitis was detected in high titre patients who also received solumedrol pulse therapy or OKT3 therapy.

We did not study CMV in the reported retinitis case because there were no other symptoms of CMV infection, e.g. fever, leukopaenia, CMV viral pneumonia, at the time