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Case Report

Cytomegalovirus colitis in a CMV-seropositive renal transplant recipient on triple drug therapy (including mycophenolate)

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Introduction

Infectious complications remain one of the major problems after renal transplantation [1]. With the recent use of more potent immunosuppressive drug regimens, such as the combination of cyclosporin (CsA), prednisone and mycophenolate mofetil (MMF), the incidence of acute rejection after renal transplantation can be reduced. The incidence of clinically important cytomegalovirus (CMV) disease however is increased in patients treated with this triple drug regimen [2–4]. Clinically important CMV colitis primarily due to vasculitis, a clinical entity well known in patients with AIDS, has been uncommon in renal transplant recipients in the last 10 years [5,6]. We describe a renal transplant patient, seropositive for CMV prior to transplantation, with CMV vasculitis of the colon, with an endoscopic image commonly associated with ischaemic colitis.

Case report

A 50-year-old Somalian man, with renal insufficiency due to hypertension, received his first cadaveric renal transplantation 1 month prior to admission. He was treated with CsA (150 mg b.i.d.), prednisone (10 mg/day) and MMF (2 g b.i.d.) as immunosuppressive therapy. No induction therapy was given. The recipient was CMV seropositive prior to transplantation. On admission the patient complained of general malaise and spiking fever (40°C) since 2 days, occurring predominantly in the morning. At physical examination no abnormalities, except fever, were found. Laboratory studies showed a serum creatinine of 185 μmol/l, blood urea nitrogen 11 mmol/l, ESR 5 mm/h, white blood cells 5×10^9/l (normal differentation), thrombocytes 212×10^9/l. An upright chest X-ray and an abdominal ultrasound were unremarkable. Blood and urine cultures for bacterial micro-organisms remained negative. CMV studies, including pp65 [7], and anti-CMV IgM were performed. Although both were negative, a presumptive diagnosis of CMV reactivation on clinical grounds was made and intravenous ganciclovir therapy was instituted (3.0 mg/kg twice daily). Within 36 h the fever resolved. Intravenous ganciclovir was stopped after 10 days. Unfortunately, two days later the patient again developed fever (38.5°C), this time accompanied by diffuse abdominal pain, nausea and bloody diarrhoea. No period of hypotension was observed. A colonoscopy reaching halfway along the descending colon was performed. The rectum and sigmoid showed the features of a severe ischemic colitis with submucosal haemorrhage and oedema without ulceration (Figure 1). In the descending colon a patchy vasculitis was present with slight oedema of the surrounding mucosa. The endoscopic aspect was consistant with either an ischaemic colitis or a vasculitis due to CMV, several biopsies were taken. A Doppler ultrasound of the abdominal arteries showed no thrombosis or dissection. Because of a strong suspicion of CMV colitis, therapy with ganciclovir was reinstituted, which resulted in a complete clinical recovery after 3 days. A repeated pp65 titer as well as an IgM anti CMV remained negative. Stool cultures, including two *Clostridium difficile* toxin assays were negative. Pathological examination of the colon biopsies revealed cytomegalovirus colitis. Inclusion bodies were found mainly in cells located in the wall or lining the lumen of submucosal blood vessels, showing features of vasculitis (Figure 2), and occasionally in epithelial cells. The diagnosis was confirmed immunohistochemically (Figure 3).

Discussion

The success of renal transplantation depends on the improved balance between rejection and infectious

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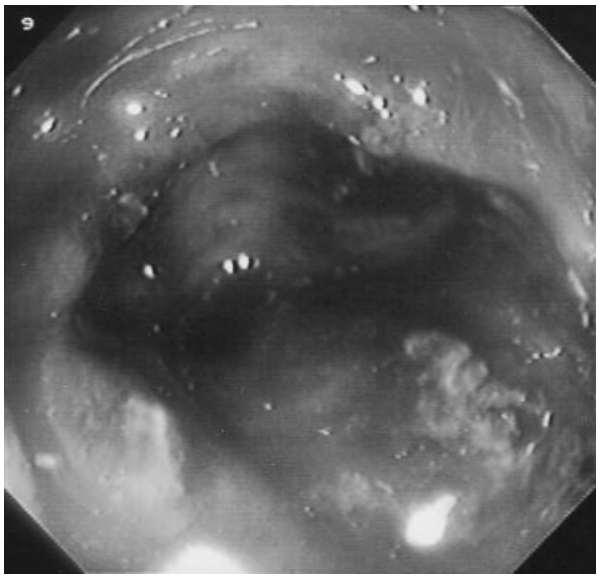

Fig. 1. The sigmoid colon showing severe submucosal haemorrhage and oedema.

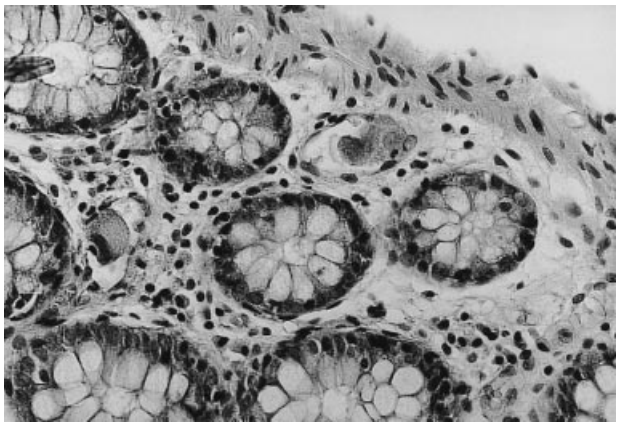

Fig. 2. Colon biopsy showing CMV inclusion bodies in cells lining the lumen of blood vessels in lamina propria (H&E × 360).

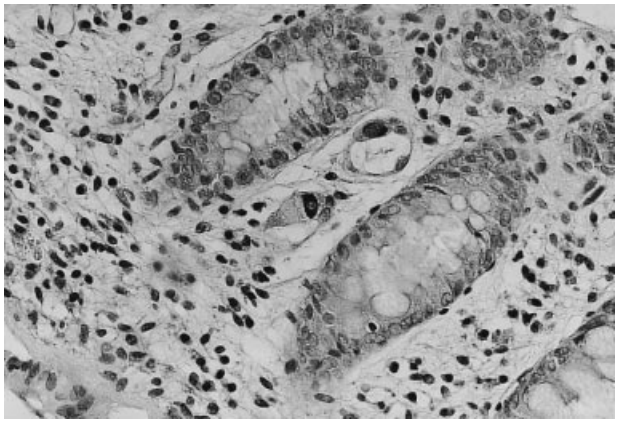

Fig. 3. Colon biopsy showing positive immunostaining of CMV inclusion bodies (immunohistochemical staining × 360).

complications. A new immunosuppressive drug, mycophenolate mofetil, has entered the scene in renal transplantation. The safety and efficacy of mycophenolate mofetil after renal transplantation has been studied in three large, double blind, controlled trials [2–4]. There is a higher risk for CMV disease in patients using MMF compared to control groups treated with placebo or azathioprine [8]. Our patient shows a severe reactivation of a CMV infection, resulting in a tissue invasive CMV vasculitis of the colon, with an ischaemic colitis. Surprisingly, on both occasions no CMV-IgM could be detected. One might speculate whether this was the result of impaired antibody production during this very severe CMV infection [9], or due to a diminished antibody production related to MMF [10]. The results of pathological examination of the colon biopsies make the diagnosis of tissue invasive CMV certain. The lesson to be learned from this CMV-seropositive patient developing CMV colitis after transplantation, is that the risk of CMV disease in patients being treated with MMF is increased and that the manifestation of CMV disease include severe tissue invasive forms. Furthermore, a high clinical suspicion for CMV disease and biopsies were necessary for prompt recognition and treatment in this patient, as customary screening methods for CMV disease remained negative. Most importantly however, clinicians must be aware of this increased risk, enabling them to respond adequately to cases like our patient.

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