Cytomegalovirus myocarditis following liver transplantation

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Summary: Cytomegalovirus (CMV) infections are commonly found in patients on immunosuppressive therapy following liver transplantation. However, acute myocarditis is an extremely rare manifestation of CMV infection in this setting. We report the case of a patient who developed acute myocarditis with severe biventricular failure with a cardiac ejection fraction of less than 10%, 6 weeks following orthotopic liver transplantation. Systemic CMV infection was diagnosed on the basis of a clinical viraemia, the presence of CMV antigen in urine, blood, and throat swab, and an associated four-fold rise in serum antibody titres to CMV. A full recovery ensued following treatment with standard anti-cardiac failure therapy and a 10 day course of intravenous ganciclovir.

Introduction

Systemic viral infections including cytomegalovirus (CMV) commonly occur in patients on immunosuppressive therapy following liver transplantation. Although successful resolution of CMV myocarditis has been reported previously following heart and renal transplantsations, successful treatment of this condition following liver transplantation has not been documented. We report the case of a patient who developed an acute CMV myocarditis following liver transplantation, which was successfully treated with ganciclovir.

Case report

A 21 year old female was admitted with a 2 week history of a dry cough, fevers, increasing dyspnoea, malaise and orthopnoea. An orthoptic liver transplant had been performed for end-stage cirrhosis secondary to autoimmune chronic active hepatitis 6 weeks previously. Both donor and recipient were CMV antibody negative and the recipient received six litres of blood (not screened for CMV) in the perioperative period. The immediate postoperative course was uneventful apart from an episode of acute cellular rejection treated with pulsed intravenous methyl prednisolone. Postoperative immunosuppressive therapy consisted of cyclosporine, prednisolone and azathioprine, the latter being discontinued at 4 weeks following liver transplant, because of bone marrow suppression. There was no previous or family history of heart or lung disease. On admission she was cyanosed, with a respiratory rate of 30 beats/minute and an irregular heart rate of 120 beats/minute. The jugular venous pressure was elevated to 6 cm above the sternal angle, the apex beat was displaced to the 6th intercostal space in the anterior axillary line and cardiac auscultation revealed a loud third heart sound. No murmurs were audible. Fine bibasal inspiratory crepitations were audible and a small right-sided pleural effusion was present. Hepatomegaly, minimal ascites and mild peripheral oedema were also noted.

Investigations revealed an arterial Po2 of 8 kPa (normal values on room air 10.6–13.3), PCO2 3.5 kPa (4.6–6) and pH 7.47 (7.35–7.45) on 21 of oxygen/minute. Leucocyte count was 4.6 × 10^9/l (48% lymphocytes), haemoglobin 10.5 g/dl and platelets 152 × 10^9/l. Serum sodium was 134 mmol/l, potassium 3.4 mmol/l, chloride 108 mmol/l, urea 11.1 mmol/l and creatinine 100 μmol/l. Serum albumin was 21 g/l, bilirubin 17 μmol/l, aspartate transaminase 135 IU/l (8–40), alanine transaminase 12 IU/l (5–42), alkaline phosphatase 111 IU/l (30–110). Although liver function was deranged on this admission, these values were significantly improved on pre-transplant levels.

Liver biopsy was not performed. An electrocardiogram (ECG), which was normal pre-operatively, demonstrated sinus tachycardia, right axis deviation and widespread T wave inversion (Figure 1). A chest X-ray revealed a small right-sided pleural effusion, cardiomegaly, bilateral upper lobe
venous dilatation and bibasal infiltrates consistent with acute left ventricular failure. Real-time echocardiography confirmed severe left ventricular dysfunction with an ejection fraction of 10%. The left ventricle and left atrium were dilated, but the right ventricle looked normal. Mild mitral regurgitation was observed and a small pericardial effusion was also noted.

Multiple blood, urine, throat and sputum cultures revealed no bacterial pathogens. CMV DNA was detected by polymerase chain reaction in blood, urine and throat washings. Additionally, early CMV antigen was detected by monoclonal antibody following 24 hour cell culture in the same samples indicating recent infection with CMV. There was no rise in antibody titre to Epstein–Barr virus, influenza A and B, mumps, adenovirus, toxoplasma, mycoplasma, chlamydia or coxsackie B. Treatment was commenced with intravenous frusemide, oxygen, digoxin, and full anticoagulation with heparin and warfarin. A 2 week course of intravenous ganciclovir (5 mg/kg/BD) was also administered. Immunosuppression was maintained with cyclosporine and prednisolone.

Following treatment, a rapid clinical recovery ensued with a repeat echocardiogram at 10 days demonstrating resolution of the pericardial effusion and marked improvement in left ventricular function with an ejection fraction of 63%. Full clinical and radiological resolution of the myocarditis had occurred by 6 months, at which time all cardiac medications were discontinued. ECG abnormalities had resolved and ejection fraction was 75% at 12 months.

Discussion

The importance of this case lies in the fact that it draws attention to a possible treatable cause of acute myocarditis in an immunosuppressed patient. CMV myocarditis is an extremely rare complication following organ transplantation and has previously only been reported in a post mortem study following liver transplantation. In the present report, the diagnosis of acute myocarditis was based on the development of painless acute severe cardiac failure with a left ventricular ejection fraction of 10% and ECG changes consistent with acute myocarditis. Systemic CMV infection was diagnosed on the basis of viraemic illness, an associated neutropenia, the presence of circulating early CMV antigen, and CMV DNA in blood urine and throat washings. An endomyocardial biopsy was not performed as it was felt that it would not substantially alter management. In addition, the myocardial lesion in viral myocarditis may be patchy in distribution and may not always be diagnosed on endomyocardial biopsy. In a recent report, the quantity of CMV present in blood
leucocytes using blot hybridization in patients following solid organ transplantation and with AIDS was shown to accurately reflect the presence of systemic CMV infection in viraemic patients. Although this method for detecting systemic CMV is still at an experimental stage, it may be useful in the future where tissue for histological examination is unavailable.

CMV is the most common opportunistic viral infection following liver transplantation and, although frequently asymptomatic, may be associated with serious complications including pneumonitis, encephalitis, nephritis and hepatitis. The rapidity of recovery in this case with ganciclovir is encouraging. Ganciclovir acts by inhibiting DNA synthesis thus blocking viral replication. There have been a number of studies demonstrating the benefit of ganciclovir in patients with systemic CMV infection post organ transplantation although none of these patients had a myocarditis.

There is experimental evidence suggesting that corticosteroids may be harmful in the early stages of viral myocarditis in animal models. It is important to note that this patient was maintained on corticosteroids and cyclosporine throughout the myocarditis without any ill effects, and azathioprine has since been reintroduced.

References

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