Pulmonary capillary leak syndrome associated with the use of intravenous cyclosporin

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Introduction

Pulmonary oedema due to pulmonary capillary leak syndrome during the use of cyclosporin, particularly when given intravenously, has been reported in some patients after bone marrow, liver, and renal transplantation \cite{1-4}. Suggested explanations for this effect have been a local high concentration of the drug in the pulmonary vessels when infused through a central line \cite{3}, or the solvent polyoxyethylated castor oil in the parenteral formulation of cyclosporin \cite{4}. However, this side-effect is not widely known and not listed in the drug information supplied by the company \cite{5}.

We report here on a patient who, after living-related transplantation, developed pulmonary oedema due to capillary leak syndrome that improved after converting from intravenous to oral cyclosporin.

Case report

A 38-year-old man with end-stage renal disease of uncertain aetiology who was on maintenance haemodialysis for 13 months, received on 23 March 1996 a donor kidney from his brother. His preoperative chest X-ray was normal. He received as immunosuppression prednisone, azathioprine, and cyclosporin. Cyclosporin was given during the first 4 postoperative days intravenously through a central line because of postoperative paralytic ileus. The cyclosporin dosage was 3 mg/kg b.w. per day, given over a 4-h period, and the trough level on day 3 was 156 ng/ml (monoclonal fluorescence polarization on TDx analyzer; Abbott Laboratories, Chicago, IL, USA).

During the first 3 days, the patient's daily urine output was 357, 1221 and 659 ml respectively. On the 3rd postoperative day he became dyspnoeic, crepitations were heard on chest examination, he was afebrile, the blood pressure was 180/70 to 135/60 mmHg and the heart rate 110/min. He was found to be severely hypoxic (pO\textsubscript{2}: 46 mmHg (6.1 kPa) on 12 litres of oxygen per minute via nasal canule), and the chest X-ray showed diffuse bilateral infiltrates. Despite a central venous pressure of only 4 cm H\textsubscript{2}O, our initial assessment was pulmonary congestion, so the patient was haemodialysed and 2 litres fluid were removed, but with no improvement in symptoms and chest X-ray findings. The following day the patient again had haemodialysis, with ultrafiltration of 3.2 litres water and a reduction of the body weight to below his dialysis 'dry weight'. However, despite this the chest infiltrates worsened. The temperature remained normal. Blood pressure was 170/90 mmHg and the white blood cell count was 14.4 x 10\textsuperscript{9}/l (having been 17.2 x 10\textsuperscript{9}/l the day after surgery). Sputum cultures revealed no growth. The pO\textsubscript{2} was 62–70 mmHg (8.3–9.3 kPa) while he was breathing 100% O\textsubscript{2} with a non-rebreathing mask.

At this stage it was felt that fluid overload had been ruled out as a cause of the pulmonary oedema. An echocardiogram was performed and confirmed normal left ventricular function. A Swan–Ganz catheter was inserted and indeed revealed a pulmonary capillary wedge pressure (PCWP) of 10 mmHg, indicating non-cardiogenic pulmonary oedema, and the patient was assumed to have developed adult respiratory distress syndrome (ARDS). As it was unlikely that opportunistic infections could develop so early in the course post-transplant and as there was no evidence of infection, a capillary leak syndrome related to i.v. cyclosporin was suspected. The i.v. cyclosporin was discontinued and replaced by oral cyclosporin. During the next 2 days the patient had one further session of ultrafiltration, removing 1 litre fluid, but again with no improvement in the X-ray findings.

Over the following days there was a gradual improvement of the oxygenation and the pulmonary infiltrates disappeared. The patient on discharge 25 days postoperatively had normal chest X-ray, and a serum creatinine level of 125 \textmu{}mol/l.
Discussion

This patient developed pulmonary oedema 3 days after living related transplantation. The central venous pressure was only 4 cm H₂O and the PCWP 10 mmHg. Although the PCWP was measured 3 h after ultrafiltration, we assume it should still be elevated if the pulmonary oedema and hypoxia, which did not improve after ultrafiltration, were caused by fluid overload. The echocardiogram showed normal left ventricle function. It was felt, therefore, that another cause of pulmonary oedema was present. In view of previous reports of capillary leak syndrome caused by i.v. cyclosporin [3,4], it was decided to discontinue it and replace it by oral cyclosporin. During the following days there was a gradual improvement of the oxygenation and chest infiltrates, despite the fact that there was no significant change in urine output and body weight during this period.

These findings support previous reports suggesting an effect of i.v. cyclosporin on the development of pulmonary oedema due to capillary leak syndrome. Transplant physicians should be aware of this rare association, because if not recognized early, it could lead to fatal complications [2]. Whether this action is due to local high concentrations of the drug when given through a central line, as in our patient, or is caused by the solvent, remains to be clarified.

References


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