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Co-administration of Caspofungin and Cyclosporine to a Kidney Transplant Patient with Pulmonary Aspergillus Infection

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A kidney transplant patient on cyclosporine treatment developed focal pneumonia due to Aspergillus fumigatus. The patient was not able to tolerate amphotericin B deoxycholate and was switched to caspofungin. The patient responded favourably without any evidence of toxicity from concomitant use of caspofungin and cylosporine.

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INTRODUCTION

Transplant patients require immunosuppressive therapy to prevent organ rejection. As a result, these patients commonly develop opportunistic infections such as aspergillosis. Mortality due to Aspergillus infection can approach 100% if it is not effectively treated. It is difficult to treat these invasive infections however, as some azoles are not effective or have many interactions with other drugs, and conventional amphotericin B is known to cause toxicity and unacceptable side-effects (1, 2).

Caspofungin is a new antifungal agent with a unique mechanism of action (3). Caspofungin stops fungal cell wall synthesis by inhibiting production of B-1,3-D glucan, an important component of the fungal cell wall, but one that is not present in mammalian cells (4). This novel mode of action is distinct from that of the azoles and polyenes agents which inhibit the synthesis of ergosterol in the fungal cell membrane (3, 5).

Caspofungin is approved for use in patients with invasive aspergillosis who are refractory or intolerant to amphotericin B. While caspofungin has been shown to be well tolerated, the concurrent use of caspofungin and cyclosporine is not recommended, because of transient liver enzyme elevations noted in healthy volunteers (3). This case report describes the treatment of a kidney transplant patient on cyclosporine who was diagnosed with a pulmonary Aspergillus infection. It is of particular interest because the patient was treated successfully with concurrent caspofungin and cyclosporine.

CASE REPORT

The patient was a 52-y-old male first diagnosed with insulin dependent diabetes mellitus in 1967. In 1991 the patient presented with right side hemiparesis that caused dysphasia. The following year the patient received a kidney transplant because of end stage diabetic nephropathy. He had received several immunosuppressive therapeutic regimens over the past few years to prevent organ rejection. These included azathioprine (75 mg/d), methylprednisolone (4 mg/d), and cyclosporine (100 mg twice daily).

In June 2002, lung abnormalities were detected by X-ray. High resolution CT scans (HRCT) revealed small cavitations in both lungs. Aspergillus fumigatus was cultured from bronchoalveolar lavage (BAL) specimens. The patient received 2 doses of amphotericin B deoxycholate (50+100 mg). His serum creatinine levels increased from 112 μmol/l to 300 μmol/l and plasma urea increased from 15.8 mmol/L to 30 mmol/L, making it necessary to stop therapy. Caspofungin (35 mg/d) was initiated. The dose was increased to 50 mg/d 5 d later, and the patient continued therapy almost 2 months (Fig. 1). The patient was hospitalized on d 55 with heart failure due to pulmonary edema, although this was probably related to prior septal infarction and coronary artery disease. After caspofungin treatment the patient received oral itraconazole (100 mg twice daily). The patient remained on cyclosporin treatment and the dose was tapered to achieve plasma levels of 100 μg/L.

On therapy with caspofungin the symptoms of infection disappeared and the Aspergillus lesions diminished appreciably. During

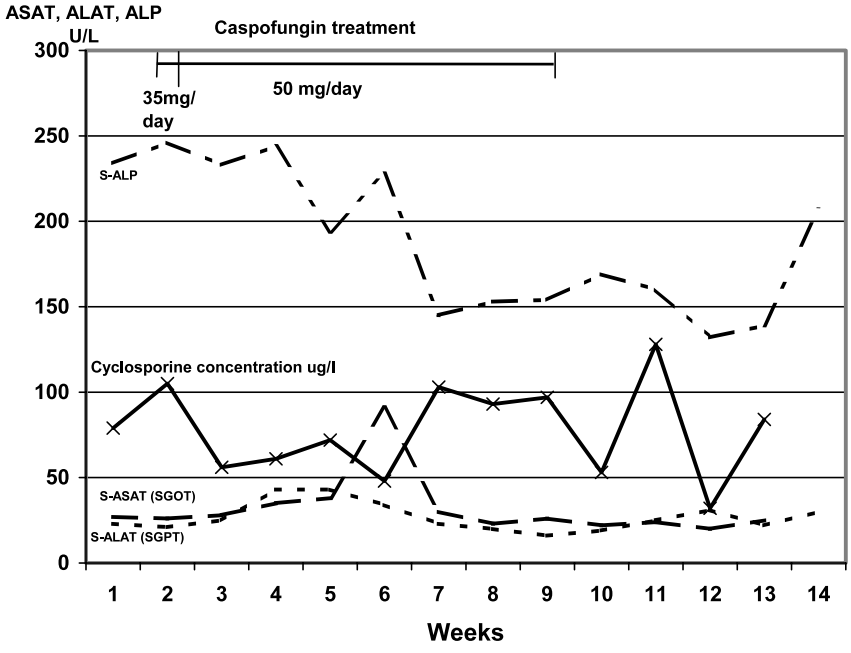

Fig. 1. Levels of liver enzymes (U/l) and cyclosporine concentration (μg/l) during Caspofungin treatment.

the time the patient received caspofungin, and following treatment, all liver enzyme values were in the normal range (< 50 U/l) except for a transient increase in ASAT (91 U/l) on caspofungin d 20. The patient was free of clinical signs and symptoms or X-ray findings consistent with Aspergillus infection until death 7 months later. The cause of death was severe coronary artery disease with myocardial infarction. At autopsy no focal lesions or signs of Aspergillus infection were detected.

DISCUSSION

The case presented here describes an immunocompromised kidney transplant patient who was diagnosed with invasive aspergillosis. This patient was not able to tolerate amphotericin B, but was treated successfully with caspofungin. Despite the severity of illness and concomitant use of cyclosporin in our patient, caspofungin was effective and well tolerated.

Caspofungin may represent a substantial improvement over existing therapy for patients who develop to aspergillosis while receiving immunosuppressive regimens. Although co-administration of caspofungin and cyclosporine was not a cause for toxicity in our patient, further studies on concomitant use are needed.

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