Case reports

Candida Parapsilosis Fungaemia Treated Unsuccessfully with Amphotericin B and Fluconazole but Eliminated with Caspofungin: A Case Report

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ABSTRACT

A case of Candida parapsilosis Hickman catheter infection with fungaemia presenting with severe hypoxia, lactic acidosis and renal failure is described. Four months previously, the Hickman catheter had become infected with Candida parapsilosis (sensitive to fluconazole and amphotericin B) with blood cultures remaining positive despite an intravenous course of fluconazole 200 mg 12-hourly increasing to 400 mg-12-hourly. Subsequently, treatment with an amphotericin B infusion (30 mg over 24 hours) for five days was associated with a progressive increase in serum creatinine from 0.042 mmol/L to 0.278 mmol/L with blood cultures remaining positive. While arrangements were being made to remove and replace the catheter via a thoracotomy, the patient developed severe hypoxia, lactic acidosis and renal failure and was admitted to the intensive care unit for further management.

An intravenous course of caspofungin (70 mg over 1 hour followed by 50 mg over 1 hour, daily) was associated with negative blood cultures and a normal plasma C-reactive protein for the first time in four months. The hypoxia was managed with spontaneous ventilation and high inspired oxygen concentrations, and the anaemia was treated with red blood cell transfusions. A rapid reversal of the respiratory failure and lactic acidosis occurred and the patient was discharged home from the intensive care unit after 10 days to continue the caspofungin infusions for a total of 6 weeks. She has subsequently remained well with negative blood cultures two months later. (Critical Care and Resuscitation 2003; 5: 20-23)

Key words: Candida parapsilosis, fungaemia, caspofungin, Hickman catheter, catheter-related infection

A case of Candida parapsilosis Hickman catheter infection with persistent fungaemia is presented. The fungaemia was resistant to a six week course of fluconazole and renal insufficiency developed following a 5 day course of amphotericin B. While awaiting an operation to remove and replace the infected Hickman catheter, the patient developed severe hypoxia, lactic acidosis, anaemia and renal failure. A daily caspofungin infusion led to a resolution of the resistant fungaemia, lung infiltrates and respiratory failure.

The patient was discharged from hospital 10 days after her admission to the intensive care unit to continue her parenteral nutrition and an additional 4 weeks of caspofungin therapy (50 mg i.v. daily) at home. She has subsequently remained well with negative blood cultures two months later.

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CASE REPORT

A 45 year old woman with a past history of intestinal pseudo-obstruction required a Hickman catheter for 22 years for long-term home total parenteral nutrition. During the course of her prolonged intra-venous nutrition she developed superior and inferior vena cava thrombosis. Central venous access became impossible by the standard percutaneous routes and her most recent central venous Hickman catheter had been inserted with difficulty (due to extensive thoracic wall venous anastomotic channels) directly into the right atrium via a thoracotomy.

While her current catheter had been infection free, after 12 months it became infected with a fluconazole and amphotericin B sensitive Candida parapsilosis. Despite a 6 week intravenous course of fluconazole (200 mg 12-hourly for 7 days increasing to 400 mg 12-hourly for 5 weeks), her blood cultures remained positive. A daily amphotericin B infusion (30 mg over 24 hours) for five days caused a progressive increase in serum creatinine from 0.042 mmol/L to 0.278 mmol/L, so it was discontinued as her condition of inaccessible central veins made the standard management of renal failure with haemodialysis impossible. As the fungaemia remained, arrangements were made to remove and replace the catheter via a thoracotomy. However, before this could happen the patient developed severe dyspnoea and was admitted to the intensive care unit severely hypoxic, anaemic with lactic acidosis and renal failure.

On presentation her blood pressure was 85/40 mmHg, respiratory rate 55 per minute, pulse 55 beats per minute (with numerous ventricular ectopic beats) and her temperature was 38.8°C. The initial arterial blood gas while breathing spontaneously (FiO₂ 100% using a circuit with an inspiratory flow rate of 50 L/min and facemask) revealed a PO₂ 47 mmHg, PCO₂ 24 mmHg, pH of 7.33, HCO₃⁻ 12 mmol/L and a lactate of 10.4 mmol/L. The laboratory investigations revealed a plasma sodium of 136 mmol/L, potassium 3.9 mmol/L, creatinine 0.433 mmol/L, lactate dehydrogenase 544 U/L, white cell count 12.7 x 10⁹/L and haemoglobin 49 g/L. A chest X-ray revealed generalised interstitial and alveolar infiltrates (Figure 1).

A course of caspofungin (70 mg i.v. over 1 hour with 50 mg i.v. daily over 1 hour) was associated with a rapid reversal of the respiratory failure, negative Candida parapsilosis blood cultures and within 12 days a normal plasma C-reactive protein (CRP) level (4 mg/L) for the first time in four months. The hypoxia was managed with spontaneous ventilation and high inspired oxygen concentrations and the anaemia was treated with 5 units of red blood cells transfused during her first 4 days in the intensive care unit.

Her temperature decreased to 36.6°C within 12 hours following the first infusion of caspofungin. The blood gas, lactate, haemoglobin and CRP levels during the first eight days of her intensive care unit stay are shown in table 1. The chest X-ray on the 10th day is also shown (figure 2).
The patient was discharged home from the intensive care unit after 10 days to maintain the caspofungin infusions (50 mg i.v. daily over 1 hour) for a total of 6 weeks. She has remained well with negative blood cultures two months later.

DISCUSSION

A candida infected central venous catheter with fungaemia in the absence of any embolic invasive infection is often managed by removal of the catheter and a short course of antifungal therapy. While the infection is often responsive to fluconazole or amphotericin B, if the infected catheter is unable to be removed the infection is usually resistant to treatment.

Caspofungin is a semisynthetic lipopeptide compound synthesised from a fermentation product of Glarea lozoyensis. It inhibits the synthesis of 1,3-beta-D-glucan which is a key step in fungal cell wall biosynthesis. It was initially marketed for the treatment of invasive aspergillosis in patients who were refractory or intolerant to other antifungal agents. However, as it has activity against fluconazole and amphotericin B resistant Candida species (e.g. C. albicans, C. tropicalis, C. parapsilosis, C. dublinensis, C. glabrata, C. guilliermondii, C. kefyr, C. krusei, C. lipolytica, C. lusitaniae, C. pseudotropicalis) it has also been recommended in these cases or in patients in who are intolerant of fluconazole and amphotericin B.

Caspofungin is administered intravenously with a standard adult dose of 70 mg initially (diluted in 0.9% saline or sterile water but not 5% dextrose) and is infused over 1 hour. This is followed by 50 mg daily. It has a half-life of 11 hours and is cleared from the circulation largely by redistribution rather than excretion or biotransformation. As it is not excreted by the kidneys the dose is not modified in renal failure. The agent is remarkably free of major adverse reactions although minor side-effects of fever, headache, diarrhoea, nausea and vomiting can occur.

In the patient described, the fungaemia was unresponsive to fluconazole and renal insufficiency developed with a 24 hour infusion of amphotericin B. While a commercial liposomal amphotericin B preparation (AmBisome®) is associated with less nephrotoxicity, compared with standard amphotericin B, the reason for this may be due to a slower delivery of the liposomal bound drug to the tissues, a hypothesis that is supported by one prospective randomised study in 80 patients with suspected or proven fungal infections that demonstrated a reduction in chills, fever, vomiting and nephrotoxicity (comparable with liposomal amphotericin B) and an improvement in mortality when amphotericin B (0.97 mg/kg) was infused over 24 hours when compared with an amphotericin B (0.95 mg/kg) infusion over 4-hours.

With this in mind it was felt that caspofungin should be tried in our patient rather than liposomal amphotericin B and was successful in clearing the resistant fungaemia and resolving the associated respiratory failure.