Septic bilateral pulmonary candidiasis successfully treated with anidulafungin therapy in two patients with peritoneal carcinomatosis

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Sir,

Although recovery of Candida from the respiratory tract is common, primary Candida pneumonia is an extremely rare occurrence, and has been described only in patients with severe forms of immunosuppression.1 Here we describe two patients with peritoneal carcinomatosis undergoing neoadjuvant chemotherapy plus extensive surgery who developed bilateral pulmonary candidiasis. Written consent for publication was obtained from each patient.

Case 1: a 67-year-old woman was admitted to our institution with a diagnosis of peritoneal carcinomatosis from lower rectal cancer. She underwent neoadjuvant systemic chemotherapy (FOLFOX; leucovorin, fluorouracil and oxaliplatin) and extensive surgery, including lower rectal resection with colo-anal anastomosis, pelvic and parietal peritoneectomy, ameontectomy, bilateral hysteroadnexectomy and intra-peritoneal hyperthermic chemotherapy (IPHC) with oxaliplatin. She had a port-a-cath (PAC) in place for chemotherapy in and a central venous catheter (CVC) placed in the internal jugular vein. On day 9 the patient developed fever (39°C) and signs of inflammatory systemic response. After three sets of blood cultures were drawn, empirical therapy with meropenem, vancomycin and fluconazole was started. On day 10 the blood cultures were negative and the CVC tip grew only two to three colonies of Candida spp. The patient developed severe respiratory failure, and chest CT demonstrated multiple, peripheral, nodular lesions involving both lungs (see Figure 1). Bronchoalveolar lavage (BAL) culture yielded Candida spp. On day 12 all blood cultures and culture of the removed PAC yielded Candida albicans plus Candida famata, and anidulafungin therapy was started at a loading dose of 200 mg followed by 100 mg every 24 h. Transoesophageal echocardiography (TEE) performed at the time of blood culture positivity excluded infectious endocarditis (IE). Fundoscopic examination revealed retinal exudates, and voriconazole was added to the therapy. After 15 days of anidulafungin a new CT scan showed disappearance of lung lesions, and the patient was discharged after 26 days of hospital stay. The 8 month follow-up was negative for relapse of infection.

Case 2: a 61-year-old woman was admitted to our institution with a diagnosis of peritoneal carcinomatosis from advanced gastric cancer. The patient was initially treated with neoadjuvant chemotherapy (cisplatin, fluorouracil and taxotere), and then underwent surgical intervention of peritonectomy, total gastrectomy plus IPHC with oxaliplatin. She had a PAC in place used for intravenous chemotherapy. After a post-operative intensive care unit (ICU) stay of 5 days the patient was transferred to a general ward. However, on day 12 the patient presented with low-grade fever, anorexia and leucocytosis. Multiple sets of blood cultures were drawn. On day 15 the patient developed severe sepsis and respiratory failure requiring non-invasive mechanical ventilation. Cultures of PAC, BAL and blood all grew C. albicans. A chest CT showed bilateral infiltrates. IE was ruled out by TEE. The patient was treated for 14 days with anidulafungin therapy (loading dose of 200 mg and then 100 mg every 24 h) followed

Figure 1. Radiological features of one patient (case 1) with septic pulmonary candidiasis at diagnosis (a) and after anidulafungin therapy (b).
by oral fluconazole for an additional 10 days with good response. A CT scan performed after 20 days demonstrated resolution of pulmonary lesions. The 6 month follow-up was negative.

Candida pneumonia is an extremely rare disease, associated with high mortality rates. A pulmonary infection caused by Candida spp. may exist in two forms: a very rare primary pneumonia due to aspiration of oropharyngeal material; and a relatively more common secondary pneumonia due to haematogenously originating from a distant site of infection. The predominant origin of septic pulmonary embolism due to Candida spp. are right-sided fungal endocarditis, CVC infection, central venous thrombophlebitis and drug addiction.

The presence of Candida in respiratory specimens may be due to contamination and there are no specific clinical and radiological pictures. The clinical syndrome is usually dominated by signs and symptoms of systemic inflammatory syndrome, while the radiographic features include a miliary nodular pattern, with feeding-vessel sign, ground-glass opacity, small nodules or multiple larger nodules with ill-defined borders randomly distributed in bilateral lungs. This pattern was prevalent in the two patients presented here. Other less common CT findings include air-space consolidation, pleural effusion, cavitation and thickening of the bronchial walls.

Conclusive diagnosis requires demonstration of the organism in lung tissues. Our two cases were not confirmed by biopsy but certain points strongly favoured the diagnosis: (i) the patients were immunocompromised; (ii) Candida spp. were repeatedly isolated from bronchial samples; (iii) tracheal and bronchial specimen cultures and blood cultures were negative for pyogenic organisms; (iv) PAC cultures were positive for Candida spp; (v) patients failed to respond to ordinary antibiotics; and (vi) there was a good clinical as well as radiological response to antifungal therapy.

To date, this is the first report of pulmonary candidiasis treated with anidulafungin therapy. Recently, Crandon et al. studied the bronchopulmonary penetration of intravenous voriconazole and anidulafungin given in combination in healthy adults, and found good anidulafungin concentrations in alveolar macrophages and optimal lung distribution. Another study found the combination of anidulafungin and voriconazole synergistic at a dosage of 5 mg/kg/day in neutropenic rabbits with experimental invasive pulmonary aspergillosis. These data seem to support the clinical use of this drug alone or in combination with voriconazole for the treatment of Candida lung infections.

In conclusion, we have described two cases of bilateral septic pulmonary candidiasis successfully treated with anidulafungin therapy. This report suggests a potential role for anidulafungin in the treatment of pulmonary fungal infections.

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**The use of linezolid in the treatment of paediatric patients with infections caused by enterococci including strains resistant to vancomycin**

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