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Medical Mycology Case Reports

Recurrent *Mucor indicus* central venous catheter infection in a five year old child on long term parenteral nutrition for short gut syndrome: could gut translocation be responsible?

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ARTICLE INFO	ABSTRACT
	A five year old girl with life-long TPN dependence for short gut syndrome presented with two episodes of non-fatal *Mucor indicus* central line associated blood stream infection (CLABSI). Each episode occurred fifteen months apart, without any evidence of ongoing mould infection whilst off antifungal therapy in the intervening time period. Both episodes were treated with removal of the infected central venous catheter (CVC) and 6 weeks of intravenous liposomal amphotericin B and/or posaconazole, with good clinical, microbiological, and radiological response. The possibility of gut translocation is supported by the repeated isolation of *Mucor indicus* in cases of intestinal mucormycosis. To our knowledge, this is the first case of recurrent episodes of blood culture positive mucormycosis in a single patient. *Mucor indicus* blood stream infection may differ significantly from invasive mucormycosis caused by other species.

1. Introduction

Invasive mucormycosis is a condition which primarily occurs in immunosuppressed patients, including those with diabetes mellitus, and is associated with significant morbidity and a high mortality rate. Typical infection sites include pulmonary, respiratory sinuses, cerebral, gastrointestinal (GI), and cutaneous infections [1,2]. Mucormycosis is also associated with intravenous drug use, in whom hematologically spread cerebral disease is overrepresented [3]. Central venous catheter (CVC) associated mucormycosis is an uncommon clinical entity; a systematic review of healthcare associated mucormycosis published in 2012 identified only 26 vascular catheter-associated infections from a total of 169 cases [2]; on review of the cited cases many of these did not meet criteria for CLABSI. The overall case fatality rate of mucormycosis is 47–56 % [1,3]. Optimal treatment requires IV antifungal therapy, with amphotericin B being first line, reversal of immunosuppression when possible, and aggressive surgical debridement [1].

Mucor indicus is a ubiquitous organism which is ethanol producing and high in omega-6 fatty acids. It is thus commonly used in industrial applications and in the fermentation of foods and beverages for human consumption [4]. It is occasionally implicated in human disease, particularly in gastrointestinal mucormycosis and cutaneous infection [5–15].

2. Case presentation

The patient, a five-year-old girl, was delivered at 30 weeks gestational age, with an antenatal diagnosis of gastroschisis requiring post-natal surgical resection of a long segment of jejunum, the entire ileum, as well as the ascending and transverse colon. She was dependent on parenteral nutrition from birth. At age 23 months a Serial Transverse Enteroplasty Procedure (STEP) was completed to increase the length and absorptive capacity of her remaining intestinal tract. Unfortunately she thereafter developed substantial gut dysmotility, and her intestinal tract became progressively more dilated and thin-walled with a high degree of stasis.

The patient experienced frequent bacterial CVC infections whilst receiving home parenteral nutrition. In 2022, at the age of four years, she presented with fever and rigors, and two sets of blood cultures were drawn from the CVC on day 0, with one of those blood cultures containing the line lock fluid from the central line. Empiric antibiotics were commenced. Both blood cultures returned positive for a zygomycete on day 2, which was soon after identified as *Mucor indicus*. Identification was achieved by conventional methods, which typically demonstrate deep yellow colonies with maximal growth at 42 °C, with microscopy demonstrating long, sympodial-branched sporangiophores. Identification was confirmed by molecular methods. The patient was commenced

on IV combination therapy with liposomal amphotericin B 5mg/kg daily and posaconazole 8mg/kg 12hrly on day 1 then daily thereafter, and the infected CVC was removed urgently. A CT head, chest, abdomen and pelvis was completed on day 4, which did not show evidence of disseminated disease. Ophthalmological examination was normal, and there were no cutaneous lesions. Immunological testing (including total immunoglobulins, neutrophil function, lymphocyte subsets, vaccine responses, CH50, and AH50) did not reveal any underlying immuno-deficiency. Fevers resolved on day 4, promptly after commencement of antifungal therapy. Susceptibility testing demonstrated an amphotericin B MIC of 0.5mg/L, and posaconazole MIC of 0.5mg/L. Given her excellent improvement at day 14, with therapeutic serum posaconazole levels of 1.7mg/L, the decision was made to switch to IV posaconazole monotherapy to complete a total of 6 weeks antifungal treatment via temporary PICC line, after which a new, tunneled CVC was inserted on the opposite side to the initial infection. Due to a suspected exogenous source of the CVC infection, TauroLockTM and additional home nursing supports were arranged on discharge to reduce the risk of recurrent CVC infections in the future.

Over the subsequent fifteen months, the patient did not have any further episodes of line sepsis. She was on long term amoxicillin-clavulanic acid, initiated by her primary team for suspected intestinal bacterial overgrowth and as a prokinetic agent to optimise her tolerance of enteral nutrition. Her intake consisted of high-calorie gastrostomy feeds only, and she had weaned off parenteral nutrition for almost two months. In 2023, on day 436, she presented with feed intolerance and significant abdominal distension with pneumatosis coli on abdominal xray. Blood cultures were collected, gut rest commenced, and IV mer-openem given for 48 hours whilst awaiting culture results and clinical progress. Symptoms improved, although significant electrolyte distur-bance prevented discharge home.

Three weeks later, on day 456, whilst the patient was still admitted to hospital, she developed a fever and dry cough. Blood cultures were collected, and IV daptomycin and meropenem were commenced due to a history of drug allergies. Two blood cultures flagged positive for a zygomycete, and IV amphotericin B and posaconazole were commenced on day 458 at the same doses used during the previous episode. Urgent CVC removal was arranged and the line tip was sent for culture; this also grew the same zygomycete, which was later confirmed as *M. indicus* by DNA sequencing. Broth microdilution demonstrated an amphotericin B MIC of 0.5mg/L and a posaconazole MIC of 1mg/L. CT chest this time demonstrated multiple lung nodules up to 10mm in diameter noted throughout both lungs, some with surrounding ground-glass opacity. CT brain and abdomen did not show any evidence of fungal disease, skin and ophthalmological examinations were normal. The patient's fever resolved on day 460 (after approximately 48 hours of antifungal ther-apy) and CRP steadily improved from a peak of 88.1mg/L, however her dry cough persisted and CT chest findings appeared to have worsening ground-glass opacity on repeat CT imaging on day 473. Biopsy was deemed high risk due to the proximity of the larger nodules to vascular structures, thus a bronchoalveolar lavage (BAL) was completed. BAL cultures grew Haemophilus influenzae, for which a 5 day course of ceftriaxone was administered. The patient's cough gradually improved thereafter. Due to lung changes of unclear aetiology, the decision was made to treat with 6 weeks of dual antifungal therapy; after an initial posaconazole level of 0.9 mg/L, the posaconazole dose was increased to 10mg/kg daily to achieve a posaconazole level of 2.3mg/L. CT chest at the end of therapy demonstrated resolution of the lung nodules. The patient has remained well off antifungal therapy over the past 16 weeks.

3. Discussion

This incredibly rare case of a child who has had *M. indicus* fungaemia twice in her lifetime, without progressing to severe disease on either occasion, highlights some interesting questions and concepts regarding *M. indicus* pathogenesis and disease progression in the relatively

immunocompetent host. A PubMed search was conducted for the phrase "*Mucor indicus*", and all cases related to human infection were reviewed. Patient ages ranged from 6 months to 82 years, with no apparent pre-dilection for onset at the extremes of age. Of the eleven human cases outlined, five had no known immunosuppressing conditions; this included two patients with gastrointestinal mucormycosis, one with concurrent fungaemia [6–16]. This organism is thus capable of causing invasive infection in seemingly immunocompetent individuals.

With regard to the source of infection, there are some suggestions that *M. indicus* infection often originates from the gastrointestinal tract [2,3,6,8,9,15]; this would potentially explain recurrent CLABSI's in our patient. Interestingly, in our case, there was never a diagnosis of active mucormycosis of the intestinal tract, however there was clear evidence of compromised mucosal integrity with pneumatosis coli on xray at presentation prior to the second episode. It is theoretically possible that long-term use of amoxicillin-clavulanic acid predisposed this patient to heavy GI colonisation with fungi. The extensive use of *M. indicus* in human food and beverage production may also explain its over-representation in gastrointestinal mucormycosis [2,4], though it is un-clear whether this would explain its occurrence in our patient, in whom all enteral nutrition is provided via commercially prepared gastrostomy feeds. The possibility of a cutaneous or iatrogenic source of infection in our patient still exists, and certainly there have been outbreaks of mucormycosis which were traced back to the same environmental source [2], however in our patient's case there was no evidence of cutaneous infection at the CVC site or tunnel, and the chance of having the same environmental source of infection is reduced by the fact that the first infection was acquired at home whilst the second was acquired in hospital.

The recurrent adherence of this organism to the CVC of our patient, as well as one other reported case of infected prosthetic material in an implanted cardiac device [11], may suggest that *M. indicus* is capable of biofilm formation. These cases suggest that the removal of prosthetic material should be considered in patients with associated *M. indicus* infection.

Finally, the excellent clinical outcome for our patient on both occa-sions indicates that some optimism can be maintained when managing patients with a similar presentation. Fungaemia due to Mucorales is an uncommon finding, and little is known about fungaemia as a prognostic marker. The only other published case of *M. indicus* fungaemia also survived [8], thus indicating that *M. indicus* fungaemia may have a good outcome when infection occurs without evidence of disseminated disease.

4. Conclusion

We present the first case of a child with recurrent episodes of *Mucor indicus* central line associated blood stream infection. This case suggests that assessment for a gastrointestinal source should be undertaken when this organism is isolated in blood cultures. A good clinical outcome may be achieved for immunocompetent patients with this infection, provided there is no evidence of disseminated disease, the infected medical device is removed promptly, and a course of antifungal therapy is administered.

Conflict of interest

There are none.

Ethical Form

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CRediT authorship contribution statement

Sarah Allen: Writing – review & editing, Writing – original draft, Project administration, Investigation, Data curation, Conceptualization.

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