CASE REPORT

Pseudozyma spp catheter-associated blood stream infection, an emerging pathogen and brief literature review

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SUMMARY

Pseudozyma spp are amorphic yeasts. They are commonly plant pathogens, but rarely cause invasive fungal disease in humans. Only three cases of central venous catheter (CVC)-associated blood stream infections due to this organism have been reported in the literature. Main underlying risk factors for *Pseudozyma* spp infection are bowel surgery, CVC and total parenteral nutrition. We present a rare case of *Pseudozyma* spp catheter-associated blood stream infection that was successfully treated with antifungal therapy and removal of CVC. It is important to recognise and differentiate this species from other yeasts as it may require the use of amphotericin B or voriconazole instead of fluconazole, to which the organism is variably resistant.

BACKGROUND

The incidence of invasive fungal infections is increasing, mainly in patient with haematological malignancy, transplant recipient or in individuals on immunosuppressive therapy. *Pseudozyma* are amorphic yeast in the Ustilaginomycetes class. *Pseudozyma* spp are common pathogen in plants that infrequently cause invasive disease in humans. Automated identifications system may mistake this organism for *Cryptococcus*. It is very important to recognise *Pseudozyma* spp as, unlike *Cryptococcus*, *Pseudozyma* frequently have high-level resistant to fluconazole.

CASE PRESENTATION

A 52-year-old woman with long-standing Crohn's disease who has required multiple bowel surgeries, including total colectomy with ileostomy, presented to the emergency room with symptoms of 3 days of fever, headache and generalised weakness. Three months earlier she had undergone port-a-cath placement in the left subclavian vein in order to receive intravenous hydration. Her medical history includes multiple central venous catheters (CVC)-associated blood stream infections with methicillin-sensitive *Staphylococcus aureus* and *Klebsiella pneumoniae*. Examination revealed a temperature of 100.2°F, heart rate 97/min, blood pressure 125/77 mm Hg and respiratory rate 18/min. The port-a-cath was functioning well and there was no surrounding erythema, induration or tenderness. The remainder of physical examination was unremarkable. Initial laboratory work-up showed a white cell count of 5300/μL, haemoglobin 12 g/dL, platelet count 149 000/μL, blood urea nitrogen 20 mg/dL and serum creatinine 1.0 mg/dL. She was started empirically on broad-spectrum antibiotics for possible catheter-associated blood stream infection. Initial blood cultures drawn from the port-a-cath grew yeast on day 2, identified as *Cryptococcus* spp by the VITEK 2 system (BioMérieuxInc, Durham, North Carolina, USA). Antimicrobial therapy was switched to fluconazole. A subsequent cryptococcal serum antigen test returned negative. Repeat blood cultures on hospital day 3 were also positive for yeast. The organism was sent to ARUP National Reference Laboratory for further identification. On day 19, the yeast was identified by using DNA sequencing of the internal transcribed spacers regions 1 and 2. The organism showed 98.4% match with *Pseudozyma* spp. Microscopic morphological characteristics correlated with the DNA sequencing identification. Identification to the species level was not able to be obtained. Based on severity of infection, fluconazole was changed to voriconazole and the port-a-cath was removed. No other obvious source of fungaemia was found. Transthoracic echocardiogram did not show evidence of endocarditis. Dilated ophthalmic examination was unremarkable. Subsequent blood cultures remained negative. Owing to delayed identification of the yeast and clinical improvement with voriconazole, susceptibility test was not requested. She received a total 2 weeks of voriconazole.

OUTCOME AND FOLLOW-UP

More than a year later she has not had recurrent fungaemia.

DISCUSSION

The incidence of invasive fungal infections has increased dramatically over recent decades. The majority of these infections occur in patients with haematological malignancies or other immunosuppressive conditions.[1] The reason for this increase is multifactorial and includes impaired host defence, haematopoietic stem cell transplantation, ablative radiation therapy and use of immunosuppressive agents.[2] *Pseudozyma* spp is amorphic yeast related to the smut fungi in the genus *Ustilago*. They are mainly isolated as pathogen from plants.[3] In 1985, Bandoni established the genus *Pseudozyma* with the species *P. prolifica*.[4] Subsequent reports suggested that this genus included more than 10 species with a broad range of phenotypic features.[3 5] However, few invasive human infections due to this species

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have been reported and little is known about its pathogenicity. As *Pseudozyma* spp are associated with infections of corn plants, a detailed dietary history of corn consumption and in particular of huitlacoche, a popular Mexican dish made from *Ustilago maydis* (used in quesadillas and other tortilla-based foods and soups) may be important when evaluating patients with invasive disease caused by these yeasts.[6] In the present case there was no history of corn or corn product consumption. Similarly in the literature the majority of cases did not describe excessive exposure to corn consumption. An exception is the case reported by Lin *et al*[7] in which the patient reported repeated consumption of corn tortilla chips.

The current case represents the fifth report of *Pseudozyma* spp blood stream infection associated with CVC.[7 8–10] Interestingly, including the present case report, four of these cases of *Pseudozyma* spp CVC infection reported in the literature also involved patients with a history of bowel surgery resulting in short bowel syndrome.[7–9] This association with short bowel syndrome is noteworthy. The fifth case involved a low-birthweight neonate.[10] In two of these cases the patients were receiving total parenteral nutrition (TPN). In all previous cases the CVC were removed, as was done in the current case. Otherwise, the spectrum of disease for this yeast includes brain abscess, pulmonary and mycetoma infection.[11–13] Two patients had an underlying malignancy. In the three cases of fungaemia due to *Pseudozyma* spp reported by Sugita *et al*[3] clinical features and clinical relevance of the isolated organisms were not presented. However, underlying conditions were listed as pneumothorax, leptospirosis, aseptic meningitis and asthma. With the exception of two cases, all the reported cases of *Pseudozyma* spp infection were in adults. The two paediatric cases reported were a *Pseudozyma aphidis* blood stream infection in a 7-year-old child and a second case reported in a 3-day-old neonate with low birth weight but without clear source.[7 10] *Ustilago* fungi also have been associated with bronchial asthma and hypersensitivity pneumonitis.[14] Recently, Mekha *et al* reported three new *Pseudozyma* spp which were isolated from clinical specimens of Thai patients. These species showed relatively low sensitivity to azole including voriconazole but were sensitive to amphotericin B. Clinical presentation and prognosis of the patients were not mentioned in the report.[15]

Identification of *Pseudozyma* spp in most of the reported cases required DNA sequencing. In past reports *Pseudozyma* spp was often initially misidentified as *Cryptococcus laurentii* by the VITEK 2 system (BioMérieuxInc, Durham, North Carolina, USA).[9] In most of the reported cases the organism was susceptible to amphotericin B, itraconzole and voriconazole but had variable susceptibility (sensitive, intermediate or resistant) to fluconazole. Interestingly three new species mentioned by Mekha *et al* showed relatively low susceptibility to voriconazole. In all reported cases *Pseudozyma* spp were resistant to echinocandins and flucytosine. In the present case susceptibility testing was not done as the patient had clinically improved after port-a-cath removal and initiation of voriconazole. It is possible that port-a-cath removal alone would have been sufficient to treat the early infection.

Pseudozyma spp are rare fungal cause of invasive disease but this and other case reports indicate that it cannot be discarded as an environmental contaminant. Patients with a history of bowel surgery who are receiving TPN through a CVC appear at increased risk for this infection. It is important to recognise and differentiate this species from other yeasts as it may require the use of amphotericin B or voriconazole instead of fluconazole to which the organism is variably resistant. There is no role for echinocandins or flucytosine to treat this infection.

Learning points

- *Pseudozyma* spp are amorphic yeasts rarely causes invasive fungal disease in humans and it cannot be discarded as an environmental contaminant.
- Main underlying risk factors for *Pseudozyma* spp infection are bowel surgery, central venous catheter and total parenteral nutrition.
- *Pseudozyma* spp is often initially misidentified as *Cryptococcus laurentii* by the VITEK 2 system (BioMérieuxInc, Durham, North Carolina, USA).
- It is important to recognise and differentiate this species from other yeasts as it may require the use of amphotericin B or voriconazole instead of fluconazole, to which the organism is variably resistant.

Competing interests None.

Patient consent Obtained.

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