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CORRESPONDENCE

Catheter-related septicemia due to *Aureobasidium pullulans*

Aureobasidium pullulans is a saprophytic dematiaceous fungus with melanin-pigmented cell wall.[1] It is the best known *Aureobasidium* species for causing emerging human diseases including peritonitis in patients on peritoneal dialysis, splenic abscess, meningitis, skin and soft tissue infections, as well as septicemia in patients with malignancies or receiving major surgery.[2] Catheter-related septicemia has rarely been reported.[2—5] We report herein one probable case and the other a confirmed case of catheter-related *A. pullulans* septicemia. The isolates were confirmed by molecular methodology, and cases of *A. pullulans* septicemia were reviewed.

A 61-year-old woman was admitted for sudden onset of loss of consciousness two years after the diagnosis and surgical resection of hepatocellular carcinoma. Her Glasgow coma score was E1M4V1 at admission. A computed tomography of the head was emergently performed and disclosed a large hemorrhagic area measuring 73 mm at the left frontal lobe. Hematoma evacuation was performed immediately and revealed a tumor measuring $3 \times 3 \times 3$ cm located superficially in the left frontal area, and pathology demonstrated metastatic carcinoma. A central venous catheter (CVC) was placed in the right femoral vein for vascular access on the 1st hospital day. Methylprednisolone 40 mg every 6 hours was given for cerebral edema and tapered off after 11 days of use.

A spiking fever of up to 39 °C developed on the 26th hospital day. Physical examination was unremarkable except for local redness over the CVC insertion site. The catheter was removed after 26 days of use due to suspicion of CVC-related infection. The catheter tip culture yielded a yeast-like organism and the colony turned black after prolonged incubation. Culture of blood from the CVC in a BACTEC 9240 Myco/F Lytic bottle (Becton Dickinson, Sparks, MD, USA) yielded a yeast-like organism after 48-hours of incubation. The colony was mucoid, and microscopic exam revealed hyaline yeast-like cells mixed with black yeast-like cells. The initial identification using VITEC identification system (Yeast Biochemical Card, bioMerieux, France) revealed 90% similarity with *Cryptococcus laurentii*. However, after 7 days of incubation on inhibitory mold agar (IMA, BBL Microbiology Systems, Cockeysville, MD, USA) the colony became brown to black (Figure 1A). Slide culture using cornmeal agar (BBL Microbiology Systems) incubated at 25 °C revealed typical morphology of *A. pullulans*; thick-walled pigmented arthroconidia with oval-shaped oval blastic conidia (Figure 1B).[1] The fever resolved after removal of the CVC and thus no antifungal agent was given. A follow-up blood culture after the catheter removal was sterile. She was transferred to another hospital on the 33rd day of hospitalization in stable condition with improved neurological status.

A 54-year-old woman was admitted for removal of a left back pleural-cutaneous fistula with left-side empyema. She had suffered esophageal rupture with surgical repair 5 years prior to this admission. Another episode of empyema complicated with pleural-cutaneous fistula had been corrected by surgery 10 months before this admission, but the surgical wound remained poorly healed. After admission, empirical treatment for her empyema was given with intravenous ampicillin/sulbactam 3 g every 6 hours and gentamicin 80 mg every 12 hours. The wound culture revealed viridans streptococci three days later. Panendoscopy on the 7th hospital day disclosed an esophageal fistula, which was removed on the 10th hospital day. Total parenteral nutrition was given after the surgery via a right femoral CVC and was reinserted over the right internal jugular vein on the 28th hospital day. Intravenous ticarcillin/clavulanate 3.1 g every 6 hours, amikacin 200 mg every 12 hours, and fluconazole 200 mg every day were started on the 32nd hospital day for *Stenotrophomonas maltophilia* pneumonia and *Candida glabrata* empyema. The fever gradually subsided with antibiotic treatment five days later.

On the 45th hospital day, her condition worsened with new fever and chills and a body temperature of 39 °C. The physical examination was unremarkable except for a tender lymph node measuring 1×2 cm near the CVC insertion site. The right internal jugular CVC was removed after 18 days of use and the CVC tip was sent for culture. Laboratory data revealed a leukocyte count of 6.58×10^9/l with segmented neutrophils 81.3%. One of the two blood fungal culture sets from peripheral blood revealed a yeast-like organism and the colony turned black after 7 days. The colony later turned black and *A. pullulans* was identified. The CVC tip culture also yielded a mucoid colony that was also identified as *A. pullulans*. Amphotericin B 0.5 mg/kg/day was given for breakthrough fungal infection under fluconazole and continued for 7 days. Oral fluconazole 100 mg/day was used as maintenance for another 56 days. The swollen lymph node resolved with the antifungal treatment. A follow-up blood culture one month later was sterile. The patient was discharged in stable condition on the 82nd hospital day.

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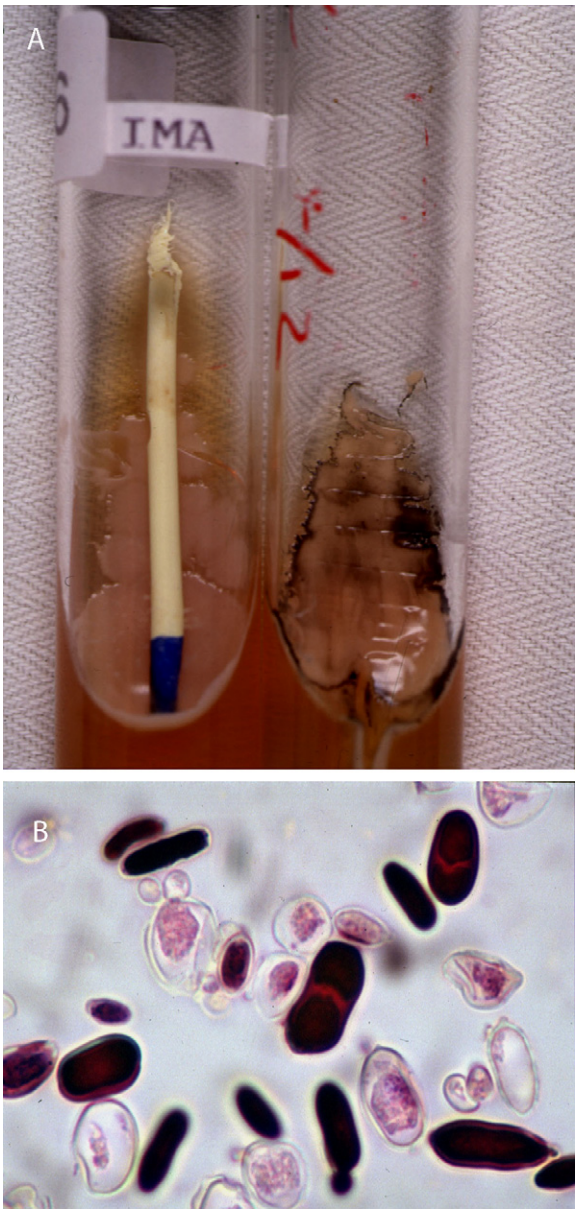

Figure 1 (A) Colonic morphology of the isolate recovered from the central venous catheter tip of patient 2, which grew on inhibitory mold agar (IMA) for 3 days (left) and that of the isolate from the blood culture, which grew on IMA for 7 days (right). (B) Microscopic examination revealed yeast-like cells (magnification ×1000).

The nucleotide sequences of the internal transcribed spacer (ITS) regions of rRNA genes (including ITS1, the 5.8S rRNA gene, and ITS2) of the two isolates were examined using two sets of primers as previously described.[6] The sequences obtained were analyzed using GCG software (Wisconsin package; version 10.1 for Unix) and the BLASTN program (National Center for Biotechnology Information Internet homepage). Both sequences showed 100% (544/544) identity to *A. pullulans* (accession number **DQ680686**).

Diagnosis of *A. pullulans* by molecular methods for confirmation may be necessary because conventional identification systems may be erroneous as previously reported and in our first case.[7] Analyzing the variable sequence area within

Table 1 Summary of *Aureobasidium pullulans* septicemia reported in the literature

Case No. [reference]	Age/gender	Underlying condition	Major surgery	Intravascular device	Treatment	Outcome
3 [2]	4 mo/M	Operation for TAPVD	Yes	Gore-Tex patch for ASD repair	Amphotericin B	Died
1 [3]	28 y/M	Severe trauma	Yes	Not reported	Fluconazole	Survived
2 [4]	53 y/F	Ovarian carcinoma, stage IIIc	No	Broviac catheter for TPN	Amphotericin B	Died
4 [5]	28 y/M	AML with neutropenic fever	No	Hickman catheter for chemotherapy	Amphotericin B	Died[a]
5 [PR]	61 y/F	Metastatic cerebral tumor bleeding with hematoma evacuation, HCC, steroid usage	Yes	Central venous catheter	Nil, catheter removed	Survived
6 [PR]	54 y/F	Operation for esophageal-pleural-cutaneous fistula with empyema	Yes	Central venous catheter	Amphotericin B then fluconazole	Survived

TAPVD, total anomalous pulmonary venous drainage; ASD, atrial septal defect; TPN, total parenteral nutrition; AML, acute myeloid leukemia; PR, present report; HCC, hepatocellular carcinoma.
[a] Died of brainstem hemorrhage after chemotherapy.

fungal ribosomal RNA genes (ITS1 and ITS2) has been noted to play an important role in characterization and identification of fungi.[8] The clinical findings of *A. pullulans* septicemia from the literature and the two cases in the present report are summarized in Table 1. These reported cases comprised patients with underlying malignancies as well as in surgical patients with prolonged intravascular catheter usage.

Treatment for *A. pullulans* is not standardized because of its rarity. Amphotericin B and fluconazole have been used for the treatment of *A. pullulans* septicemia[2,3] (Table 1). Catheter removal should perhaps be mandatory as in our first patient, who did not receive any antifungal agents and recovered solely after catheter removal. The need for catheter removal has also been emphasized in peritoneal dialysis-related peritonitis caused by *A. pullulans*.[2] A similar experience has also been reported in catheter-related Aspergillus fungemia.[4]

These two cases have several implications: first, although encountered rarely, *A. pullulans* can cause CVC-related septicemia and catheter removal may be necessary. Second, physicians and laboratorians should raise their suspicion of *A. pullulans* when an atypical mucoid yeast isolate is found, especially if the colonies turn black after prolonged incubation and a commercial identification system misidentifies these as *Cryptococcus* species.

Conflict of interest: No conflict of interest to declare.

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