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Candida utilis catheter-related bloodstream infection

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ABSTRACT

Central venous catheter-related fungemia are increasing in the last years, also due to rare fungi. We report the case of a Candida utilis catheter-related bloodstream infection in a patient with metastatic carcinoma of the bladder and a long term totally implanted venous catheter. The diagnosis was done by paired blood cultures and differential time to positivity. The Candida species was rapidly identified by MALDI-TOF mass spectrometry. The patient was successfully treated with anidulafungine.

1. Introduction

The incidence of candidemia is increasing worldwide, also for the larger use of indwelling vascular catheters. In the last years, *Candida* species – also very rare – have been more frequently isolated as causative agent of catheter-related bloodstream infections. *Candida utilis* is anamorphic form of *Pichia jadinii*, known for its industrial applications and rarely associated with disease. To the best of our knowledge, there are only very few reports of *C. utilis fungemia*. Here we present a new report of bloodstream infection caused by this yeast in humans and the first in our hospital and in Italy.

2. Case

A 66-years old man (smoker, electrical engineer), with a history of nasopharyngeal cancer with lymph node metastases and with a more recent diagnosis of poorly differentiated carcinoma of the bladder and lymph node, lung and skeletal metastases, was admitted to our hospital for pain at the right thigh. Six months before admission, the patient had undergone transurethral resection of the bladder (TURB). After surgical intervention, he suffered for urinary infection caused by *Enterococcus faecalis*. He was treated with ampicillin/sulbactam, with improvement of urinary symptoms. During the following weeks, the patient had intermittent fever, that was not investigated. In spite of the fever, one month before admission to our hospital, a totally implanted long-term central venous catheter was inserted and chemotherapy with methotrexate, vinblastine, adriamycin and cisplatin was started. On the day of admission, the patient urgently underwent surgery for a pathological fracture of the femur. During the period after surgical intervention, parenteral nutrition through the totally implanted venous catheter was administrated. On day 14th, the patient presented high-grade fever (39 °C). Blood cultures were performed both from central catheter and peripheral vein. Also urine culture was performed. A chest x-ray was normal. Empirical therapy with vancomycin 2 g/die and piperacillin/tazobactam 13.5 g/die was started. After 22 h of incubation, the BACTEC Fx blood culture system (BD Diagnostics, 7 Loveton Circle, Sparks, MD) signaled the Mycosis IC/F blood vial to be positive. Blood cultures were performed with BACTEC Fx inoculating two different blood culture vials Bactec Mycosis IC/F and Aerobic/F. Gram stains were done directly from positive blood culture vials, specimens were subcultured onto Saboraud agar plate (Kima, Italy) and relevant agar plates (blood, chocolate and MacConkey agar), and incubated at 37 °C for 24 h. Smooth and cream colored colonies that formed on Saboraud agar plate were identified within few minutes to the species level by MALDI-TOF mass spectrometry on a Microflex LT mass spectrometer (Bruker Daltonics Germany) with standard routine laboratory procedures. Briefly, yeast culture samples were mixed with 300 mL of sterile water and 900 mL of absolute ethyl alcohol, after centrifugation at 13000 g for 2 min the pellet was resuspended in 70% formic acid and 100% acetonitrile (Sigma-Aldrich, Lyon, France) before centrifugation. One microliter of supernatant was applied onto a polished steel target plate, air-dried and covered with 1 μL of the matrix saturated solution of a-cyano-4-hydroxycinnamic acid (HCCA) in 50% acetonitrile and 2.5% trifluoroacetic acid (TFA) (Sigma-Aldrich, Lyon, France) [Fig. 1]. A total of six blood cultures and one central venous catheter specimen were found

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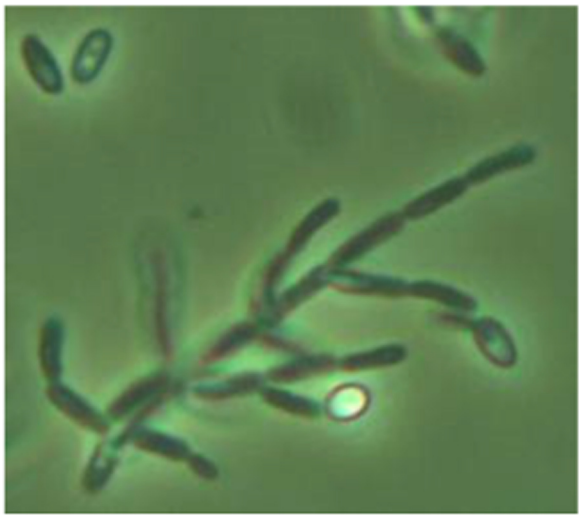

Fig. 1. Clinical isolate was grown on saboraud agar, stained with lactophenol cotton blue dye and observed with conventional microscopy.

to be positive for *C. utilis*. In urine specimen sent to the clinical microbiology laboratory the same *Candida* species was detected.

Blood culture drawn from central venous catheter was positive six hours before those from peripheral vein. Gram-stained smear of the Mycosis IC/F bottle contents showed the presence of yeast cells afterwards identified as *C. utilis* by MALDI-TOF mass spectrometry. Thus, a diagnosis of *C. utilis* catheter related bloodstream infection was done (Fig. 1).

Antifungal susceptibility test was performed by the Sensititre YeastOne Y0-10 panel (Trek Diagnostics Systems) according to the manufacturer's instructions, *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258 were tested as quality control reference strains.

MIC values and susceptibility categories for the nine antifungal agents tested in this study and are summarized in Table 1.

Anidulafungin was started and antibacterial therapy was discontinued. An examination of fundus oculi and a Transthoracic Echocardiogram (TTE) did not show metastatic foci of *Candida* infection. The central venous catheter was removed and the culture of the tip was positive for *C. utilis*. After two days, the fever disappeared and the patient improved. After one week, a blood culture was performed with no growth of yeast. Antifungal treatment was continued for two weeks after the negative blood cultures.

Following the interpretative breakpoints applied for antifungal susceptibilities tests based on values recommended by the CLSI and EUCAST (Clinical and Laboratory Standards Institute, document M27-A3, 2008), European Committee on Antimicrobial Susceptibility Testing Antifungal Agents Breakpoint tables for interpretation of MICs Version 4.1, the specimen was sensitive to all antifungal agents used.

3. Discussion

C. utilis is considered a non-pathogenic yeast extensively used in the food industry since it is capable of nonethanolic fermentation reactions and of using alcohols as a carbon source [1]. The yeast shows low virulence even in immunosuppressed mice [2] and has been rarely isolated from superficial clinical specimens and in the digestive tract of hospitalized patients [3]. Documented cases of fungemia caused by this yeast have been vey rare [4,5,6].

We report a case of *C. utilis* related fungemia in a man with a history of nasopharyngeal cancer with lymph node metastases and with a more recent diagnosis of poorly differentiated carcinoma of the bladder and lymph node lung and skeletal metastases. This is the first case of *C. utilis* candidaemia in our hospital and in Italy. Regarding the possible pathogenesis of infection, the patient was deeply immunosuppressed for his neoplastic diseases and for subsequent chemotherapy. During the weeks before surgery, he presented relapsing urinary infections, only once investigated and treated appropriately. At the time of possible relapses, no diagnostic examinations were performed and the patient remained febrile. It can be assumed that one of the episodes of untreated urinary tract infection (UTI) was caused by *C. utilis*, with a transient bacteremia and subsequent extra-luminal colonization of the catheter through the hematogenous route. In fact in previous papers recurrent UTIs were associated with *C. utilis* bacteremia [7,8]. During the following weeks, surgical intervention and parenteral nutrition might have determined the central venous catheter-related bloodstream infection (CRBSI). Alternatively, an other pathogenetic way can be assumed, the direct intra-luminal colonization of the catheter during the administration of parenteral nutrition, in a deeply immunosuppressed patient after a major surgical procedure.

Table 1
Susceptibility data of *Candida utilis*.

Drug	MIC (μg/ml) at 24 h
Amphotericin B	0.25
Anidulafungin	0.016
Caspofungin	0.06
Flucytosine	0.006
Fluconazole	2
Itraconazole	0.125
Micafungin	0.03
Posaconazole	1
Voriconazole	0.5

In automated blood culture systems the microrganism growth is constantly monitored by colorimetric detection of CO_2. The time to positivity correlates inversely with the microrganism load so it may be used to compare the concentrations of microrganisms in samples of blood collected simultaneously from central venous catheter and peripheral vein [9], so the positivity of the blood culture drawn from central venous catheter six hours before those from peripheral vein was assumed for the diagnosis of catheter-related candidemia in our patient, according to current guidelines [10]. Moreover, IDSA guidelines recommend the early removal of central venous catheter from patients with candidemia [10,11].

The surveillance for emerging fungal pathogens is very important for the monitoring of the spread of non-albicans candidiasis. Moreover as geographical differences seem to occur in the epidemiology of candidemia between different countries [12], a systematic monitoring of the trends of incidence, species distribution and antifungal susceptibilities profiles is needed. The rapid and accurate identification of the etiological agent of fungal infection and its susceptibility is required and may improve patient management and clinical outcome of candidiasis. The recent introduction of mass spectrometry applied to microorganisms identification allows a faster detection of the pathogen in comparison with conventional identification systems such as API and VITEK (bioMerieux), or PHOENIX (BD Diagnostics) and its use in routine diagnostic labs will reduce delays in diagnosis and treatment of infections.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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