Fungemia Caused by *Hansenula anomala*: Successful Treatment with Fluconazole

Satoshi HIRASAKI, Toshiharu IJICHI, Naohisa FUJITA*, Shin-ichi ARAKI, Hideo GOTOH and Masao NAKAGAWA

Fungemia, due to *Hansenula anomala*, developed in an adult patient with small cell lung cancer who received anti-cancer chemotherapy and plasmapheresis for a sensori-motor neuropathy complication. Treatment with intravenous infusion of fluconazole in addition to the removal of the central venous catheter was successful in treating the fungemia. Pathogenic *Hansenula anomala* infections are rare, but reports of this infection have been increasing. The use of fluconazole treatment for this infection has not been reported in the literature, and this is the first case of an adult infection of *Hansenula anomala* in Japan.

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Key words: compromised host, small cell lung cancer, central venous catheter, plasmapheresis, chemotherapy

Introduction

*Hansenula anomala*, an ascosporogenous yeast of the class Ascomycetes, is a free-living organism isolated from many environments, including from normal or transient flora of the human throat and alimentary tract (1). Although it has been recognized as an opportunistic pathogen, infections with this organism are very rare. Previous reports have implicated *H. anomala* in pulmonary infection (2), infectious endocarditis (3), urinary tract infection (4), oral mucosal infection (5) and fungemia (6-10). This organism has been reported to be sensitive to amphotericin B and flucytosine (9); however its sensitivity to fluconazole has not been evaluated. Here we report a case of fungemia due to *H. anomala* treated with fluconazole.

Case Report

A 63-year-old female was diagnosed as having an advanced small cell lung cancer complicated with a carcinomatous sensori-motor neuropathy in March 1990. She was treated three times with PVP therapy (CDDP plus etoposide) for the cancer and four times with double filtration plasmapheresis for the neuropathy.

Parenteral nutrition was infused through a central venous catheter. The catheter was replaced on July 13. Antibiotics had not been administered since the middle of June. Only July 30, she developed a fever and general fatigue. Physical examination revealed a temperature of 39.9°C, a pulse of 90 beats/min and blood pressure of 120/80 mmHg. There were no palpable lymph nodes. Chest and abdominal examination were normal. Laboratory tests revealed a WBC count of 7,200 cells/mm³, C-reactive protein of 7.6 mg/dl, and an ESR of 120 mm/h.

Microscopic examination of the urine revealed the presence of *Pseudomonas aeruginosa* but no yeast. By parenteral infusion of antibiotics through the same catheter, urinary *P. aeruginosa* disappeared, but imipenem/cilastatin, fosfomycin, erythromycin, and clindamycin were not effective in treating the fever. Blood cultures obtained on July 30, 31, August 1, and 3 revealed the presence of *H. anomala*. The catheter was removed, and on August 4 the patient was started on a regimen of 200 mg/day parenteral fluconazole.

The fever was alleviated on the following day. Cultures from the catheter tip were negative for *H. anomala*. Blood cultures obtained on August 7 were sterile. A total of 3,000 mg of fluconazole was administered over 16 days (Fig. 1).

Mycological studies

Blood culture bottles were incubated at 35.0°C on NR16A and NR17A (Becton and Dickinson Corp, 465 Kajii-cho, Kawaramachi Hirokoji, Kamigyo-ku, Kyoto 602, Japan)
Sunnyvale, CA, USA). Positive blood cultures were detected by a semiautomated radiometric method (Bactec 460, Johnston Laboratories, Towson, MD, USA). Yeast was grown in the positive culture bottles within 24 hours of the inoculation. Globose to hat-shaped ascospores were observed (Fig. 2). The microorganism isolated was identified as *H. anomala* using a microcapsule carbohydrate assimilation system (API 20C, Analytab Products, Plainview, NY, USA).

The yeast gave positive reactions for the assimilation of nitrate, glucose, maltose, sucrose, raffinose, cellobiose, trehalose, and soluble starch. Assimilation of lactose and urease production were negative. The growth inhibition study was performed using a synthetic aminoacid medium, fungal (SAAMF), as described by Yamaguchi et al (11). The 99% inhibitory concentration was found to be 6.25 µg/ml for fluconazole, 3.13 µg/ml for amphotericin B and 12.5 µg/ml for flucytosine.

**Discussion**

Infection with *H. anomala* was first described by Csillag et al (12) in 1953. They reported that a 2.5-month-old infant died due to interstitial pneumonia (12, 13). The microorganism isolated from the lungs was identified as *H. anomala* by Wang and Schwarz (14) in 1958. Regarding adult infection of this organism Klein et al (9) reported 2 cases and reviewed 6 cases in the literature. Two additional cases were described following their report (4, 10). Including the present case, all 11 patients reported (3, 4, 7-10) had severe underlying diseases: malignancies, hematological disorders, multiple sclerosis, or kidney transplantation. However, other risk factors have been implicated in the candidemia (15, 16): surgery, central venous catheters, hyperalimentation, neutropenia, antibiotics, corticosteroids, and chemotherapy. The present case had 4 risk factors (central venous catheter, hyperalimentation, administration of antibiotics, and chemotherapy), and it can be speculated that the plasmapheresis which she received as a treatment for the neuropathy was an additional risk factor. Munoz et al (10), reported that *H. anomala* was isolated from the catheter tip in their case, but in the present case the cultures from the catheter tip were negative. However, considering that antibiotics and sugar-rich solutions were administered through the same catheter,
it is highly probable that the catheter was the origin of the fungemia as speculated by Klein et al (9).

Previous data have shown that *H. anomala* was sensitive to amphotericin B and flucytosine. In the present case, the susceptibility studies showed that fluconazole was as effective as these other 2 agents in treating *H. anomala*. To our knowledge, the effects of fluconazole (which has not been reported to cause any significant effects (17) have not been evaluated. This is the first description of the effects of this antifungal agent on *H. anomala*.

The incidence of *H. anomala* infection has been increasing with the expanding use of corticosteroids, immunosuppressive drugs, and antibiotics. In conclusion, the potential of *H. anomala* infection as an opportunistic pathogen should be recognized, because the prognosis of this fungal infection in compromised hosts is poor without appropriate treatment.

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**References**