Fungemia due to *Trichosporon dermatis* in a patient with refractory Burkitt’s leukemia

**TO THE EDITOR:** This is a rare case report of fungemia caused by *Trichosporon dermatis* in a patient with refractory Burkitt’s leukemia who was administered prophylactic voriconazole.

*Trichosporon* species may be normal flora in the gastrointestinal tract and transiently colonize the skin and respiratory tracts in humans [1]. Invasive infection caused by *Trichosporon* has emerged as an opportunistic infection in immunocompromised patients with hematological malignancies, post-SCT malignancies and solid tumors [1, 2]. *Trichosporon dermatis* (*T. dermatis*) was recently transferred to *Trichosporon* species from *Cryptococcus humicola* complex [3]. We report a patient with refractory Burkitt’s leukemia whose venous blood culture during the neutropenic period after chemotherapy with administration of prophylactic voriconazole (VRCZ) revealed fungemia caused by *T. dermatis*. To our knowledge, this case is the first reported case report of fungemia caused by *T. dermatis* during administration of VRCZ.

**CASE**

A 47-year-old female who had suffered from obstructive jaundice and ascites for two months was admitted to our hospital for further examinations. A peripheral blood smear revealed lymphoblastic cells with blue cytoplasm and cytoplasmic vacuoles, and a CT scan showed swelling of multiple lymph nodes in the peritoneal cavity. She was diagnosed as having acute lymphoblastic leukemia of Burkitt’s type confirmed by karyotype analysis of a bone marrow aspiration sample showing 47, XX, t(8;14)(q24;q32), +mar in 9 out of 20 cells and FISH analysis of bone marrow showing IgH/c-MYC fusion signals. Combination chemotherapy with rituximab+hyper CVAD followed by high-dose methotrex-
Fusariosis caused by Trichosporon. She died of refractory leukemia 2 weeks after initial chemotherapy. Three months after the start of chemotherapy, serum β1D-gulucan became positive, and the anti-fungal drug was therefore changed from FLCZ to VRCZ because of covering aspergillosis even without characteristic features of aspergillosis shown by a CT scan of the chest and sinus. After that, galactomannan and β1D-gulucan remained negative, but she was administered prophylactic VRCZ at 300 mg BID because of transient increase of galactomannan and continuous myelosuppression after repeated chemotherapy (Fig. 1). Nine months after the diagnosis, she suffered from high fever in a severe neutropenic period (white blood cell count of 0.1-0.6×10^6/L) after salvage chemotherapy. Venous blood culture taken through the CVC showed Corynebacterium species and Trichosporon mucoides (T. mucoides) by a conventional morphological identification method. At that time, both Cryptococcus antigen and β1D-gulucan were negative and culture of the removed CVC was also negative. Although the optimal therapy for invasive trichosporonosis is still not known and the identified Trichosporon was susceptible to VRCZ in vitro (MIC was 0.060 μg/mL), clinical anti-fungal effect of the drug was not sufficient. Therefore, VRCZ was switched to L-amphotericin B (L-AMB). Thereafter, Trichosporon species was not identified by repeated venous blood samplings. She died of refractory leukemia 2 weeks after the diagnosis of fungemia by Trichosporon. The stocked isolate was genetically analyzed later and identified as belonging to T. dermatis by DNA sequencing of the intergenic spacer 1 region [4].

DISCUSSION

Several species of Trichosporon have been reported to cause opportunistic fungemia [5]. T. dermatis was newly detected from an infected human skin lesion and was also recognized as a cause of summer-type hypersensitivity pneumonitis (SHP) [3, 6]. T. dermatis is closely related to T. mucoides morphologically and biochemically and is easily misdiagnosed as T. mucoides [7]. Therefore, previous reports concerning trichosporonemia should be reevaluated. Although it had been unknown whether this species was pathogenic to humans, fungemia caused by T. dermatis has been reported since 2006 [7, 8]. Retrospective gene analysis of 22 Trichosporon sp. blood stream isolates sequentially obtained from different patients in Brazil showed only one case of T. dermatis [9]. Similarly, Ruan et al. reported that no T. dermatis infection was identified from 14 patients with fungemia [1]. Although Rodriguez-Tudela et al. documented eight cases of T. dermatis causing infections, only one case showed bloodstream infection [10]. Therefore, fungemia caused by T. dermatis is very rare. Although Fekkar et al. reported that T. dermatis antigens were cross-reactive with both Aspergillus galactomannan and Cryptococcus capsular antigen, serum of our patient did not show cross-reactivity [8].

Fungemia caused by T. dermatis in our patient occurred during administration of prophylactic VRCZ and levofloxacin at standard doses. Although amphotericin B and echinocandins were not active against Trichosporon isolates in vitro, azoles, especially VRCZ, have been reported to show good potency [1]. In vitro susceptibility testing of T. dermatis to antifungal agents has been reported to be similar to that of other pathogenic Trichosporon species [3, 9], and it was in fact also susceptible to VRCZ in vitro in this case. Profound immunosuppression after repeated chemotherapy, severe neutropenia and oral administration might be the main reasons for the ineffectiveness of VRCZ at a standard dose. Monitoring plasma VRCZ levels might be necessary to avoid subtherapeutic levels [11]. Risk factors for invasive trichosporonosis are prior antibiotic therapy, use of a central catheter, malignancy, prior chemotherapy and neutropenia, all of which were present in our patient and all of which are also risk factors for candidemia [1, 12]. Since fungemia by T. dermatis was resolved after removing the central venous catheter in this patient, the influence of central venous catheter might be a major reason of fungemia. Although the clinical effect of L-AMB in our patient was not clear because of early death after the switch of agents, Trichosporon species was no longer identified by repeated venous blood samplings. Careful attention should be paid to breakthrough fungal infection in patients with severe immunosuppression and neutropenia even if they are administered wide-spectrum anti-fungal drugs.

In conclusion, this is the first report of T. dermatis infection during administration of VRCZ. Careful attention should be paid to invasive fungal infection in patients with immunosuppression even with administration of prophylactic anti-fungal drugs because of the high mortality rate of invasive trichosporonosis, especially in patients with malignancies [1]. Molecular techniques are necessary for accurate and definitive diagnosis of trichosporonosis.

Satoshi Hashino1, Shojiro Takahashi1, Rena Morita1, Hiroe Kanamori1, Masahiro Onozawa1, Takahito Kawamura1, Kaoru Kahata1, Takashi Kondo1, Issei Tokimatsu1, Takashi Sugita1, Koji Akizawa1, Masahiro Asaka1

1Department of Gastroenterology and Hematology, Hokkaido University School of Medicine, Sapporo, 2Internal Medicine II, Oita University Faculty of Medicine, Oita, 3Department of Microbiology, Meiji Pharmaceutical University, Kiyose, 4Department of Clinical Laboratory and Transfusion, Hokkaido University Hospital, Sapporo, Japan
Correspondence to: Satoshi Hashino
Department of Gastroenterology and Hematology, Hokkaido University Graduate School of Medicine, Kita-15, Nishi-7, Kita-ku, Sapporo 060-8638, Japan
E-mail: shashino@med.hokudai.ac.jp

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Authors’ Disclosures of Potential Conflicts of Interest
No potential conflicts of interest relevant to this article were reported.

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TO THE EDITOR: The co-expression of CD3 in B-cell lineage lymphomas or the aberrant co-expression of CD20 in T-cell lineage lymphomas has been rarely reported. We describe a 72-year-old female, who presented with systemic lymphadenopathy and a 2 cm-sized gastric mass. Biopsies of the lymph node and the gastric mass showed diffuse sheets of large, atypical lymphoid cells. The tumor cells were positive for B-cell antigens such as CD20 and CD79a as well as for the T-cell antigen CD3 and cytotoxic molecule TIA-1. In situ hybridization for Epstein-Barr virus-encoded RNA (EBER) showed positive signals in the nuclei of the majority of tumor cells. Molecular studies revealed rearrangements of the immunoglobulin heavy chain (IgH) region and the T-cell receptor (TCR)-γ genes, but not the TCR-β genes. The patient was treated with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP), which resulted in near-total remission. This case illustrates the difficulty of lineage determination of non-Hodgkin lymphomas with only pan-B- and pan-T-cell markers. Unlike the previously reported cases, the present case showed molecular markers of both the B- and T-cell lineages, which further complicates the interpretation. The association of CD3-positive diffuse large B-cell lymphoma (DLBCL) with the Epstein-Barr virus (EBV) warrants further study.

Lymphoma diagnosis is based on histomorphology, immunophenotyping, flow cytometry, and molecular studies. Lymphomas are broadly classified as being of the B-cell and T-cell lineages, using immunohistochemistry and/or flow cytometry. Among the markers to determine B- and T-cell lineages, CD20 and CD3 are the most commonly used. T-cell lymphomas with aberrant expression of the B-cell marker CD20 or B-cell lymphomas with aberrant expression of T-cell associated antigens such as CD5, CD43, CD7, CD2, CD4, and CD8 have been reported [1-5]. However, cases of B-cell lymphoma with CD3 co-expression are extremely rare [6, 7]. Herein, we report a case of diffuse large B-cell lymphoma (DLBCL) in an elderly patient, with an aberrant co-expression of the T-cell associated antigen CD3 and cytotoxic molecule TIA-1, an infection with EBV, and a dual rearrangement of the immunoglobulin heavy chain (IgH) and T-cell receptor (TCR)-γ genes, but not...