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Trichosporon asahii pneumonia in a patient with acute graft-versus-host disease

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ABSTRACT

Trichosporon asahii is a yeast usually found as a part of the normal microbiota on skin and gastrointestinal tract, with a pathogenic potential if the host is immunocompromised. We report a case of a median-age male patient with diagnosis of acute myelogenous leukemia who came to our clinic, where he began the Mexican non-ablative conditioning regimen to start a stem cell transplantation from his HLA-compatible female sibling, but complicates with graft-*versus*-host disease which was successfully treated, and then ended with a fatal pneumonic fungal infection due to *T. asahii*.

Key words: acute graft-*versus*-host disease, pneumonia, *Trichosporon asahii*.

Neumonía por *Trichosporon asahii* en un paciente con enfermedad aguda de injerto contra huésped

RESUMEN

Trichosporon asahii es una levadura que habitualmente se encuentra como parte de la microbiota normal de la piel y el aparato gastrointestinal, con potencial patogénico si el huésped está inmunodeprimido. Se comunica el caso de un paciente de mediana edad con diagnóstico de leucemia aguda mieloblástica a quien se hizo un trasplante de células hematopoyéticas alogénicas con el régimen de acondicionamiento mexicano no ablativo, con células hematopoyéticas de su hermana con compatibilidad HLA. El paciente padeció enfermedad aguda de injerto contra huésped que fue tratada exitosamente, pero que se complicó con una infección fúngica pulmonar fatal por *T. asahii*.

Palabras clave: enfermedad aguda de injerto contra huésped, neumonía, *Trichosporon asahii*.

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BACKGROUND

Graft-*versus*-host disease is a major complication of allogeneic hematopoietic cell transplantation. This syndrome has certain features resembling autoimmune and other immunologic disorders, such as immunodeficiency and cytopenias.[1] On the other hand, nosocomial infections caused by opportunistic fungi are becoming more frequent, mainly among immunodeficient patients. *Candida* has been the causative agent in the majority of fungal infections along time, but in recent years other fungi species has appeared to be related in patients with immunologic diseases.

The genus *Trichosporon* causes localized or systemic infections in immunocompromised patients.[2] In the taxonomy of *Trichosporon,* 38 species has been described and eight of those are recognized to cause different clinical manifestations: *Trichosporon asahii*, *T. asteroides*, *T. cutaneum*, *T. inkin*, *T. mucoides*, *T. ovoides*, *T. pullulans*, and *T. loubieri*.[3] These species are causative agents of cutaneous infections such as piedra in immunocompetent patients,[4] which is a superficial infection of the hair shaft, as well as localized or disseminated mycoses, particularly in patients with underlying hematological malignancies.[5] *Trichosporon asahii* is the most frequent agent of *trichosporonosis* and is the responsible of 90% of all cases of infections of *Trichosporon* in immunocompromised patients.[6]

T. asahii is an anamorphic yeast with distinct morphological characteristics of budding yeast cells and true mycelia that disarticulate to form arthroconidia,[7] which is considered to be part of the human microbiota in the human skin and gastrointestinal tract,[5] and can be found in soil and water. However, it exhibits an opportunistic behavior as it causes systemic infections in patients with predisposing conditions, mainly among those who uses urinary or central venous catheters, who has pleural and/or chest drains, and in immunosuppressed patients by hematologic malignancies, different types of cancer and AIDS who went through surgical procedures, coupled with factors such as the use of intravenous chemotherapy, immunosuppressive, corticosteroids and broad-spectrum antibiotic drugs, and between those transplanted or with mechanical ventilation.[2,6]

In this report, we present the case of an adult male with diagnosis of acute myelogenous leukemia who was given a stem cell transplantation after a conditioning regimen, but then complicated with a graft-*versus*-host disease which culminated with a fatal infection with *T. asahii*.

CASE REPORT

A 51-year old male patient with a negative history of allergies, smoking, alcoholism, drug abuse, transfusions or surgery was found to have acute myelogenous leukemia in May 2013. After being under a chemotherapy scheme not remembered by the patient, he was referred to our clinic to begin a Mexican non-ablative conditioning regimen which employs busulfan, cyclophosphamide and fludarabine,[8] with which he goes into a partial remission with 1.2% minimal residual disease, and then he started to be given stem cell transplantation from his HLA-compatible (7/8) female sibling. The patient was given 1.2 x 10^6 CD34+ cells per kilogram on February 5, 2014, and on day +17 the patient became a full chimera with 94% donor cells. After being recovered in both his platelets and granulocytes, he developed fever, rhinorrhea, myalgias and arthralgia, but his chest X-rays film were reported to be normal. He then started symptomatic treatment based on levofloxacin and oseltamivir. On day +19 the diagnosis of graft-*versus*-host disease was suspected because of the presence of watery diarrhea and cutaneous rash. The patient then started therapy with 200-mg/day intravenous methylprednisolone without resolution of his symptoms, and 48 hours later with 10-mg/day

subcutaneous alemtuzumab for five consecutive days. The symptoms then resolved and the patient was discarded with oral prednisone, cotrimoxazol and itraconazole. Twelve days after that he was re-admitted as a result or fever, hypotension, malaise and dyspnea; the chest X ray film disclosed a right apical nodule with bilateral pleural effusions as well as consolidation and bilateral nodular infiltrates (Figure 1).

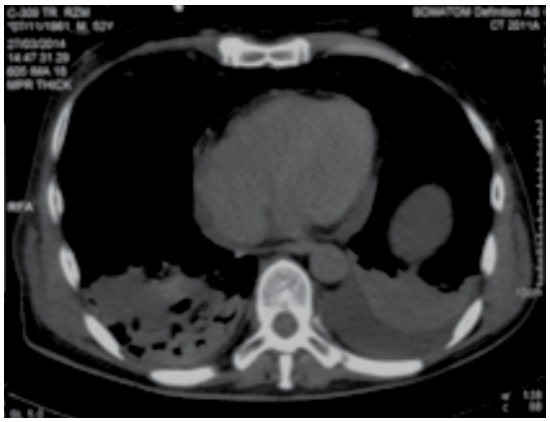

Figure 1. Chest computed tomography scan showing pleural effusions and consolidation areas.

The patient started a regimen with meropenem and fluconazole, but he fell in persistent shock and progressive hypoxemia. As a result of it, he was admitted in the intensive care unit in where an endotracheal tube was inserted. A bronchoscopy was done (Figure 2) and a mucous plug was removed. The patient started on 200 mg voriconazole every 12 hours.

Trichosporon asahii, *Staphylococcus epidermidis* and *Enterococcus faecalis* were isolated in the material obtained from the bronchial plug. *Candida albicans* was isolated from the blood, and the galactomanan antigen was negative. *Trichosporon asahii* was found also in the bronchial biopsy (Figure 3). The patient died during septic shock on day + 57 after the allograft.

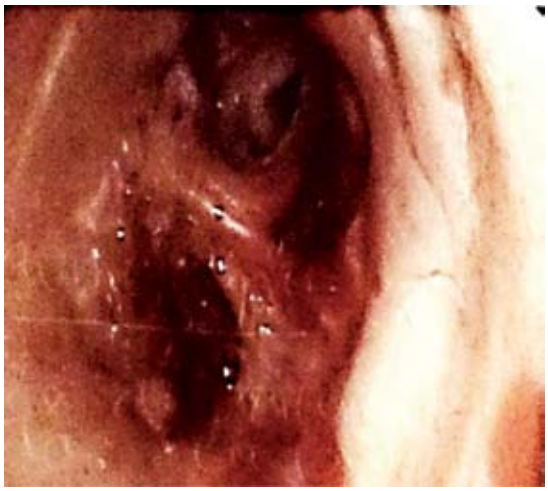

Figure 2. Abundant secretions were found as well as a mucous plug in the bronchoscopy of the patient.

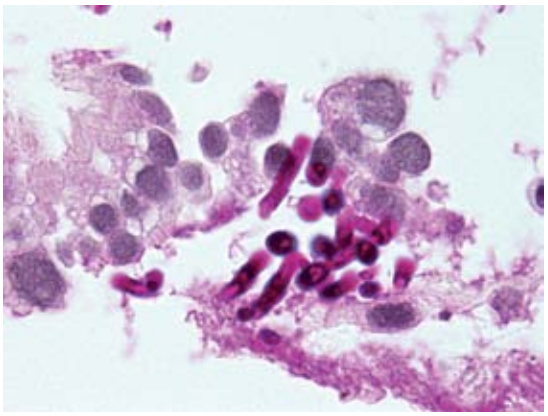

Figure 3. Bronchial biopsy with PAS staining showing bronchial epithelium with loss of their morphology and inflammatory infiltrate, and presence of *Trichosporon asahii*.

DISCUSSION

Trichosporon species are emerging pathogens in immunocompromised hosts, and *Trichosporon asahii* is the most frequently specie involved in disseminated infections. Most of the cases have been reported in neutropenic adults with hematological malignancies, although trichos-

poronosis has also been recently reported after solid organ transplantation.[9] Systemic infections with *Trichosporon asahii* are uncommon and are associated with poor prognosis, with a mortality rate estimated to be approximately 70-80% even with therapy with amphotericin B.[3,4,6] Pulmonary involvement, with respiratory symptoms and radiological features of alveolar or interstitial infiltrates, is observed in many cases of pulmonary graft-*versus*-host disease (GVHD).[10,11] In this case, the initial diagnostic suspicion was pulmonary acute GVHD since the pulmonary manifestations appeared, together with the ensue of diarrhea and rash as other evidences of GVHD. However, the material obtained during the bronchoscopy revealed the infectious nature of the condition. *Trichosporon* species has been isolated on culture of the sputum in some cases, but some authors disagree with this evidence. There are several reports that indicate that the skin and pulmonary lesions are the most common presentation, and others less frequently report liver and splenic abscesses.[11] Susceptibilities of *Trichosporon* species to antifungal agents are variable in the literature, and it is of relevance to show that *in vitro* activity does not always correlate with efficacy *in vivo*.[3] Recently, new azoles have appeared as promising therapies for this infection, as some *in vitro* studies have shown that azoles, particularly voriconazole, may be more potent than amphotericin B.[6,11,12] In the present case, voriconazole exhibited a minimum inhibitory value against *Trichosporon asahii*. The outcome of this patient highlights the critical requirement for early diagnosis and a rapid and appropriate therapy of trichosporonosis to obtain a favourable outcome.

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