**Acremonium Pneumonia Successfully Treated in Patient with Acute Myeloid Leukemia: A Case Report**

### Abstract

Invasive fungal infection is a major cause of morbidity and mortality in patients who receive treatment for acute myeloid leukemia (AML). We present the case of successful treatment of *Acremonium* spp. pneumonia in a patient with acute myeloid leukemia who underwent chemotherapy.

**Keywords:** Mycotic pneumonia; *Acremonium* spp.; Acute myeloid leukemia; Voriconazole

### Introduction

Fungal infection remains a significant cause of morbidity and mortality in patients with AML. Moreover, there has been an increase in the fungal infections incidence caused by moulds such as *Mucorales*, *Fusarium* and *Scedosporium* [1] and other rare micromycetes [2]. There is a paucity of the literature data devoted to mycotic pneumonia caused by *Acremonium* spp. in patients with AML. Acremonium infection is difficult to diagnose. It is necessary to distinguish airway colonization and involvement of lung tissue. This case report also highlights the difficulties in diagnosing invasive pulmonary mycosis (caused by *Acremonium* spp.) and the importance of correct antifungal therapy.

### Case

In February 2013 a 78-year-old man with AML was hospitalized to the Hematology department of Military Medical Academy (St. Petersburg, Russian Federation) for induction chemotherapy. The patient had (in the first day of chemotherapy) leukocytes - 45,7*10⁹/L, blasts - 37.5%, granulocytes - 1%. The cytoreductive therapy was started with hydroxycarbamide (dose 1-3 g). The result - partial clinical and hematological remission. The patient had neutropenia throughout the treatment period (14 days).

On the 10th day after admission, the patient presented fever (38.5-39.0˚C) without any additional clinical signs (day 0), while white blood cells (WBC) count was 400/ml with zero neutrophil per ml. The patient was treated with small doses of cytosar. Fever persisted with the onset of a dry cough and impaired general condition.

The computed tomography (CT) scans of the chest showed interstitial infiltrates in the right lower lung. Galactomannan test (Platelia Aspergillus, Bio-Rad) in serum was negative. The material was sent to the P.Kashkin Research Institute of Medical Mycology at I.Metchnikov North-Western State Medical University for the identification of species. The obtained fungal culture was identified as *Acremonium* spp. Growth of *Acremonium* spp. culture was also received from the lung tissue samples (Figure 2).

On the 10th day after admission, the patient presented fever (38.5-39.0˚C) without any additional clinical signs (day 0), while white blood cells (WBC) count was 400/ml with zero neutrophil per ml. The patient was treated with small doses of cytosar. Fever persisted with the onset of a dry cough and impaired general condition.

The computed tomography (CT) scans of the chest showed interstitial infiltrates in the right lower lung. Galactomannan test (Platelia Aspergillus, Bio-Rad) in serum was negative. The patient was treated empirically by ceftriaxone 6 g/day and amikacin 1.5 g/day. After 3 days of continuous high fever, the antibiotic therapy was changed to imipenem 2.0 g/day and linezolid 1.2 g/day for 10 days.

Due to the progression of infection in the right lung, the patient was treated empirically by caspofungin 50 mg/day. On day +14 his condition worsened (dyspnea was growing) and he was transferred to ICU. He had persistent pyrexia despite treatment with imipenem, linezolid, and caspofungin. The CT scans of his chest were repeated and revealed a large abscess in the right lower lung.

CT of the chest at 14th day revealed interstitial infiltrates with abscess in the right lower lobe (Figure 1).

The bronchoscopy and transbronchial biopsy of the lung lesions were performed. Septate mycelium was found by microscopy of the bronchoalveolar lavage (BAL) and lung tissue histology. Abundant growth of moulds was received. The material was sent to the P.Kashkin Research Institute of Medical Mycology at I.Metchnikov North-Western State Medical University for the identification of species. The obtained fungal culture was identified as *Acremonium* spp. Growth of *Acremonium* spp. culture was also received from the lung tissue samples (Figure 2).

Other tests, which included blood cultures, respiratory viral PCR, culture and PCR for *Mycobacterium tuberculosis* in BAL samples, were all negative.

On the basis of this investigation mycotic pneumonia (agent - *Acremonium* spp.) was diagnosed. Antimycotic therapy was changed to oral voriconazole 200 mg twice daily. The outcome was favorable. On April 15, 2013 white blood cell count was restored (2.4 x 10⁹/L) by colony-stimulating factor. The total duration of agranulocytosis, from the first day of treatment, was 48 days.

After 7 days of voriconazole therapy the patient had a marked improvement in his general health condition (no fever or cough). After 3 month of antifungal treatment by CT was noted complete resolution of the mycotic pneumonia (Figure 3).

**Additional Information**

**Volume 2 Issue 5 - 2016**

**Nikolay N Klimko,1 Sofya N Khostelidi*,1 Yulia E Melekhina1, Dmitry A Gornostaev,2 Vyacheslav N Semelev2, Tatyana S Bogomolova1 and Vadim V Tirenko2**

1Department of Clinical Mycology, Allergology and Immunology, North-Western State Medical University, Russia
2SM Kirov Military Medical Academy, Russia

*Corresponding author:* Sofya N Khostelidi, Department of Clinical Mycology, Allergology and Immunology, North-Western State Medical University named after Il Mechnikov, 194291, Santuyo de Cuba str, Build 1/28 Saint-Petersburg, Russia, Tel: +78123035146; Email: sofianic@mail.ru

Received: June 30, 2016 | Published: October 04, 2016

The total duration of antimycotic therapy was 130 days. Later, the patient was treated with voriconazole for secondary prophylaxis on each course of chemotherapy. He was still alive and in complete remission of mycotic pneumonia in a 6-months follow-up.

Discussion and Literature Review

*Acremonium* spp. is a genus of fungi, formerly known as *Cephalosporium*, in the phylum *Ascomycota*, *Hypocreales* order, *Hypocreaceae* family. *Acremonium* spp. has a worldwide distribution, it is commonly found in the environment in soil and on dead plant material as well as in hay and rotting plants; some species can be also found in food stuff [1,2,3]. *Acremonium* is a large polyphyletic fungal genus that comprises approximately 150 species. Most species of *Acremonium* are saprophytic and non-pathogenic. However, certain species are pathogenic to plants and humans. Species that have been reported to cause infections in humans are *Acremonium alabamensis*, *Acremonium kiliense* (now *Sarocladium kiliense*), *Acremonium roseogriseum* (now *Gliomastix roseogrisea*), *Acremonium strictum* (now *Sarocladium strictum*), *Acremonium potronii* and *Acremonium recifei*. The species of *Acremonium* are morphologically very similar to each other and can be distinguished only by subtle differences, which makes their identification difficult. Therefore, in most of the clinical cases the etiological agent was reported only as *Acremonium sp.* that expanding the list of the *Acremonium* genus possible pathogens [1,2,3].

*Acremonium* spp. penetrate to macroorganism mainly through damaged skin or mucous membranes usually causing mycetoma or keratitis [4,5,6]. In immunocompromised patients micromycetes can penetrate not only through lesions (which can appear as results of injury or maceration of the skin in places of catheter fixation), but also via inhalation affecting paranasal

**Figure 1**: Computed tomography of the chest on the 14th day of antibiotics therapy. The interstitial infiltrates with abscess were observed in the right lower lobe.

**Figure 2**: Culture from the lung tissue samples (*Acremonium* spp.), microscopy of culture (x400).

Other tests, which included blood cultures, respiratory viral PCR, culture and PCR for *Mycobacterium tuberculosis* in BAL samples, were all negative.

**Figure 3**: Computed tomography of the chest on the 130th day of antifungal therapy (no interstitial infiltrates in the right lower lobe).
In immunocompromised patients, Acromenium spp. lung disease was observed in a few cases [17-19]. The main risk factors for invasive fungal infections were prolonged neutropenia, allogeneic HSCT and graft-versus-host disease, primary immunodeficiency syndromes, prolonged stay in the ICU, peritoneal dialysis, etc. [20-24]. According to the data of Kcromery V et al. [22] up to 10% oncohematological patients with invasive mycosis suffer from Acromenium spp. infection [22].

It should be noted that the disease pattern in immunocompromised patients is similar to that in other invasive fungal infections. At the same time, it was noted and reflected in the published literature that if the risks of invasive fungal infections persist in the presence of the Acromenium spp. infection of the internal organs the fungemia develops rapidly [22-24, 25,26].

The high-resolution computed tomography is performed to determine the prevalence of pathological process in lungs, paranasal sinuses, abdominal organs. It should be noted that the CT signs of organ damage, for example in the lungs, are similar to those of other invasive fungal infections. Serologic diagnostic methods for Acromenium infection have not been developed yet [1,2,3,27].

The main method that allows to diagnose invasive fungal infections caused by Acromenium spp. is mycological - identification of the causative agent in pathological material by microscopy, cultural and histological examination. It should be noted that the members of the Acromenium genus grow slowly; therefore, the Petri dishes should be viewed not less than 14 days. Another method of diagnosis is pathomorphological study but identification of Acromenium spp. may be difficult, because the hyphae structure and branching in the tissues resemble Aspergillus spp [1,2,28]. In the analyzed publications identification of the pathogen species failed in more than 50% of patients. Among the most frequently identified pathogens were Acromenium kiliense and Acromenium strictum (18% and 18%, respectively) [2,29].

Thus, the main criteria for the diagnosis of invasive fungal infections caused by Acromenium spp. in immunocompromised patients is identification of the fungi of the genus Acromenium in mycological examination, combined with the presence of risk factors, clinical symptoms and instrumental examination data.

It should be mentioned that Acromenium spp. are resistant to many antifungals in vitro. According to the data of some researchers, certain species of Acromenium spp. can be susceptible to amphoterin B and some azoles [28,29,30]. Fluconazole, flucytosine and echinocandins are not active against Acromenium [29,31]. The first described cases reported about the use of amphoterin B, ketoconazole, fluconazole, itraconazole as antifungal therapy. Further retrospective survival analysis showed that the use of liposomal amphoterin B and surgical treatment was prospective [29].

Triazole antifungics (voriconazole, posaconazole, and ravucanazole) exhibit different degrees of activity against Acromenium spp. [30,31,32]. According to the new international guidelines for the treatment of fungal infections caused by Acromenium spp. in immunocompromised patients with invasive process the drug of choice is voriconazole (All) [29]. Surgical treatment (removal of the infection source) and removal/replacement of the central venous catheter also bring some success (ClI). Amphoterin B can be used in the absence of the first-line drugs (ClI). The patients with lesions of the skin and soft tissues can also be treated with amphoterin B (BI) and its lipid fractions [29].

Disease prognosis in immunocompromised patients depends on the clinical form and severity of the underlying disease. Survival rate in immunocompromised patients with local forms (lesions of the skin, soft tissues, bones, joints) is up to 100%; with invasive lesions of the internal organs - 75%; with acute disseminated process in the cases of early antifungal therapy - about 50% [28,29].

In the described clinical case the invasive pulmonary mycosis caused by Acromenium spp. in patient with acute myeloid leukemia was promptly diagnosed. Thus the empirical echinocandin therapy was replaced by a standard dose of voriconazole and at the same time the recovery of the granulocyte level was achieved. Adequate antifungal therapy and stabilization of the underlying disease allowed to keep the patient alive.

In conclusion, acute myeloid leukemia, cytostatic chemotherapy and prolonged neutropenia are risk factors for invasive fungal infections caused by Acromenium spp. Combination of adequate antifungal therapy and correction of risk factors is important for successful treatment of fungal infections.

References


