

***Acremonium Potronii* Associated Pneumonia in an Allogeneic Stem Cell Transplantation Recipient**

Allojeneik Kök Hücre Nakli Yapılan Bir Olguda Gelişen *Acremonium Potronii* İlişkili Pnömoni

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ABSTRACT

Infections are one of the major causes of morbidity and mortality after allogeneic hematopoietic stem cell transplantation. Clinically significant graft versus host disease, steroid therapy, cytomegalovirus infection, recurrent neutropenia and relapsed/refractory disease are the recognized risk factors for invasive fungal infections. *Acremonium*, which is a large polyphyletic fungal genus, is present in soil, insects, plants and other environmental substrates. Disseminated infections are rare with the reported cases limited to immunocompromised patients with a large clinical spectrum including pneumonia, arthritis, osteomyelitis, endocarditis, peritonitis, meningitis and sepsis. *Acremonium* species present low susceptibility to most antifungals including imidazoles, fluorocytosine and amphotericin B. For the clinically relevant species, the minimum inhibitory concentrations for all antifungal agents are high, except terbinafine. As *Acremonium* spp grow slowly, cultures should be kept for at least 2 weeks to ensure detection of a positive sample. Clinicians should be aware that *Acremonium* spp, particularly *A. Potronii*, might be one of the causative fungi of systemic infection in severely immunocompromised allogeneic hematopoietic stem cell transplantation recipients.

Key Words: *Acremonium potronii*, pneumonia, stem cell transplantation, multiple myeloma, immunosuppression

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ÖZET

Enfeksiyonlar allojeneik kök hücre nakli yapılan hastalarda önemli morbidite ve mortalite nedenidir. Graft versus host hastalığı, steroid tedavisi, sitomegalovirus enfeksiyonu, nötropeni ve relaps/dirençli hastalık invaziv fungal enfeksiyonlar için bilinen risk faktörleri arasındadır. *Acremonium* toprakta, böceklerde, bitkilerde ve diğer çevresel yapılarda bulunabilen bir mantar türüdür. Nadir olarak immunsupresif hastalarda pnömoni, artrit, osteomyelit, endokardit, peritonit, menenjit ve sepsis gibi disemine enfeksiyonlara neden olabilmektedir. İmidazol, florositozin, amfoterisin B gibi antifungal ajanlara karşı duyarlılığı düşüktür. Terbinafin dışındaki tüm antifungal ajanlar için minimum inhibitör konsantrasyonu yüksektir. Yavaş üreme özelliğine sahiptir, bu nedenle üremenin sağlanması için kültürler en az iki hafta süreyle bekletilmelidir. *Acremonium*, özellikle olgumuzda tespit edilen *Acremonium potronii*, allojeneik kök hücre nakli yapılan ağır immunsupresif hastalarda gelişen sistemik mantar enfeksiyonlarında düşünülmesi gereken bir mantar türüdür.

Anahtar Sözcükler: *Acremonium potronii*, pnömoni, kök hücre nakli, multipl myelom, immunsupresyon

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INTRODUCTION

Multiple myeloma (MM) remains to be an incurable disease despite novel treatment strategies. Allogeneic hematopoietic stem cell transplantation (AHST) is the only treatment option with a curative potential so far. However, the potential cure comes at a price; transplant related mortality (1,2). Infections represent up to 63% of the causes of death in myeloablative AHST recipients. Early infections are less common in non-myeloablative AHST recipients as a result of less mucositis and neutropenia. However, patients may remain susceptible to opportunistic infections for an extended period in the post-transplant course due to the slow recovery of T cell immunity (3-5). Disseminated *Acremonium* infections are rare with the reported cases limited to immunocompromised patients with a large clinical spectrum including

pneumonia, arthritis, osteomyelitis, endocarditis, peritonitis, meningitis and sepsis (6-10).

Here, we present a case of MM who underwent non-myeloablative AHST and developed pneumonia associated with *Acremonium potronii* along with graft versus host disease (GVHD) and cytomegalovirus (CMV) reactivation.

CASE REPORT

A 61-year-old male patient, who was diagnosed as Stage IIIA MM, received an autologous HSCT after 6 cycles of VAD (Vincristine, Doxorubicine and Dexamethasone) chemotherapy. Eight cycles of bortezomib/dexamethasone and a lenalidomide-based combination were administered post autologous HSCT for progressive disease. He received a non-myeloablative AHST from his HLA identical brother.

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On day +180, he developed skin and gastrointestinal GVHD and was started on cyclosporine A, mycophenolate mofetil and methyl prednisolone with posaconazole prophylaxis. On day +190, he was hospitalized due to neutropenic fever. He had CMV reactivation with a CMV polymerase chain reaction (PCR) level of 1380 copies/mL. Piperacillin-tazobactam and gancyclovir were commenced. A progressive increase in CMV DNA level reaching up to 26000 copies/mL on gancyclovir treatment was observed. Early antiviral modification with foscarnet resolved CMV infection. However, the patient remained to be febrile and hypoxic. Piperacillin-tazobactam was stopped and an extended antibacterial treatment including meropenem and linezolid was commenced. High resolution chest tomography (HRCT) revealed peribronchovascular patchy areas of consolidation with air bronchograms (Figure 1 & 2). Bronchoscopy was not feasible because of refractory thrombocytopenia. Based on radiological evidence, bacterial bronchopneumonia was the most possible diagnosis, however *Pneumocystis jirovecii* or fungal infection could not be ruled out.

Prophylactic posaconazole was stopped, empiric voriconazole and trimethoprim sulfamethoxazole were started. Soon after, he was transferred to the intensive care unit for mechanic ventilation support. A few days after his death, *Acremonium potronii* grew in his sputum culture which was taken before intubation. The morphologic identification of *Acremonium* on genus level was done according to colony morphology on Sabouraud dextrose agar (SDA) plates. Microscopic evaluation of the colonies was also performed for identification. The genotypic identification was done by using DNA sequencing. 500 bp region of the fungal internal transcribed spacer (ITS) DNA was sequenced in ABI Prism TM 310 Genetic Analyzer (Applied Biosystems, USA). The sequence data analyzed using the National Center for Biotechnology Information (NCBI, Bethesda, Md.,USA) BLAST system (available at <http://www.ncbi.nlm.nih.gov/BLAST/>). Fungal DNA isolated from colony was identified as *Acremonium potronii*. Antifungal susceptibility was performed according to reference methods proposed by Clinical Laboratory Standards Institute (CLSI) by M38A microdilution method. Amphotericin MIC value was 2 µg/ml, it was 4 µg/ml for voriconazole, 32 µg/ml for fluconazole and 0.5 µg/ml for itraconazole.



Figure 1 Peribronchovascular patchy areas of consolidation with air bronchograms on high resolution chest tomography (horizontal section)



Figure 2 Peribronchovascular patchy areas of consolidation with air bronchograms on high resolution chest tomography (sagittal section)

DISCUSSION

Despite feasible antifungal prophylaxis, fungal infections remain to be a major cause of mortality in patients with hematologic disorders, with an incidence of 15,1% in AHST recipients (7-9). Clinically significant GVHD, steroid therapy, CMV infection, recurrent neutropenia and relapsed/refractory disease are the recognized risk factors for invasive fungal infections (3-5). Our patient had several risk factors including advanced age, GVHD, steroid therapy and CMV reactivation some of which were interrelated. *Acremonium* species present low susceptibility to most antifungals including imidazoles, fluorocytosine and amphotericin B. Voriconazole treatment was shown to be successful in some cases. However, the appropriate treatment for *Acremonium* spp infections is currently undetermined (7,10). As *Acremonium* spp grow slowly, cultures should be kept for at least 2 weeks to ensure detection of a positive sample (8). Nevertheless, relatively noninvasive samples such as sputum are typically positive for *Acremonium* only in disseminated infection. An earlier bronchoalveolar lavage sampling might have saved the patient's life with prompt diagnosis and treatment. The dismal outcome of the presented patient might as well be due to inherent resistance of the microorganism besides the delayed diagnosis. To our knowledge, this is the first case in the literature presenting with *Acremonium potronii* associated pneumonia.

The most interesting part of this case is that we identified a distinct clinical isolate among the large family of *Acremonium* spp that had not been previously reported as a causative agent for pneumonia in humans. It is important to note that we lack sufficient clinical information to make a definite comment on the clinical relevance of this uncommon microorganism.

Conflict of interest

No conflict of interest was declared by the authors

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