A Localized Macular Rash in an Immunocompromised Patient with Pneumonia and Necrotizing Enterocolitis

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Abstract

A 21-year-old male with T-cell acute lymphoblastic leukemia (ALL) was admitted for fever and neutropenia. Despite 72 hours of antibiotic therapy, he remained febrile and developed new abdominal and pleuritic chest pain. A computerized tomography (CT) scan demonstrated necrotizing enterocolitis and a left lower lobe pneumonia with early cavitation versus abscess formation. His antimicrobial regimen was broadened to meropenem and voriconazole. On hospital day 5, an asymptomatic rash appeared on his left face consisting of erythematous macules that blanched with pressure. Within 24 hours, the skin lesions expanded and developed a central, non-blanching violaceous hue. Liposomal amphotericin B was added and a biopsy of the rash was obtained. Mucor spp was confirmed by tissue culture. Repeat imaging showed interval development of diffusely scattered and innumerable hypodense lesions throughout the liver and spleen, as well as diffuse myositis and within the brain and spine. Care was withdrawn and the patient expired on hospital day 11. Risk factors for developing invasive aspergillosis and mucormycosis are similar. This case illustrates similarities in their clinical presentations, highlights potential gaps in coverage by antifungal agents that are commonly used for empiric coverage, and reviews treatment options.

**Keywords:** Mucormycosis; Immunocompromised host

Introduction

Aspergillosis and mucormycosis are both molds that can cause invasive infections in immunocompromised hosts, however effective management differs. Although aspergillosis is encountered more commonly, the incidence of mucormycosis may be rising, particularly among those with hematologic malignancies [1].

Case Presentation

We present a 21-year-old male with T-cell acute lymphoblastic leukemia (ALL) who was incidentally noted to be febrile and tachycardic in clinic while neutropenic. The patient had been diagnosed with T-cell ALL 4 months ago and was in remission, receiving consolidation chemotherapy. He had not experienced any infectious complications and was previously healthy. He had not received any antifungal prophylaxis prior to this admission. His absolute neutrophil count (ANC) had been <500 cells/μL for 11 days and <100 cells/μL for 4 days. Blood cultures were obtained from his port and he was started on cefepime. On hospital day 2 his blood culture revealed Gram-negative rods and so tobramycin was added. The Gram-negative rods were speciated as Neisseria elongata. All subsequent blood cultures were negative. Despite 72 hours of antibiotic therapy, he remained febrile and developed new abdominal and pleuritic chest pain. On hospital day 3 a computerized tomography

(CT) scan demonstrated necrotizing enterocolitis and a left lower lobe pneumonia with early cavitation versus abscess formation (Figure 1).
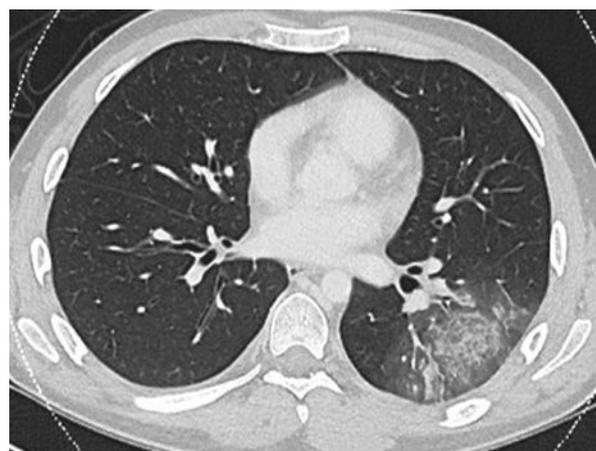
Figure 1: CT scan of the chest demonstrates a 1.8 cm density within the left lower lobe.

His antimicrobial therapy was broadened to meropenem and voriconazole on hospital day 4. Over the next 24 hours, he defervesced. Although supplemental oxygen was added for mild desaturations during sleep, his exam remained stable without tachypnea, increased

work of breathing, or worsening abdominal pain. On hospital day 5, a new asymptomatic rash appeared on his left face consisting of erythematous macules that blanched with pressure (Figure 2).


Figure 2: Localized blanching erythematous macules.

Figure 3: Interval change in rash appearance over 24 hours to non-blanching violaceous papules.

Laboratory investigation revealed persistent profound neutropenia (ANC <100 cells/µL), a C-reactive protein of 8.0 mg/L (normal range, <1.0 mg/L), aspartate transaminase of 64 U/L (normal range, 10-40 U/L), and alanine transaminase of 149 U/L (normal range, 7-56 U/L). Serum galactomannan enzyme immunoassay (EIA) and (1-3)-β-D-Glucan testing were pending. Within 24 hours, the skin lesions expanded and developed a central, non-blanching violaceous hue (Figure 3).

No new skin lesions developed. Liposomal amphotericin B was added and a biopsy of the rash was obtained for culture and histopathology. Grocott methenamine silver-stained tissue was significant for innumerable angioinvasive hyphae (Figure 4).
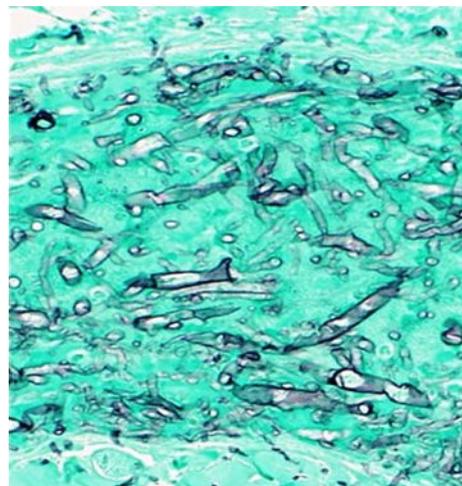
Figure 4: Grocott methenamine silver-stained tissue (200x) significant for innumerable angioinvasive hyphae.

Final Diagnosis

Disseminated mucormycosis.

Hospital Course

The following day fevers returned and respiratory support escalated. He also complained of new left-sided groin pain and weakness of the left lower limb. Ultrasound and Doppler evaluation of the hip and left inguinal region were normal. Magnetic resonance imaging (MRI) of the left hip revealed diffuse myositis within the musculature of the proximal anterior compartments and hyperintense foci within the left femoral head. MRI of the spine was normal. Serum creatine kinase was 160 U/L (normal range, 52-336 U/L). Trans-thoracic echocardiogram was normal. After 48 hours of incubation, his skin culture revealed white colonies on Sabouraud dextrose agar that were identified as Mucor spp. Voriconazole was discontinued and caspofungin was added on hospital day 7. Due to increasing respiratory depression with PCA use, the patient was intubated. On hospital day 8, bronchoscopy revealed black, necrotic lung tissue with histopathology also consistent with mucormycosis. MRI of the brain and spine showed 4 rounded intracerebral enhancing lesions concerning for abscesses and enhancement of the occipital sulci around these lesions. Repeat CT imaging of his abdomen and pelvis on hospital day 10 showed diffusely scattered and innumerable 1-3 cm hypodense lesions throughout the liver and spleen. Serum galactomannan EIA and (1-3)-β-D-Glucan testing remained negative throughout his hospital course. Care was withdrawn and patient expired on hospital day 11.

Discussion

In a recent prospective cohort, mucormycosis accounted for more than 10% of invasive mold infections among children [2]. Risk factors for developing aspergillosis and mucormycosis are similar [3,4]. Pneumonia is the predominant clinical presentation for both infections, and there is significant clinical and radiologic overlap, although dissemination favors mucormycosis [3,4]. Given the rarity of isolation via blood culture and absence of serologic markers, tissue

biopsy is almost always necessary for definitive diagnosis of mucormycosis; however, this is often challenging in patients with multiple comorbidities. Voriconazole is a recommended empiric antifungal therapy for neutropenic fever that has less toxicity [5] and improved survival benefit over amphotericin B among those with aspergillosis, [6] but this therapy is not active against mucurmycosis [7]. Concern for an increased rate of adverse events without survival benefit [2] likely limits recommendations for empiric combination antifungal therapy, but some high-risk populations may benefit from its judicious use. Isavuconazole is an alternative for treatment of aspergillosis [8] that some suggest could provide equivalent survival benefit to amphotericin B against Mucormycosis [9]. In populations with risk factors, and in presentations that are concerning for invasive mold infection, consider starting an empiric therapy that is effective against both aspergillosis and mucormycosis.

Acknowledgement

Conflict of Interest

The authors have no conflicts of interest to declare.

Declaration

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