A young female with fever, pulmonary infiltrates and pancytopenia
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Learning Objectives

• Semi-invasive pulmonary aspergillosis (Semi-IPA) is an uncommon cause of fever of unknown origin.
• Semi-IPA triggering hemophagocytic lymphohistiocytosis (HLH) is a rare presentation that may pose a diagnostic challenge.

Case Description

A 43-year-old African American female with history of hypertension and smoking was brought to the emergency department due to unresponsiveness. She was last known well one week prior to presentation.

Physical examination:
• Temperature 40°C, heart rate 140/min, and oxygen saturation 92% on ambient air
• Confused and obtunded
• Petechial rash on bilateral lower extremities
• Bilateral crackles on lung auscultation

Differential diagnosis:
• Community-acquired pneumonia, aspiration, primary CNS infection, vasculitis

Initial work-up and management on admission:
• CBC: Hb 10.5 g/dL, WBC count 2000/cumm, absolute neutrophil count 1500/cumm, and platelet count 47,000/cumm.
• Peripheral blood smear: anisopoikilocytosis, rare schistocytes, granulocytopenia, thrombocytopenia
• Inflammatory markers: C-reactive protein was 89.4 mg/L and ferritin was 5262 ng/mL
• Started on empiric ceftriaxone and azithromycin
• CT showed bilateral consolidations located in the left lower lobe and right middle and lower lobes (Figure 1)
• Patient had persistent fever, hypoxemia and pancytopenia

Further work-up during admission:
• Serum 1,3 Beta D glucan was >500 pg/mL
• Bronchoscopy: BAL showed Aspergillus fumigatus (Figure 3)
• Bone marrow: normal flow cytometry, normocellular marrow, no evidence of hemophagocytosis
• Soluble CD25 was elevated at 2577 pg/mL

Figure 1. CT chest at presentation showing consolidations in the right middle lobe (panel A) and bilateral lower lobes (panel B)

Figure 2. Post-treatment CT chest at 3-month follow up showing small residual opacity in the right middle lobe (panel C) and near-complete resolution of lower lobe consolidations (panel D)

Figure 3. Aspergillus spp. identified in the bronchial aspirate-branaching, septate hyphae with conidiophores and conidia

Management during admission:
• Treated with systemic corticosteroids 1mg/kg after bone marrow biopsy for management of cytokine storm
• G-CSF was administered after bone marrow biopsy results with interval improvement of ANC
• Treated with micafungin and then switched to voriconazole 200mg BID after BAL wet prep showed Aspergillus spp (Figure 3)
• Fever, pancytopenia and hypoxia resolved, ferritin downtrended
• Steroid taper was started

Follow up at 3 months:
• Patient continued to show clinical improvement
• Repeat chest CT showed near-resolution of bilateral consolidations (Figure 2)
• Voriconazole trough levels monitored as outpatient with plan for 6-month duration of therapy

Discussion

• Semi-IPA presenting in an immunocompetent patient is an uncommon presentation.
• Among infectious causes of HLH, Semi-IPA as a trigger has been rarely described.
• Bone marrow biopsy revealing hemophagocytosis is not a required criterion for HLH diagnosis in an appropriate clinical scenario (our patient had H-score indicating 70% probability of HLH).
• With successful treatment of the underlying infection, HLH-specific cytotoxic chemotherapy was avoided.

References