A 64-Year-Old Male With Fever and Persistent Lung Infiltrate

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Acute fibrinous and organizing pneumonia is a newly recognized pattern of lung injury. It may be idiopathic or secondary to a variety of lung injuries. In this case report we describe a 64-year-old male with acute fibrinous and organizing pneumonia caused by decitabine. He had substantial clinical and radiological improvement after the discontinuation of decitabine and a course of corticosteroids. *Key words: acute respiratory distress syndrome, ARDS, acute lung injury, ALI, decitabine, myelodysplastic syndrome, drug induced pneumonitis, acute fibrinous and organizing pneumonia.*
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Introduction

A wide variety of drugs can cause pulmonary injury and should be considered during the evaluation of lung infiltrate.[1] Early diagnosis is important because unrecognized toxicity can be progressive and even fatal. Drug-induced lung injury may manifest in a variety of histological patterns.[1] Acute fibrinous and organizing pneumonia is a distinct pattern of reaction of the lung to injury.[2] It is characterized by intra-alveolar fibrin balls and organizing pneumonia. The absence of hyaline membranes, granulomatous inflammation, and eosinophilic deposition are important distinguishing features.

Case Report

A 64-year-old male came to our hospital with dry cough, fever, and chills, of 2 weeks duration. He had a history of myelodysplastic syndrome, developing after the successful treatment of acute myelogenous leukemia. Four weeks earlier he had received 50 mg of intravenous decitabine daily for 5 days. At the time of hospitalization he had just completed a second course of decitabine. On examination his temperature was 102°F, blood pressure was 134/62 mm Hg, heart rate was 98 beats/min, oxygen saturation was 88% on room air, and respiratory rate was 18 breaths/min. His lung examination had inspiratory crackles in the left lung base. The rest of his physical examination was unremarkable. He had pancytopenia, with white-blood-cell count of 0.7×10^9 cells/L (normal range of $4–10\times10^9$ cells/L), hemoglobin of 7.9 g/dL (normal range of 14–17 g/dL), and platelets of 12,000 cells/L (normal range of 140,000–400,000 cells/L). His differential count showed 20% neutrophils, 70% lymphocytes, and 10% monocytes. His serum sodium, potassium, creatinine, magnesium, calcium, and liver function test were all within normal limits. Blood and urine cultures were negative. The chest radiograph showed an ill-defined left-lower-lobe infiltrate.

He was started on broad-spectrum antibiotics, including an anti-fungal agent. The computed tomography scan of his chest (Fig. 1) revealed a left-lower-lobe consolidation. Computed-tomography-guided needle aspiration of the left lower lobe was non-diagnostic. He underwent bronchoscopy with bronchoalveolar lavage, which was non-diagnostic. His bronchoalveolar lavage fluid showed 48% macrophages, 32% neutrophils, and 20% lymphocytes. He remained febrile despite treatment with antibiotics. A repeat computed tomography of the chest (Fig. 2) 10 days later showed worsening of the left-lower-lobe consolidation. The patient underwent video-assisted thoracoscopic wedge biopsy of the left lower lobe. The open-lung biopsy from the left-lower lobe (Fig. 3) showed patchy areas of organizing pneumonia with fibrin balls within the alveoli and air spaces. There was no hyaline membrane. The diagnosis of acute fibrinous and organizing pneumonia sec-

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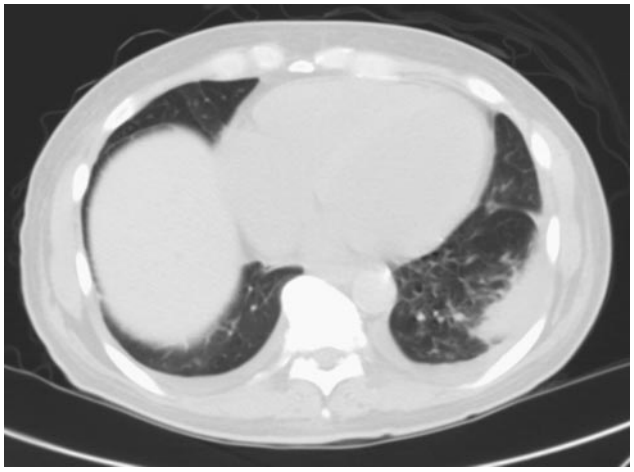

Fig. 1. Computed tomogram shows a left-lower-lobe consolidation.

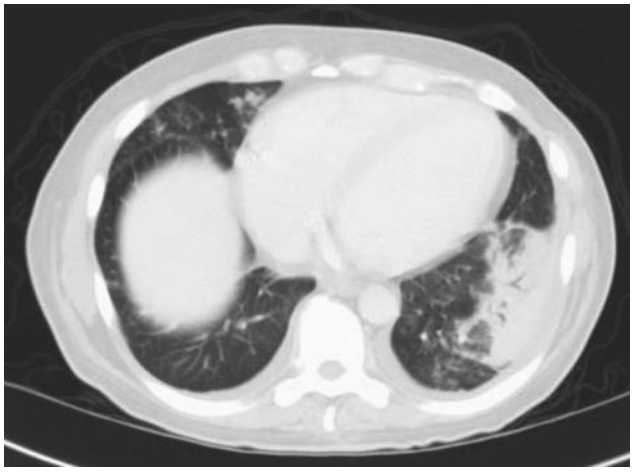

Fig. 2. Repeat computed tomography 10 days later shows worsening of the left-lower-lobe consolidation.

ondary to decitabine was established. He was started on methylprednisone 60 mg intravenously, every 6 hours, followed by 40 mg of oral prednisone daily. He had substantial clinical and radiological improvement after discontinuation of decitabine and a course of corticosteroids.

Discussion

Acute fibrinous and organizing pneumonia was first described by Beasley et al[2] in 2002. In their paper they noted several conditions associated with acute fibrinous and organizing pneumonia, including collagen-vascular disease, lymphoma, amiodarone, and infections caused by *Haemophilus influenzae* and *Acinetobacter baumannii*. Recently, acute fibrinous and organizing pneumonia has also been reported in patients with dermatomyositis,[3] acute lymphocytic leukemia,[4] severe acute respiratory syndrome,[5] and secondary to drugs, including abacavir[6] and busulfan.[7]

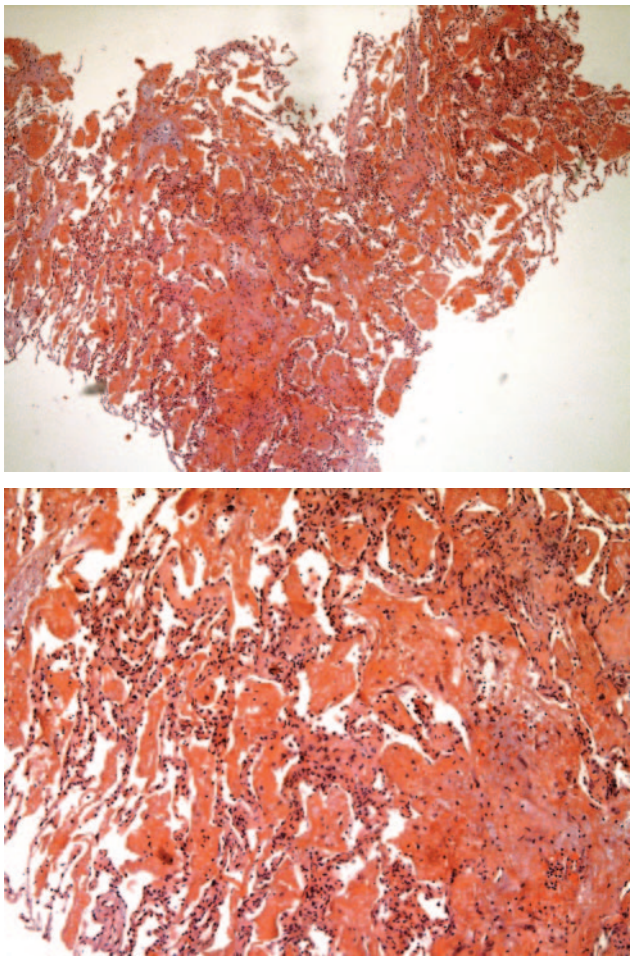

Fig. 3. Micrograph from the open-lung biopsy of the left-lower lobe shows patchy areas of organizing pneumonia with fibrin balls in the alveoli and air spaces.

Patients with acute fibrinous and organizing pneumonia may have an acute or subacute clinical course. The pattern of the acute form resembles the clinical picture of acute lung injury. Decitabine[8] is a hypomethylating agent that was recently approved by the Food and Drug Administration for the treatment of myelodysplastic syndrome. The major adverse effect of decitabine is myelosuppression. Other adverse effects, including fever, nausea, vomiting, diarrhea, bone aches, hyperbilirubinemia, and skin rash, have also been described. To the best of our knowledge this is the first case describing acute fibrinous and organizing pneumonia pattern of lung injury secondary to decitabine.

The classic histological findings of acute fibrinous and organizing pneumonia include intra-alveolar fibrin balls with organizing pneumonia. This pattern must be distinguished from diffuse alveolar damage, bronchiolitis obliterans organizing pneumonia,[9] and eosinophilic pneumonia.[10] Fibrin deposits are found in diffuse alveolar damage and bronchiolitis obliterans organizing pneumonia, but,

unlike acute fibrinous and organizing pneumonia, these deposits do not represent the major findings. The air-space involvement in acute fibrinous and organizing pneumonia is patchy in distribution, as opposed to diffuse involvement in diffuse alveolar damage. Hyaline membranes, granulomatous inflammation, and eosinophilic infiltrates are absent in acute fibrinous and organizing pneumonia.

The retrospective review by Beasley et al[2] demonstrated that approximately 30% of patients with acute fibrinous and organizing pneumonia required mechanical ventilation. Notably, all those patients who needed mechanical ventilation died. The acute fibrinous and organizing pneumonia pattern portends a poor prognosis, with a mortality rate of more than 50%. The clinical course of these patients is similar to those with diffuse alveolar damage, and, indeed, acute fibrinous and organizing pneumonia may be a fibrinous variant of diffuse alveolar damage. Treatment with corticosteroids and discontinuation of the underlying drug may be attempted.

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