



# The Creative Clinician

## Alphabet Soup: RAEB, HMA, DOE, and AFOP

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**Medications have long been associated with acute lung injury.** We describe a case of a patient with acute fibrinous and organizing pneumonia (AFOP) after receiving decitabine.

### CASE PRESENTATION

A 64-year old man with a history of cardiac transplant in 2000 secondary to idiopathic nonischemic dilated cardiomyopathy presented with pancytopenia in July 2009 and was diagnosed with the myelodysplastic syndrome **refractory anemia with excess blasts-2 (RAEB-2)**. His blast count bordered on qualifications for acute myeloid leukemia, and he was initially treated with standard induction consisting of seven days of standard-dose cytarabine followed by three days of daunorubicin. A repeat bone marrow showed persistent blasts and he was then treated with high-dose cytarabine which he also failed. Subsequently, his treatment regimen was changed to decitabine at the standard dose of 20mg/m<sup>2</sup> days 1-5 dosed every 4 weeks. He received 3 cycles of decitabine. His only other medications were cyclosporine 75mg daily, prednisone 5mg daily, and omeprazole 20mg daily.

Within three months of the first dose of decitabine, his chest radiographs began to show bilateral diffuse opacities. On the day of admission, he presented to an outpatient cancer center with worsening fatigue, dyspnea on exertion, a nonproductive cough, and tachypnea. On examination, temperature was 37.8 degrees Celsius, blood pressure 130/80 mmHg, respiratory rate was 30/minute, and his oxygen saturation was 100% on room air. Lungs were clear to auscultation but during the course of his hospitalization he developed diffuse rales bilaterally.

High-resolution **computed tomography (CT)** of the chest (Figure 1) showed innumerable bilaterally centrilobular nodules most prominent in the dependent regions of the lung. There were subpleural reticular changes with thickening of the interlobular septae but no evidence of architectural distortion or honeycomb cystic change.

Bronchoscopy was performed and microbiological studies for bacterial, fungal, and viral etiologies were negative. A transbronchial biopsy showed no evidence of infection or leukemic infiltrate but was concerning

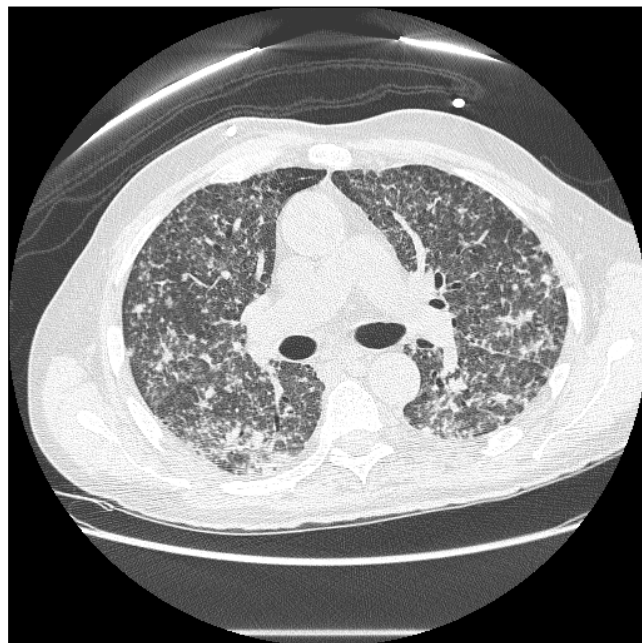


Figure 1: High resolution computed tomography (CT) showing bilateral centrilobular nodules and subpleural reticular changes with thickening of the interlobular septae. Image courtesy Rhode Island Hospital Department of Diagnostic Imaging.

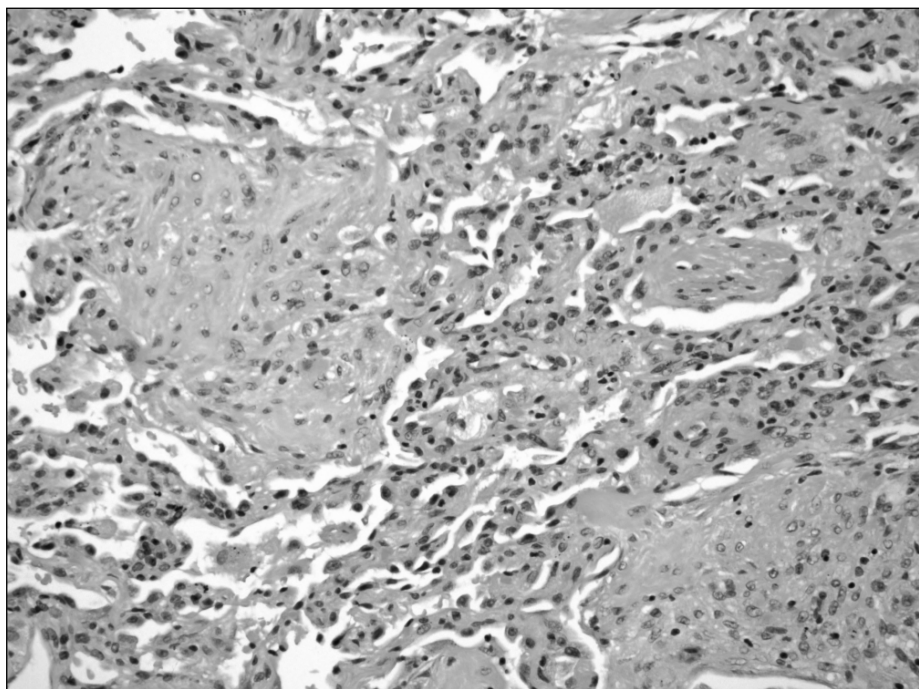


Figure 2: Pathology specimen from an open lung biopsy shows intra-alveolar fibrin balls and lack of classic hyaline membranes. This is consistent with the histologic description of acute fibrinous and organizing pneumonia. Image courtesy Bassam I. Aswad, MD.

for diffuse inflammation. An open lung biopsy was performed which was consistent with acute fibrinous and organizing pneumonia (Figure 2). The patient was started on high-dose intravenous methylprednisolone (250mg IV every 6 hours for three days) and subsequently transitioned to oral prednisone (40mg daily) with significant improvement in his symptoms. At a follow-up visit several weeks after discharge, the patient's respiratory symptoms had resolved and he was tapered to his baseline prednisone dose of 5mg daily.

## DISCUSSION

Myelodysplastic syndromes (MDS) have been reported with a higher frequency in patients receiving solid organ transplants.<sup>1</sup> Decitabine is a cytosine analog that serves as a **hypomethylating agent** (HMA) by inhibiting DNA methyltransferase and is indicated for the treatment of myelodysplastic syndromes including **refractory anemia with excess blasts (RAEB)**.<sup>2</sup> Commonly, it is associated cytopenias although pneumonia and respiratory failure have also been reported.

**Acute fibrinous and organizing pneumonia (AFOP)** was first described in 2002 as a variant of diffuse alveolar damage.<sup>3</sup> Characterized by intra-alveolar fibrin balls and organizing pneumonia, the pathologic specimens are notable for absence of granulomatous inflammation and hyaline membranes. In a series of Canadian patients diagnosed with the **severe acute respiratory syndrome (SARS)** a significant number of patients were noted to have AFOP on post-mortem analysis.<sup>4</sup> AFOP has also been described after **hematopoietic stem cell transplantation (HSCT)** as well as after decitabine administration.<sup>5</sup>

Treatment usually includes steroids, although antibiotics and cyclophosphamide have also been used. Recently, use of mycophenolate mofetil has been used as an adjunct to corticosteroids in treating AFOP.<sup>6</sup> In patients who have received decitabine, particular attention should be paid to the patient's respiratory status and cessation of decitabine considered if the patient develops clinical or radiographic findings to suggest acute lung injury.

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## Disclosure of Financial Interests

The authors and/or spouses/significant others have no financial interests to disclose.

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