Organizing Pneumonia And Diffuse Alveolar Damage: An Incidental Finding In An Immunocompromised Patient By EBUS-FNA

B Lowenthal, F Hasteh

Abstract
Diffuse Alveolar Damage (DAD) is a clinicopathologic syndrome depicting a deposition of intraalveolar red blood cells, fibrin, and hemosiderin-laden macrophages coming from the alveolar capillaries. The causes of DAD originate from injury to the alveolar circulation. The typical computed tomography scan pattern of DAD comprises of diffuse ground glass opacities with or without consolidation. There is no evidence of DAD presenting as a mass in the literature. Endobronchial ultrasound-guided fine needle aspiration (EBUS-FNA) is not a popular method for diagnosis of DAD. This case report is an example of an immunocompromised patient undergoing induction chemotherapy for myelofibrosis transforming into acute myelogenous leukemia presenting with a left upper lobe mass on imaging. The clinical diagnosis was concerning for fungal pneumonia versus less likely malignancy. EBUS-FNA was performed on the left upper lobe mass to reveal groups of reactive looking pneumocytes wrapping around fibrin deposits forming a pseudopapillary architecture with a background of mixed inflammatory cells, necrotic material, histiocytes, giant cells, and occasional clusters of crowded epithelioid cells. The cell block revealed fibrin deposits and collection of histiocytes consistent with DAD and organizing pneumonia. Special stains and immunohistochemistry did not reveal microorganisms. This case report demonstrates EBUS-FNA of a mass-like lesion showed features of DAD and organizing pneumonia in an immunocompromised patient. EBUS-FNA can be used as a non-invasive procedure for diagnosis of DAD and organizing pneumonia. The cytopathologist should be familiar with these features to help improving the diagnostic accuracy.

INTRODUCTION
Diffuse Alveolar Damage (DAD) is a clinicopathologic syndrome depicting a deposition of intraalveolar red blood cells, fibrin, and hemosiderin-laden macrophages coming from the alveolar capillaries. All the causes of Diffuse Alveolar Damage originate from injury to the alveolar circulation. We present a patient who presents with hemoptysis, anemia, hypoxic respiratory failure, and pulmonary infiltrates on x-ray. There are many causes of Diffuse Alveolar Damage, which includes underlying connective tissue disorder, seropositive systemic vasculitides, bland pulmonary hemorrhage, drug injury, coagulation disorders, and infections. Bronchoalveolar Lavage (BAL) is the diagnostic choice for Diffuse Alveolar Damage as it demonstrates progressively hemorrhagic serial samples. However, the underlying cause is not diagnosed with BAL, but is identified with history, physical examination, laboratory and serologic testing. The typical computed tomography (CT) scan pattern of DAD demonstrates diffuse ground glass opacities with or without areas of consolidation. There is no evidence in the literature of DAD presenting as a mass. This case report will demonstrate a case where endobronchial ultrasound-guided fine needle aspiration (EBUS-FNA) of a mass like lesion can be utilized for diagnosis of incidentally found DAD in addition to the underlying cause.

CASE REPORT
We report a 67 year old male with a history of myelofibrosis with transformation to acute myelogenous leukemia, latent tuberculosis infection, diabetes mellitus, and hypertension.
who presents to our institution for induction chemotherapy. Over the course of the hospital stay, the patient developed neutropenic fevers and was found to have blood culture positive for extended-spectrum beta-lactamase producing E. coli. On the 29th day of hospitalization, his fevers recurred resulting in a chest CT scan to be ordered. This scan demonstrated a new left upper lobe mass concerning for a fungal pneumonia versus less likely malignancy (Figure 1). The patient had been sub-therapeutic on Posaconazole up to this point due to the adverse side effects. The clinicians were thus worried that the mass represented a fungal ball lung infection. Interventional Radiology performed the EBUS-FNA.

The rapid evaluation showed atypical pneumocytes, questioning a reactive process. Following the procedure, the patient developed hypoxia, hypotension, and atrial fibrillation with rapid ventricular response. He was then transferred to the intensive care unit (ICU) where he was found to have a large left-sided effusion. In the ICU, a chest tube was placed draining 2 liters of blood. After 24 hours, the patient stabilized and was transferred out of the ICU. His fevers resolved and the lung mass soon decreased in size. Despite negative cultures and cytologic results (see below), the patient was treated for aspergillus pneumonia. The patient was ultimately discharged to follow-up with his referring Oncologist.

CYTOPATHOLOGIC FINDINGS
The left upper lobe mass tissue was procured through a transbronchial needle aspiration utilizing a 22 gauge needle. Three fine needle aspirations are performed under direct ultrasound visualization (EBUS-FNA) in the interventional radiology suite. The aspirates were evaluated with a rapid on site evaluation (ROSE) by the Cytopathologist. The specimen was sent for routine cytology and cytology cell block. The specimen was sent to Pathology in two containers. The first container produced two air dried smears stained with Diff Quik® for ROSE and three alcohol-fixed smears for Papanicolaou staining. The second container consisted of 20 ml of tan-red fluid with fragments of tissue within the suspension, which was sent to make a cell block.

The EBUS-FNA smears consisted of multiple groups of crowded cells with scant cytoplasm. There were occasional tiny nucleoli in the background of few giant cells, histiocytes, and a large number of reactive-appearing pneumocytes. This can be seen in Figure 2. The cell block demonstrated some fibrin deposits with features consistent with organizing pneumonia. Diffuse Alveolar Damage was also considered in the diagnosis due to the fibrin deposition and extensive reactive pneumocytes. The cytology did not show well-formed granulomas, viral cytopathic effect, or malignant cells. GMS and AFB special stains were performed and negative for fungal microorganisms and acid fast bacilli, respectively. CMV and Adenovirus immunohistochemical stains (Ventana Medical Systems, Tucson, AZ) were negative for cytomegalovirus and adenovirus. Overall, the diagnosis of the EBUS-FNA from the new left upper lobe lung mass was consistent with organizing pneumonia with some fibrin deposits.

Figure 1
Chest CT scan in the transvers plane highlights the left upper lobe mass-like opacity.
Figure 2a
The aspirate smears reveal groups of crowded cells with scant cytoplasm, background fibrin, a large number of reactive-appearing pneumocytes with background histiocytes and few giant cells (A- Diff Quik, 200x, B- Papanicolaou, 200x).

Figure 2b
The aspirate smears reveal groups of crowded cells with scant cytoplasm, background fibrin, a large number of reactive-appearing pneumocytes with background histiocytes and few giant cells (A- Diff Quik, 200x, B- Papanicolaou, 200x).

DISCUSSION
Bronchoalveolar Lavage is an established diagnostic tool in evaluating inflammatory and immune processes of the lungs, especially located within the lower airways4. This is because most cells and solutes recovered in BAL specimens are derived from the alveolar spaces and interstitium within the lower respiratory tract5. Diffuse Alveolar Damage is an inflammatory process of the lung located within the lower respiratory tract as the red blood cells, hemosiderin-laden macrophages, and fibrin deposition all takes place within the alveolus and nearby interstitium. Organizing pneumonia can be located throughout the interstitium of the lung and will demonstrate reactive-appearing pneumocytes, histiocytes and potentially microorganisms, granulomas, or viral cytopathic effects.

A recent study examined the diagnostic utility of ROSE of BAL specimens in patients with Acute Lung Injury or Acute Respiratory Distress Syndrome. Of the 71 patients studied, BAL was found to give a specific diagnosis to 41% of patients, give typical features of DAD without a specific diagnosis to 39% of patients, and give no specific information to 20% of patients6. Bronchoalveolar lavage is a diagnostic test of choice because it is minimally invasive with a low morbidity and has a good diagnostic value when history, physical examination, and laboratory data is not helpful for diagnosis. In inflammatory and immunologic pulmonary conditions, BAL is superior to open lung biopsy and transbronchial biopsy because the lavage samples a much larger area of lung7. In addition to the ability of BAL to obtain a more diffuse lung sample, BAL is recommended in immunocompromised patients with DAD and infections investigating the underlying pneumonia as compared to open lung biopsy8.

Fine Needle Aspiration (FNA) is not typically used as a diagnostic modality in Diffuse Alveolar Damage or organizing pneumonia due to the pinpoint nature of the procedure. FNA is usually utilized in specific radiologic lesions such as malignancy or nodule as a way to evaluate a specific site. In this case, the patient was found on work-up to have a new left upper lobe mass that was concerning for fungal pneumonia versus less likely malignancy due to the clinical picture. As a result of the radiology reading, EBUS-FNA was the diagnostic method of choice over Bronchoalveolar Lavage. The finding of an organizing pneumonia in a background suggestive of Diffuse Alveolar Damage was an unexpected incidental finding in this
immunocompromised patient. The concomitant diagnosis of Diffuse Alveolar Damage and organizing pneumonia in an immunocompromised patient via EBUS-FNA was not found in the literature. This case report demonstrates a EBUS-FNA of a mass-like lesion showing features of DAD and OP in an immunocompromised patient. FNA biopsy can be used as a non-invasive procedure for diagnosis of DAD and OP. The Cytopathologist should be familiar with these features to help improving the diagnostic accuracy.

References
Author Information

Brett Matthew Lowenthal, MD
Department of Pathology, University of California San Diego Medical Center
San Diego, California
blowenthal@ucsd.edu

Farnaz Hasteh, MD
Department of Pathology, University of California San Diego Medical Center
San Diego, California