CASE REPORT

Alcoholic leukopenic pneumococcal sepsis

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ABSTRACT

Alcohol abuse has been associated with an increased mortality and morbidity due to increased aspiration, delirium tremens, and seizures. The association of pneumococcal lung infections and leukopenia in the setting of alcohol abuse are rarely reported; however, when present, severe lung infections can happen with severe lung injury and poor response to conventional therapy and ultimately, death. We are reporting a case of 55-year-old-man presented with shortness of breath, cough and altered mental status and eventually found with severe pneumococcal lung infection in the setting of leukopenia and long-term alcohol abuse representing alcoholic leukopenic pneumococcal sepsis syndrome.

Key words: Alcohol abuse, leukopenia, pneumonia

INTRODUCTION

Alcohol abuse is a recognized significant risk factor for serious pulmonary infections. These infections are usually severe and have been association with an increased two- to four-fold risk of adult respiratory distress syndrome (ARDS) compared to non-alcoholics. In addition, leukopenia with a white blood cell count of lesser than 4,000 has been reported in alcoholics, which increase their risk for severe infections and death. Pneumococcal pneumonia with leukopenia and alcohol abuse can lead to a clinical entity that was termed the alcoholic leukopenic pneumococcal sepsis ("ALPS") syndrome with mortality rate as high as 83.3% compared to general population.[1]

CASE REPORT

Alcohol abuse and subsequent leukopenia led to a significant and devastating illness in a 55-year-old man. The patient presented with 2 day history of shortness of breath, cough, fever, chills, confusion, and altered mental status. The patient was found unconscious at the day of admission by a friend and there was no witnessed seizure or trauma. The patient was last seen conscious was 12 h before this presentation. The patient had a significant history of alcohol abuse with the multiple admissions to the hospital due to alcohol withdrawal.

On examination, he was unconscious. The patient was intubated on arrival and placed on assist- control mechanical ventilation. Vitals were significant for sinus tachycardia and hypotension that mandated the use of vasopressors. The chest shows right-sided decreased air entry with diffuse crackles. The rest of examination was unremarkable. Initial work-up revealed complete blood count shows white blood cells 0.8×10^9/L (reference range 4.5-11.0), absolute neutrophil count 360 mm^3, hemoglobin 8.1 g/L (14.0-17.5), and platelets 109,000 and creatinine 3.5 mg/dl, potassium 4.5 meq/L. Chest X-ray showed right lower lobe consolidation with the right costophrenic angle obliteration suggestive of right pleural effusion [Figure 1]. Computed tomography - Angiography of the chest confirmed the findings of right lower lobe consolidation with no pleural effusion on both lung window [Figure 2a transverse cut and 2b coronal cut] and mediastinal window [Figure 3a transverse cut and 3b coronal cuts]. Bronchial secretions culture grows gram-positive diplococci (*Streptococcus pneumoniae*). Given the radiographic and microbacterial findings along the history of alcohol abuse and leukopenia, the diagnosis of "ALPS" syndrome was made. The patient initially was admitted

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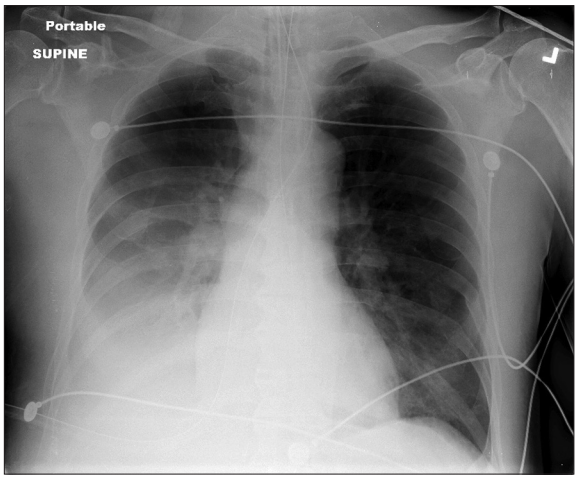

Figure 1: Chest X-ray showed right lower lobe consolidation with the right costophrenic angle obliteration suggestive of right pleural effusion

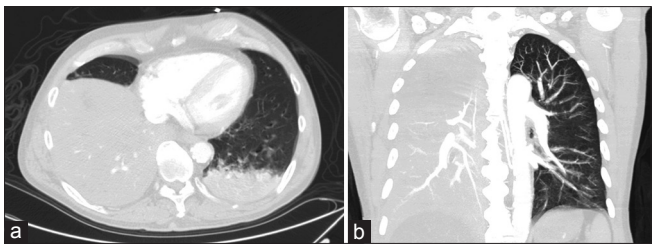

Figure 2: Computed tomography - Angiography of the chest confirmed the findings of right lower lobe consolidation with no pleural effusion on both lung window ([a] transverse cut and [b] coronal cut)

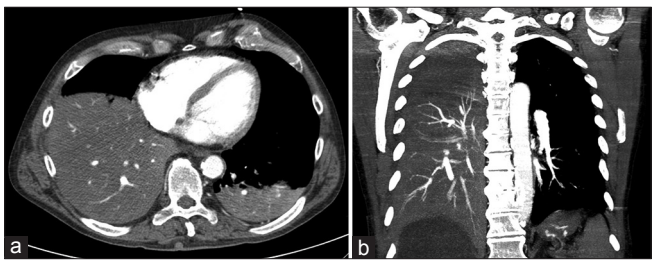

Figure 3: Computed tomography - Angiography of the chest confirmed the findings of right lower lobe consolidation with no pleural effusion on both mediastinal window ([a] transverse cut and [b] coronal cut)

to the intensive care unit and started on vancomycin and piperacellin/tazobactam antibiotics. Few days later, he made remarkable recovery and was discharged in stable condition.

DISCUSSION

The patient's presentation initially raised suspicious of a syndrome included alcoholism, leukopenia, and pneumococcal sepsis. Alcohol abuse has been well-recognized as a significant risk factor for serious pulmonary infections with tissue-damaging gram-negative pathogens, such as *Klebsiella pneumoniae*,[1] or for bacteremia and shock from typical pathogens, most notably *S. pneumoniae*.[2] In addition, alcohol abuse independently increases the risk of ARDS two- to four-fold in at-risk individuals, and this is exacerbated by the fact that alcohol abuse also increases the risk for trauma, sepsis, and other acute illnesses that lead to ARDS.[3] Furthermore, chronic alcohol abuse also increases the risk of multiple organ failure and ventilator associated pneumonia, complications that exacerbate the morbidity and mortality associated with the ARDS.[4] The influence of alcohol abuse on morbidity and mortality among patients with community-acquired pneumonia is substantial. The mortality among alcoholic patients hospitalized for community-acquired pneumonia may reach up to 65%, which was much higher than the predicted death rate for hospitalized patients (approximately 20%).[1] Leukopenia with a white blood cell count of lesser than 4,000 cells per cubic millimeter (mm^3) of blood is another aspect of fatal association between alcohol abuse and pneumonia. This has been remarkably notable pneumococcal pneumonia and can lead to a clinical entity that has been termed the "ALPS" syndrome. This was identified in previous studies that showed alcoholic patients with pneumococcal bacteremia and leukopenia had a mortality rate reaching up to 83.3%, whereas the mortality in the rest of the cohort was only 22%.[2]

The mechanisms by which alcohol abuse increases the risk of pneumonia likely are multifactorial and include increased risk of aspiration of gastric acid and/or pathogens from the upper part of the throat. Alcoholic patient are predisposed to pathologic changes in the oropharyngeal flora where the prevalence of oropharyngeal colonization with pathogens such as *K. pneumoniae* may be as much as 4 times higher in alcoholic compared with the non-alcoholic patients. This combined with the acute intoxicating effects of alcohol and the subsequent depression of the normally protective gag and cough reflexes, leads to more frequent, and severe pneumonias from gram-negative organisms.[5] Another key factor is a decreased mucous-facilitated clearance of bacterial pathogens from the upper airway, - alcohol ingestion impairs the function of the cilia (hair-like projections from cells) that swing mucus out of the lungs, in part by disrupting the normal coordinated ciliary beating that clears pathogens from the airway.[6] Furthermore, alcohol abuse impairs pathogen ingestion (i.e., phagocytosis) by white blood cells in the air sacs of the lungs (i.e., alveolar macrophages) and other infection-fighting white blood cells (i.e. neutrophils) as well as it suppresses the responses of small proteins involved in immune function (i.e., chemokines).[7] These changes are often sub-clinical and may not manifest as detectable lung impairment until challenged by an acute insult such as sepsis or trauma.

In alcoholic patients who are presenting with pneumonia, clinicians have to triage patients based on severity of

presentation and homodynamic stability. Direct admission to the hospital usually is indicated, especially in patient presenting with septic shock. ALP with respiratory failure requires intubation and mechanical ventilation. Antibiotic therapy is the mainstay of treatment with especial attention to *K. pneumoniae*. Experimentally, chronic alcohol ingestion decreases the expression of granulocyte macrophage colony-stimulating factor (GM-CSF) receptors in the airway epithelium and macrophages and as a result, GM-CSF–dependent functions in each cell type are suppressed. Thus, treatment with recombinant GM-CSF restores GM-CSF receptor expression and normalizes both alveolar epithelial barrier function 7 and alveolar macrophage immune function[8,9] A small clinical trial has evaluated GM-CSF treatment for acute lung injury in patient with septic shock, and results showed demonstrated that patients who received recombinant GM-CSF treatment had less severe lung injury than those who received a placebo.[10] It is considered that GM-CSF treatment might be efficacious in alcoholic individuals with ARDS, which might augment alveolar macrophage immune functions and improve outcomes in alcoholic subjects with severe community- or hospital-acquired pneumonia; however, this strategy has not been expanded into a larger clinical trial.[8]

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