

A Case of Necrotising Pneumonia in the Setting of Influenza Infection

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Abstract

A 37 year old male with past medical history of HIV (unknown CD4+ count and viral load, on HAART with questionable compliance), IV drug abuse, presented to ER with complaints of three day cough productive of yellow/brownish sputum, subjective fevers, chills, chest pain aggravated by coughing and deep breaths, diarrhea, vomiting. He reported being in contact with people who had flu. Vitals showed temperature of 38.3 Celsius, respirations 22/min, heart rate of 114/min, O₂ saturation of 97% which rapidly decompensated to 85% on room air. On physical exam patient was in moderate to acute distress, with rhonchi in bilateral lung fields, tachypneic, tachycardic, occasionally producing blood tinged sputum. Labs showed severe neutropenia with bands, normal hemoglobin and hematocrit, elevated lactate, and anion gap metabolic acidosis. Influenza A test was positive. Blood cultures did not show any growth, and rapid strep test was negative. Gram staining was used to identify bacterial morphology. Repeated arterial blood gas analysis showed increasing A-a gradient with progressively worsening PO₂:FiO₂ ratio. Chest X-ray showed infiltrates in right upper and left middle lung. He was treated for sepsis secondary to pneumonia with intravenous fluids, azithromycin and ceftriaxone (switched to vancomycin and cefepime) neupogen. Patient went into severe sepsis and septic shock, was intubated and started on vasopressors. He subsequently developed massive hemoptysis with expectoration of approximately 3 liters of blood. Patient expired after 45 minutes of resuscitation, 19 hours after admission.

Case Report

A 37 year old male presented to ER with complaints of cough productive of yellow/brownish sputum for three days, subjective fevers with chills, chest pain aggravated by coughing and deep breaths. He had past medical history of HIV with unknown CD4+ count and viral load, was on HAART with questionable compliance, acquired through intravenous drug abuse. He reported being in contact with people who had flu. He worked as a doorman without any limitations until three days prior to admission. Vitals showed blood pressure of 104/65 mmHg temperature of 100.9 F, tachypnea 22/min, tachycardia at a rate of 114/min, O₂ saturation of 97% which rapidly decompensated to 85% on room air.

Physical exam showed a patient in moderate to acute distress, with crackles in both lung fields, tachypneic, tachycardic, occasionally producing blood tinged sputum. Labs showed severe neutropenia with bands (wbc 1.2/nL), normal hemoglobin (16 g/dL) and hematocrit (50%), elevated lactate (6.96 mEq/L), and anion gap metabolic acidosis (HCO₃ 15mEq/L). Influenza A rapid test was positive.

Blood cultures did not show any growth, and rapid strep test was negative. Gram staining was used to identify bacterial morphology. Repeated arterial blood gas analysis showed increasing A-a gradient (95 mmHG) with progressively worsening PO₂:FiO₂ ratio suggestive of ARDS. Chest X-ray showed infiltrates in the right and left upper lung fields. He was treated for sepsis secondary to community acquire pneumonia (CAP) with intravenous fluids, azithromycin and ceftriaxone. Tamiflu was given for Influenza infection. Since patient's condition failed to improve, he was provided broader coverage with vancomycin and cefepime for MRSA.

Neupogen was given for neutropenia. Patient progressed to severe sepsis and was intubated and started on vasopressors. Condition progressed to septic shock and patient developed a sudden onset massive hemoptysis with expectoration of approximately three liters of blood. Patient expired after 45 minutes of resuscitation, 19 hours after admission.

The final autopsy report of the respiratory system in our case showed diffuse necrosis and superficial ulceration of the laryngeal mucosae extending into bilateral bronchi. Both lungs were consolidated and meaty after extruding large amounts of hemorrhagic fluid. The trachea and bronchi were necrosed. The pulmonary arteries were unremarkable. Hilar lymph nodes were unremarkable. The lungs were diffusely consolidated and hemorrhagic with no discrete foci, necrosis, or cystic changes. No small vessel thromboemboli were seen. Small bronchi/bronchioles had necrotic debris.

Official microscopic diagnosis: Both lungs had diffuse congestion and hemorrhage. There was bilateral focally necrotizing bronchopneumonia with numerous clusters of cocci suggestive of staphylococcus. Cocci were intracellular consistent with ante-mortem. There was necrotizing tracheitis, bronchitis, and bronchiolitis. There was focally necrotizing vasculitis. Infection was greater on left, but right lung had focal areas of alveolar damage. A few areas bilaterally showed interstitial inflammation.

Discussion

We present a case of Influenza A infection with superimposed necrotizing pneumonia and rapid fatal outcome. Necrotizing pneumonia is a relatively rare condition and fatal in one-half to three quarters of cases [1,2]. It is commonly characterized by leukopenia, fever, sudden onset respiratory failure, hemoptysis, and a high

mortality rate. Patients are mostly children or young adults who present with influenza-like symptoms which rapidly progress to respiratory failure and septic shock. In our case, patient was immune compromised with HIV infection, non-compliant to HAART, that may have contributed to a rapid clinical deterioration. He had a hospital course of only 19 hours during which he remained hemodynamically unstable requiring pressors. That prevented the CT scan investigation, as well as doing sputum cultures.

Based on studies done in mice solely infected with Influenza virus, virus plus bacteria, or bacteria only, it appears that viral infection accelerates death in the mice infected with bacteria [3]. *Streptococcus Pneumoniae* is the most frequently isolated causative agent of community-acquired pneumonia (CAP). However, in patients admitted to ICU with severe CAP, *Staphylococcus aureus* and respiratory viruses, esp. Influenza, must always be considered. Of particular concern are Pantone-Valentine leukocidin (PVL) positive strains of *S. aureus*, H5N1, as well as H1N1 Influenza strain, which has also been associated with 1918. pandemic of flu [3,4].

Autopsies usually reveal hemorrhagic necrosis and destructions of wide areas of the lungs [5]. Lung histopathology in our case was similar to other described cases in literature and involved diffuse inflammation, parenchymal necrosis with alveolar damage, accumulation of bacterial clusters of cocci and lymphocytic infiltration. Larger bronchi showed acute mucosal inflammation and epithelial necrosis [6]. The role of PVL toxin in necrotizing pneumonia is thought to be related to its pro-inflammatory and cytotoxic effects on neutrophils, monocytes, and macrophages. This leads to rapid cell necrosis which largely lacks any apoptotic features. Subsequently, serine proteases and other proteolytic enzymes spill from host immune cells and cause lung tissue damage [7].

Therapeutic modalities for necrotizing pneumonia are difficult to evaluate because this is a relatively rare condition. Empirical treatment against *Staphylococcus Aureus* should be started immediately with a beta lactam antibiotic such as piperacillin-tazobactam and vancomycin. If a rapid fall in the leukocyte count is observed in this setting, PVL producing *S. Aureus* should be suspected and an antibiotic that blocks toxin expression should be rapidly added to any ongoing antibiotic therapy. In the early lifethreatening stages of the disease, goal should be to encounter the effects of the toxin, inhibit its production and biological effects rather than to obtain bacterial clearance [2].

Earlier reports suggest that in the setting of leukopenia, sepsis, multilobar superimposed pneumonia with influenza and hemoptysis, there is high mortality secondary to necrotising process in lungs [7]. Vancomycin is used to cover MRSA but results have not shown significant improvement in mortality. In our case, patient deteriorated inspite of getting vancomycin. Some reports have suggested combining linezolid with clindamycin as this would cover MRSA and also decrease toxin production [1]. In the setting of these case reports which signify that linezolid and clindamycin work better in cases of necrotizing pneumonia, our case further signifies that immunocompromised patients with suspected pneumonia and hemodynamic instability should be empirically treated with linezolid. A randomized controlled trial on empiric trial of linezolid vs. vancomycin in such cases would be helpful. The use of intravenous immune globulin (IVIG) should be considered in the most severe cases [2]. In addition to antimicrobial and antiviral therapy

(neuraminidase inhibitors), modalities to establish adequate gas exchange (endotracheal intubation), hemodynamic stability (intravenous hydration and vasopressors) and controlling hemoptysis must be applied.

Limitations of our case report are the lack of proven bacterial strain and a subtype of Influenza virus. Nevertheless, presence of rapid worsening of symptoms, leukopenia, hemoptysis and severe respiratory failure with Influenza A virus infection and Gram positive clusters of cocci and intracellular cocci suggest a possible PVL *S. aureus* infection. non-specific symptoms and rapidly worsens and develops hypoxemia and leukopenia. Therapy should be started as early as possible with an anti-staphylococcal antibiotic before disease enters into a septic and lung destructive stage. If this happens, effective therapy is almost impossible accounting for high mortality rate. People with HIV/AIDS are at increased risk from serious complications related to influenza, one of them being necrotizing pneumonia There is an increased risk for heart- and lungrelated hospitalizations in people infected with HIV during influenza season (October to May) as opposed to other times of the year, and a higher risk of influenza-related death in HIV-infected people.

Because of these serious consequences, it is recommended that HIV-infected people receive influenza vaccine [8,9]. Although there have been no randomized controlled trials or studies proving benefit of linezolid/clindamycin over vancomycin/zosyn, our experience and the review of past literature makes us feel it is time to study lowering the threshold for using linezolid/clindamycin in cases of suspected necrotizing pneumonia.

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