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Case Report

Dyspnea in Acute Myeloid Leukemia – An Uncommon Presentation of Diffuse Alveolar Hemorrhage

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Abstract

Diffuse alveolar hemorrhage is a life-threatening condition characterized by acute hypoxic respiratory failure, hemoptysis, and acute blood loss anemia. Most common etiologies are related to systemic vasculitis due to ongoing vessel inflammation. Diagnosis, however, can be challenging due to variety of non-specific symptoms. We present a challenging case of a 65-year-old male with newly diagnosed acute myeloid leukemia undergoing induction chemotherapy who developed diffuse alveolar hemorrhage.

Keywords: Pulmonary hemorrhage; Acute myeloid leukemia; Hematologic complication

1. Introduction

Acute myeloid leukemia (AML) is a disorder which involves immature myeloid cell proliferation thus causing bone marrow failure. It is characterized by "blast" cells in the peripheral blood along with in the bone marrow. It is the most common acute leukemia in adults with approximately 20,000 cases diagnosed annually. Treatment involves aggressive induction chemotherapy following the '7+3' regimen with cytarabine and an anthracycline agent. Such treatment leaves one immunocompromised and exposed to drug toxicities, infections, and coagulopathy.

2. Case Presentation

A 65-year-old male factory worker presented to the emergency department with weakness, fatigue, shortness of breath and a new rash. Patient reported having unusual malaise for two weeks along with a dry cough, rhinorrhea, and congestion. He denied weight loss, fevers, chills, bleeding episodes, recent infection and travel. Physical exam revealed normal vital signs. Patient appeared pale and fatigued, with a petechial rash over his torso. The remainder of the exam was unremarkable. Lab values revealed hemoglobin 8 gm/dL, hematocrit 23%, white blood cells 58 × 10^9/L, platelets 26 × 10^9/L, and peripheral blasts 26%. Computed tomography of the chest revealed patchy infiltrates of the right and left upper lobes indicative of pneumonia (Figure 1).

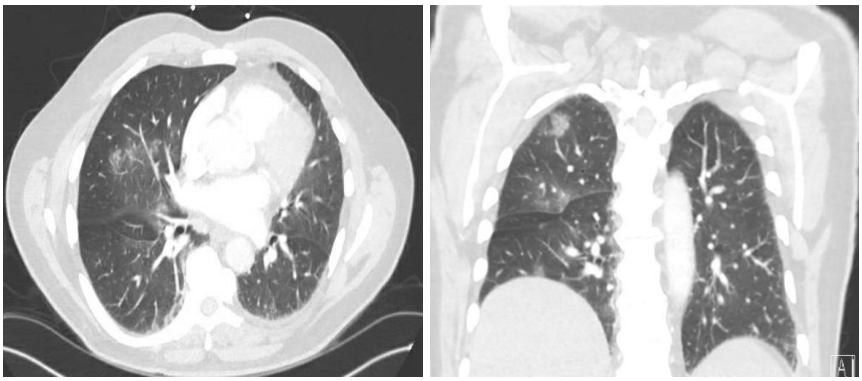

Figure 1: CT Scan of the chest, axial and coronal view with patchy opacities bilaterally.

A multiple-gated acquisition scan revealed normal size of atria and great vessels. The right and left ventricle was of normal size and contractility. The left ventricular ejection fraction was estimated to be within normal range. The patient underwent a bone marrow biopsy on the same day of admission which confirmed acute myeloid leukemia with 38% myeloid blasts.

The patient was started on induction chemotherapy with a '7+3' regimen with cytarabine and daunorubicin and antibiotics were initiated with ceftriaxone 1g IV q24h. On day 5 of admission patient had neutropenic fever, denied cough, abdominal pain, and dysuria. Chest x-ray (CXR) revealed new opacities in the mid-lower left lung. Antibiotics were escalated to azithromycin 500 mg IV q24h, vancomycin 1.24g IV q12h, and meropenem 1gm IV q8h. On day 8 the patient became hypoxic requiring up to 8 liters of oxygen on nasal cannula and labs were significant for pancytopenia with transfusion requirements and transfer to intermediate care status. On day 9 patients had worsening oxygen requirements which warranted ICU transfer. Patient required intubation with mechanical ventilation and bronchoscopy with bronchoalveolar lavage which confirmed diffuse alveolar hemorrhage (Table 1).

Repeat CT chest revealed increase in ground-glass opacities throughout the lung (Figure 2) and the patient was started on systemic glucocorticoids.

	Day 1	**Day 5**	**Day 8**	**Day 9**	**Day 19**
Clinical Status	Fatigue, shortness of breath, petechial rash, non-productive cough	Neutropenic fever	Fatigue, denies cough, hemoptysis, shortness of breath	Shortness of breath, hypoxia	Hypoxia and hypotension, PEA arrest
Laboratory Findings	Hemoglobin 8 gm/dL, white blood cell 58 × $10^{\wedge 9}$/L, platelet 26 $10^{\wedge 9}$/L	Hemoglobin 7.9 gm/dL, white blood cell 2.1 × $10^{\wedge 9}$/L, platelet 19 $10^{\wedge 9}$/L	Hemoglobin 6.3 gm/dL, white blood cell 0.6 × $10^{\wedge 9}$/L, platelet 9 $10^{\wedge 9}$/L	Hemoglobin 7.2 gm/dL, white blood cell 0.4 × $10^{\wedge 9}$/L, platelet 16 $10^{\wedge 9}$/L	Hemoglobin 7.3 gm/dL, white blood cell 0.2 × $10^{\wedge 9}$/L, platelet 46 $10^{\wedge 9}$/L
Imaging Findings	CT Chest: Patchy inflates of the right and left upper lobes	CXR: New opacities in the mid-lower left lung	CTA Chest: Interval worsening of ground-glass opacities throughout the lungs. No pulmonary embolism.	CT Chest: Persistent ground-glass opacities seen throughout the lungs	CXR: Persistent bilateral pulmonary infiltrates
Treatment	"7+3" regimen with cytarabine and daunorubicin + ceftriaxone 1 gm q24h	Day 5 of chemotherapy + azithromycin 500 mg IV q24h, vancomycin 1.24 g IV q12h, meropenem 1 gm IV q8h	Oxygen supplementation + Transfusion (PRBC/Platelet)	Intubation on mechanical ventilation + bronchoscopy with BAL	Started on norepinephrine drip, increased PEEP 18, CPR

Table 1: Patient's Clinical Course.

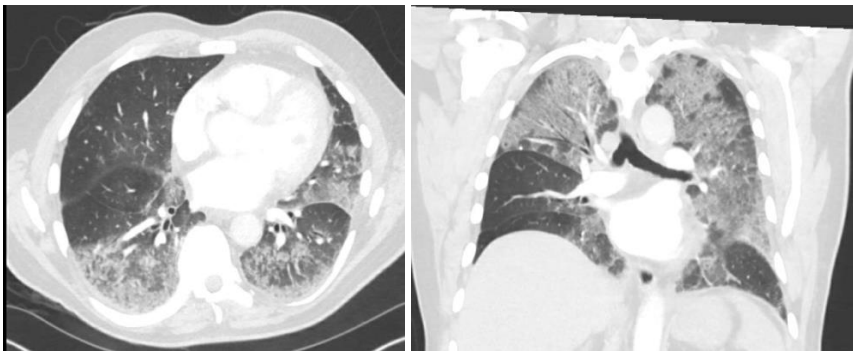

Figure 2: CT of the Chest, axial and coronal view with worsening bilateral ground glass opacities as compared to admission.

During the subsequent days the patient had difficulty weaning from ventilation and was dependent on blood products. He then became hypoxic and hypotensive and underwent resuscitative measures for PEA arrest and unfortunately succumbed to his illness.

3. Discussion

Diffuse alveolar hemorrhage is a life-threatening illness which can be caused by a variety of disorders [1]. Although it is most commonly seen in systemic vasculitides, it can be also be secondary to malignancy, cytotoxic drug therapy, and coagulopathy [2]. Although, the exact mechanism is not yet understood, it is believed that coagulopathy is the foundation of destruction to the alveolar-capillary membrane. Presentation often varies from febrile episodes, cough, dyspnea, hemoptysis, and hypoxia; however, all symptoms are acute in nature [3, 4]. Diagnosis commonly includes anemia with imaging often showing non-specific ground glass opacities, however, bronchoscopy with bronchoalveolar lavage is diagnostic [1].

Our patient deteriorated despite being on adequate antimicrobial coverage which led us to revisit the diagnosis as it is quite difficult to differentiate infectious and non-infectious infiltrates on imaging solely based on the symptom of dyspnea. Diagnosis can be challenging among our immunocompromised cancer patients receiving chemotherapy, as they will be both pancytopenic and predisposed to infections as seen in our patient. This can muddy the diagnosis and clinicians must have a high degree of suspicion when there are unexplained alveolar infiltrates. Treatment is targeted at supportive care to maintain oxygenation, reversing coagulopathy, and eliminating insulting agents.

4. Conclusion

Diffuse alveolar hemorrhage is a known but uncommon complication in those receiving chemotherapy, specifically in acute myeloid leukemia. Clinicians must have a high index of suspicion to make movement towards decreasing morbidity and mortality.

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