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Fatigue and Cytopenia, A Case Report of Acute Myeloid Leukemia

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Abstract

Acute Myeloid Leukemia (AML) manifests with vague symptoms including weakness, fatigue, and dyspnea. A 56-year-old man with a history of smoking and alcohol cessation presented with progressive dyspnea, leg edema, anorexia, weight loss, fatigue, and weakness over three months. Physical exam findings were unremarkable, except for pallor. Laboratory results indicated pancytopenia and elevated liver enzymes, with negative viral and hepatitis screenings. A chest X-ray revealed left basilar pneumonia with small pericardial and bilateral pleural effusions. He was managed with blood product transfusion and antimicrobials.

Further workup with a bone marrow biopsy showed 90% hypercellular marrow with 30-35% blasts, indicating AML. Chromosomal analysis suggested a poor prognosis. The patient initially consented to a 7+3 daunorubicin and cytarabine therapy, but later declined a stem cell transplant, opting instead for outpatient palliative chemotherapy and electing for a do-not-resuscitate status. Vague symptoms with pancytopenia should raise suspicion for AML. Early recognition, prompt diagnosis, and treatment initiation are vital for optimizing patient outcomes.

Introduction

Acute Myeloid Leukemia (AML) is a malignant disorder of the hematopoietic stem cells of bone marrow. It is characterized by the rapid proliferation and accumulation of abnormal myeloid precursors. These aberrant cells disrupt normal hematopoiesis, leading to bone marrow failure and resultant cytopenias. Clinically, AML presents with symptoms of anemia, infection, and hemorrhage due to the suppression of normal blood cell production [1]. The disease demonstrates an incidence rate of 4.3 annual cases per 100,000 individuals in the United States [1]. The clinical incidence of AML has risen by 15%, and its proportion among all leukemia cases has grown by 27% over the past 30 years [2]. AML accounts for the highest percentage of leukemia-related deaths at 60%, making it one of the most fatal types of leukemia [2]. AML predominantly affects older adults, with a median age at diagnosis of 68 years [1].

Furthermore, AML exhibits a slight male predominance, with a male-to-female ratio of approximately 5-to-3 [1]. Specific genetic disorders and syndromes elevate the risk of AML. For example, individuals with Down syndrome face a notably higher risk, with AML ranked among the most prevalent malignancies in this demographic during childhood [3]. Genetic predispositions such as ataxia-telangiectasia and Li-Fraumeni syndrome are associated with an increased susceptibility to AML [4]. The prognosis for AML overall remains guarded, with a five-year relative survival rate of 32% [5]. Despite advancements in understanding the molecular pathogenesis of AML and the development of targeted therapies, the survival rates emphasize the aggressive nature of the disease and the need for novel treatment strategies. In this context, we present a case of AML, characterized by vague symptoms and pancytopenia. This case illustrates the diagnostic challenges and highlights the necessity for early recognition and comprehensive diagnostic workup to facilitate early, effective management. It is important to recognize how clinical presentation can vary, as well as to offer a personalized treatment plan to improve outcomes in AML.

Case Presentation

A 56-year-old man presented to the emergency department (ED) in July 2023 with three months of progressive dyspnea on exertion, bilateral lower extremity edema, anorexia, weight loss, fatigue, and weakness. He smoked 2 packs of cigarettes daily and had recently quit drinking alcohol. He did not regularly see a primary care physician and took no prescription medication. On presentation, his vitals were: temperature 98.9 degrees Fahrenheit, blood pressure 126/59 mm Hg, pulse 93 beats per minute, and 100% saturation on room air. The patient denied fever, headaches, chest pain, hematuria, abdominal pain, nausea, vomiting, or blood in stools. Physical examination was significant for 2+ lower extremity edema and generalized pallor. Electrocardiogram (EKG) showed sinus tachycardia with no signs of acute ischemia or infarct. Chest X-ray revealed small pleural effusions bilaterally with possible left basilar consolidation (Figure 1). Initial laboratory tests showed elevated liver enzymes and pancytopenia (Table 1).

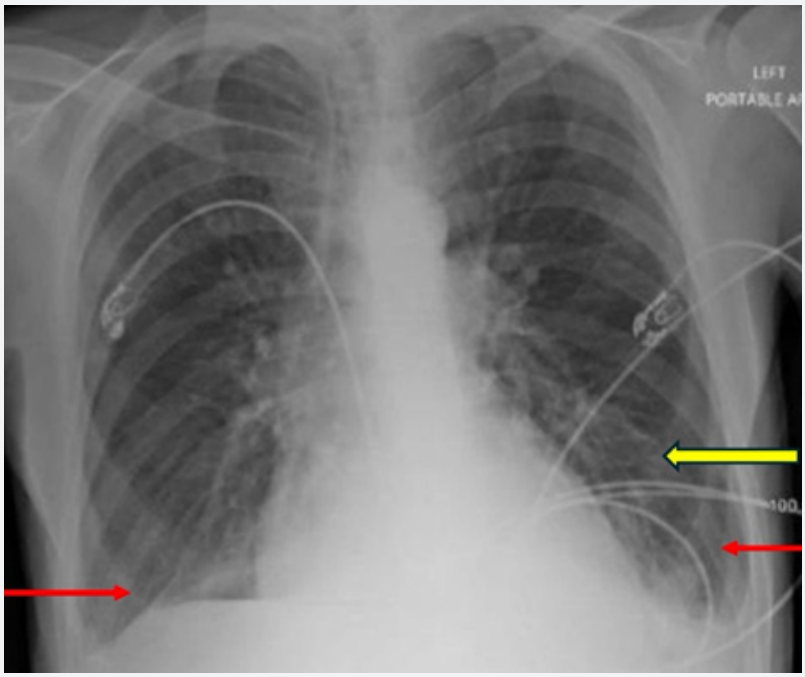

Figure 1: Chest X-ray: Small bilateral pleural effusions with left basilar consolidation
Red arrows indicate pleural effusions. Yellow arrow indicates consolidation.

Table 1: Lab Results at Presentation.

Lab test	Lab result	Reference range (units)
CBC		
White blood cells	23,000*	4000 - 11,000/L
Hemoglobin	5.9*	13.5 - 17.5 g/dL
Hematocrit	19.8*	40.5 - 52.5%
MCHC	29.8*	32.0 - 36.4 g/dL
RDW	36.4*	12.4 - 15.4%
Platelets	73,000*	135,000 - 450,000/L
Lymphocytes absolute	900	1000 - 5100/L
Neutrophils Absolute	700*	1700 - 7700/L
CMP		
Sodium	128*	136 - 145 mmol/L
Potassium	3.9	3.5-5.1 mmol/L

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Anion gap	17*	Mar-16
Creatinine	10	9-13 mg/L
Calcium	83	83-106 mg/L
Total bilirubin	23*	0-10 mg/L
ALP	120	40-129 U/L
ALT	201*	10 - 40 U/L
AST	91*	15 - 37 U/L

ALP: Alkaline Phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BUN: Blood Urea Nitrogen; CBC: Complete Blood Count; CMP: Comprehensive Metabolic Panel; CO2; Bicarbonate; MCHC: Mean Corpuscular Hemoglobin Concentration; RDW: Red Cell Distribution Width.
* Indicates pertinent abnormal value

ALP, alkaline phosphatase. ALT, alanine aminotransferase. AST, aspartate aminotransferase. BUN, blood urea nitrogen. CBC, complete blood count. CMP, comprehensive metabolic panel. CO2, bicarbonate. MCHC, means corpuscular hemoglobin concentration. RDW, red cell distribution width. The left lower lobe infiltrate was treated with IV ceftriaxone and azithromycin for community acquired pneumonia, and blood cultures were obtained, eventually with negative growth. The patient received two units of blood, and the threshold for further blood product transfusion was for hemoglobin less than 7 g/dL or platelets less than 10 k/μL. Hematology was consulted due to pancytopenia, and a bone marrow evaluation was recommended due to suspicion for hematologic malignancy. The human immunodeficiency virus (HIV) antibody was negative, and the patient was not a hepatitis carrier. The infectious disease team started antifungal and antiviral prophylactic treatment with fluconazole and valaciclovir, and antibiotics were adjusted to levofloxacin for neutropenia. Cardiology was consulted for new onset atrial fibrillation with rapid ventricular rate, which was treated with IV diuresis, digoxin and diltiazem. While edema and dyspnea improved, the patient continued to feel fatigued.

A bone marrow biopsy showed 90% hypercellular marrow indicative of AML, with 35% myeloblasts. Prognosis was poor based on fluorescence in situ hybridization (FISH), molecular studies, and cytogenetics showing a complex karyotype consisting of del5q, del7q, loss of RUNX1/21q, and TP53 mutation. Goals of care were discussed, and the patient elected to proceed with treatment. He started intensive induction therapy with 7+3 daunorubicin and cytarabine. Around this time, he developed a rash on the inner thighs, abdomen, and upper extremities, which was treated with diphenhydramine and topical triamcinolone with resolution.

On day 14 of chemotherapy, a bone marrow biopsy was repeated but did not change the course of treatment as it was inconclusive. There was concern for possible residual leukemic blasts, but in less than 5% of cellular marrow. Pathology could not rule out underlying myelodysplastic syndrome (MDS) or possible regenerative marrow. After a discussion with the medical team and family, it was decided to defer granulocyte colony-stimulating factor, with a plan to repeat the biopsy around day 28 of chemotherapy or when blood levels should recover. The best chance of cure was deemed with allogeneic stem cell transplant. However the patient was suffering from significant fatigue, and he declined, insisting on outpatient palliative care while continuing chemotherapy. He elected for a code status change to Do Not Resuscitate Comfort Care Arrest and was discharged after a month-long hospitalization. His lab trends during hospitalization and chemotherapy treatment are noted in (Figures 2-3).

At his first outpatient appointment, the patient was found to be in rapid atrial fibrillation and was subsequently re-admitted. Cultures were obtained, and he was administered 1L of normal saline. He was started on metoprolol and cardiac ablation was discussed, however the patient declined further invasive procedures. He expressed a desire to transition to hospice, stating that he wished to spend the remaining time getting his affairs in order and being with his loved ones. As he was of sound mind, the patient was discharged to home with home hospice per his decision. The chronological course is shown in (Figure 4).

Discussion

With a five-year relative survival rate of 32%, AML remains among the most aggressive and fatal types of leukemia. Vague symptoms along with pancytopenia should raise a clinical suspicion for AML [5]. With the prevalence of chromosomal abnormalities in more than half of cases, early evaluation through hematology and cytogenic analysis remains crucial. Due to the nonspecific symptoms in our patient case, clinical suspicion initially pointed towards heart failure and superimposed infection. Meanwhile without improvement, a bone marrow biopsy had been obtained, confirming the patient's diagnosis with hypercellular marrow and 30-35% blasts. The cytogenic analysis demonstrated deletions in 5q33 and 7q31, loss of RUNX1/21q, and a TP53 mutation, indicating a poor prognosis due to the complex karyotype [6].

The standard treatment for AML includes induction chemotherapy, typically with a 7+3 daunorubicin and cytarabine regimen which the patient received. This treatment regimen remains the standard treatment to put AML in complete remission, despite new advancements in targeted therapies,

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due to its prolonged established efficacy [7]. Unfortunately, the patient declined a stem cell transplant, instead opting for outpatient palliative care. Literature supports allogeneic stem cell transplant in patients with high-risk cytogenetics to improve survival, highlighting a critical decision point in managing the patient's condition [8]. Some complications arose during the case including arrhythmia and rash, which prompted adjustment to the treatment regimen. These complications are not atypical in patients with AML and can be associated with significant adverse effects such as infections and organ toxicity [9].

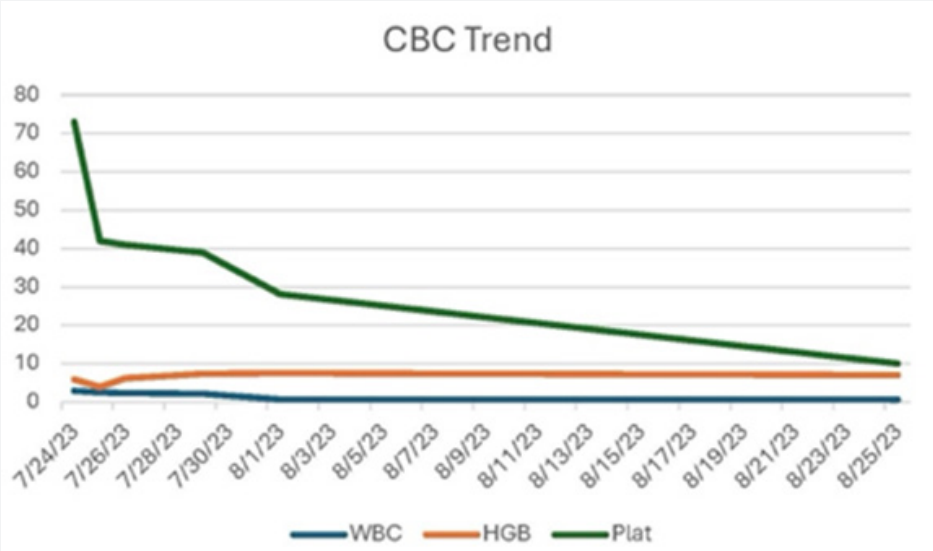

Figure 2: CBC trend through hospitalization
CBC, complete blood count. HGB, hemoglobin. Plat, platelets. WBC, white blood count.
WBC reference range: 4000-11,000/L
HGB reference range: 13.5-17.5 M/uL
Plat reference range: 135,000-450,000/L

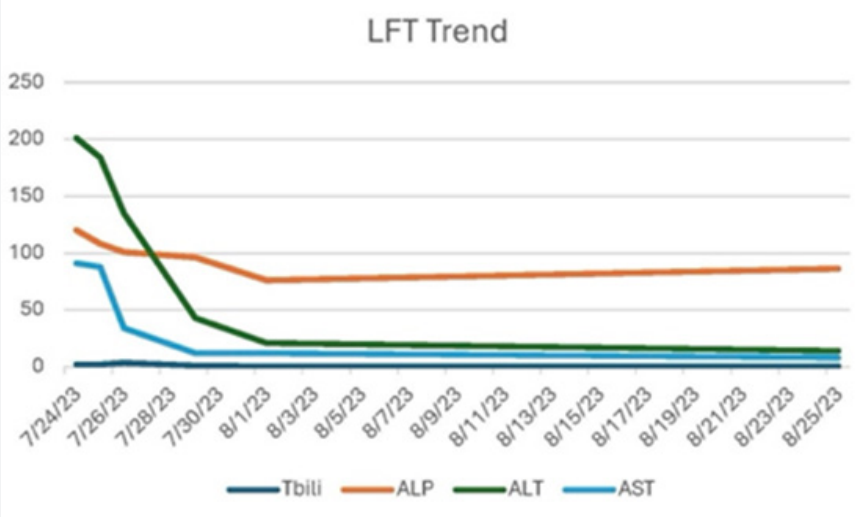

Figure 3: LFT trend through hospitalization.
ALP, alkaline phosphatase. ALT, alanine aminotransferase.AST, Aspartate aminotransferase. LFT, liver function tests. Tbili, total bilirubin.
Tbili reference range: 0-1 mg/dL
ALP reference range: 40-129 U/L
ALT reference range: 10-40 U/L
AST reference range: 15-37 U/L

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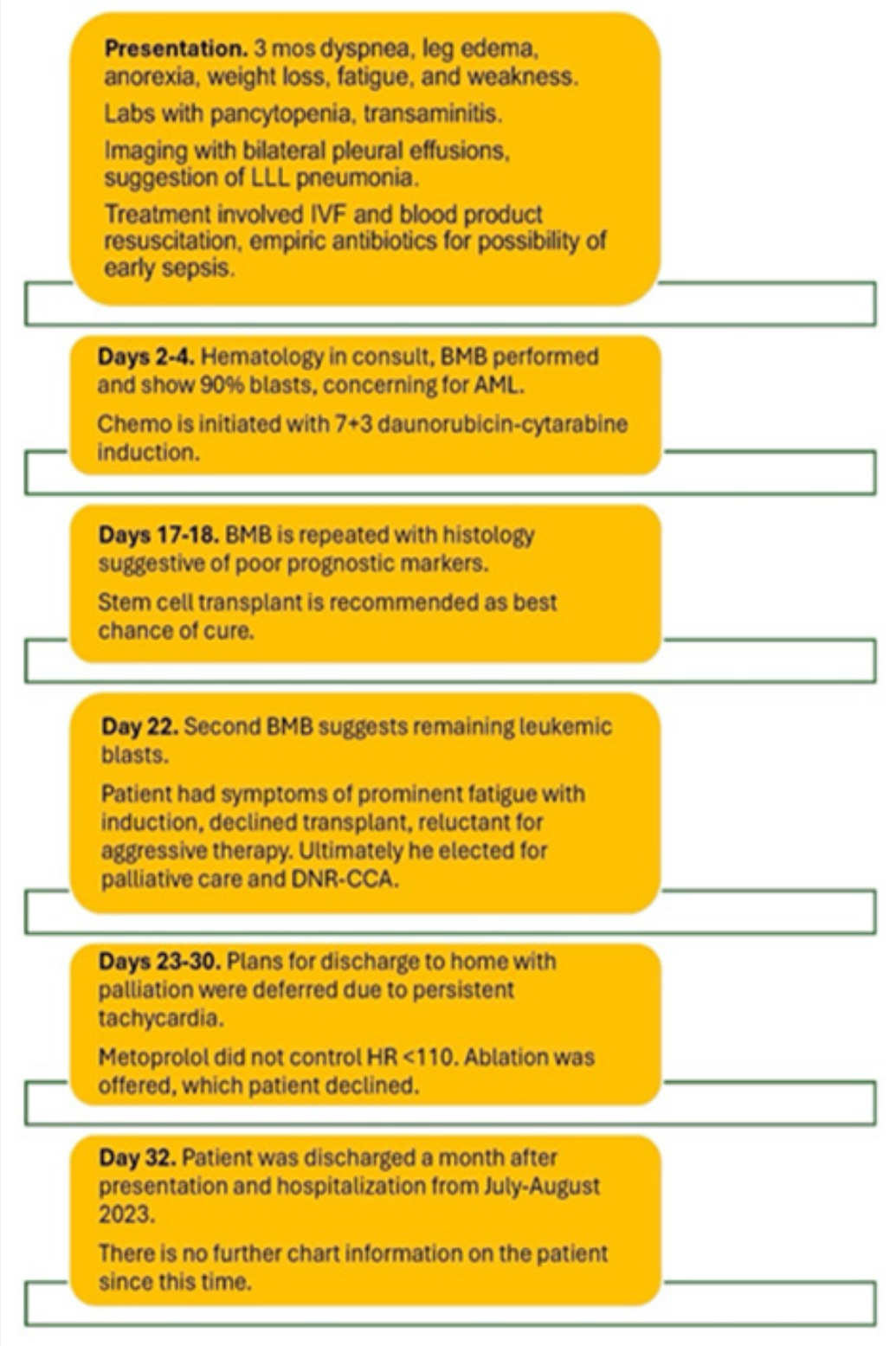

Figure 4: Chronologic course of symptoms, diagnosis, management and outcomes

AML, acute myeloid leukemia. BMB, bone marrow biopsy. DNR-CCA, do-not-resuscitate comfort care. HR, heart rate. IVF, intravenous fluids. LLL, left lower lobe. Mos, months.

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Recent advancements in the treatment of AML include targeted therapies such as Feline McDonough Sarcoma (FMS)-like tyrosine kinase (FLT) 3 inhibitors, isocitrate dehydrogenase (IDH) 1 and 2 inhibitors, and B-cell lymphoma (BCL) 2 inhibitors, which have shown promise in improving the outcome of specific genetic subtypes of AML [10]. These new agents show a significant shift towards personalized medicine in AML management. However, the efficacy and safety of these treatments compared to traditional chemotherapy are still under scrutinous investigation [11]. These new targeted therapies show promise in the realm of improved survival with fewer adverse effects however long-term data is still unknown [12]. Our patient was diagnosed after three months of symptoms in an advanced stage of disease and with poor prognostic markers. He received the standard of care therapy during an intensive hospitalization, but further care was ultimately limited to side effects, overall symptoms, and his spiritual and mental well-being. Providers provided careful attention to treatment options and outcomes and ultimately honored the patient's wishes.

Conclusion

Vague symptoms such as dyspnea, fatigue, and weakness, with an associated pancytopenia in a 56-year-old male, should raise suspicion for AML. A bone marrow biopsy should confirm the diagnosis, and standard treatment entails 7+3 daunorubicin and cytarabine induction chemotherapy. Due to poor cytogenetic prognostic markers, allogeneic stem cell transplant may be recommended. In our patient's case, his wishes to transition to palliative and hospice care may have resulted in a less favorable clinical outcome, but we continue to individualize patient care and honor their overall well-being in the treatment plan. Further research explores targeted therapies, such as FLT3 and IDH inhibitors, which may offer promising alternatives with potentially fewer adverse effects.

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