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Acute Myeloid Leukemia Presenting as Thrombotic Thrombocytopenic Purpura: A Case Report

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Abstract

We would like to present a case of Acute Myeloid Leukemia (AML) with myelodysplasia-related changes that presented as thrombotic Thrombocytopenic Purpura (TTP). Our patient presented to with the classic pentad of TTP symptoms: anemia, thrombocytopenia, fever, elevated creatinine, and altered mental status. After a failure to respond to plasmapheresis therapy, we proceeded with a bone marrow biopsy and fluorescent *in situ* hybridization, which supported formal diagnosis of acute myeloid leukemia with myelodysplasia-related changes. Our case is an extremely rare presentation of a rare condition, as there have been no reported cases of acute myeloid leukemia with myelodysplasia-related changes presenting as thrombocytopenic thrombotic purpura. This case highlights the importance of a high clinical index of suspicion for acute myeloid leukemia in patients who present with unexplained cytopenias and constitutional symptoms even when there are distracting symptoms and an absence of blasts on peripheral smear.

Keywords: Thrombotic thrombocytopenic purpura; Acute myeloid leukemia; Microangiopathic hemolytic anemia; Ttp; Aml; Myelodysplastic; Thrombocytopenia

Introduction

Acute Myeloid Leukemia (AML) is a type of cancer in which the bone marrow makes abnormal myeloblasts, red blood cells, or platelets [1]. Proliferation of abnormal cells in the bone marrow interfere with normal production of normal blood cells [1]. Classically, patients present with lethargy, easy bleeding and bruising, and increased risk of infection. Thrombotic Thrombocytopenic Purpura (TTP) is a rare blood disorder caused antibodies against the enzyme ADAMTS13, which results in the fragmentation of platelets by uncleaved von Willebrand multimers and subsequent formation of blood clots in microvasculature throughout the body [2]. Classically, these patients present with low-grade fevers, anemia, thrombocytopenia, acute kidney injury, altered mental status, and schistocytes on peripheral blood smear [2]. We would like to present a patient whose clinical presentation aligned with TTP, but upon further investigation, was found to have a rare form of AML.

Case Presentation

This is a 75-year-old male who presented to the emergency department with altered mental status, non-bloody diarrhea, subjective fevers, and intermittent epistaxis, each of which had been present for the past two weeks. Past medical history was notable for non-insulin-dependent diabetes mellitus, paroxysmal atrial fibrillation, anticoagulated with apixaban 5 mg BID, and hypertension. At this time, physical exam was notable for a lethargic, obese male in no acute distress, epistaxis from right nostril, 3/6 crescendo-decrescendo murmur in the right upper sternal border, hepatosplenomegaly, and petechiae scattered across the patient's bilateral lower extremities.

Complete Blood Count (CBC) with differential was ordered on arrival, which revealed the patient's hemoglobin, mean corpuscular volume, and platelets to be 9.2 grams per deciliter (g/dL), 78.7 liters per cell, and 11,000 per microliter (μL), respectively. Comprehensive Metabolic Panel (CMP) was remarkable for a creatinine of 1.5 micrograms per deciliter (mg/dL), which was increased from his baseline of 1.1 mg/dL. The patient was given one unit of platelets and the CBC was rechecked post-transfusion. The platelets had decreased from 11,000 per μL to 9,000 per μL. At this time, coagulation studies were ordered and found to the following: Prothrombin Time (PT) 17.1, Partial Thromboplastin Time (PTT) 36.5, D-dimer 1.67 micrograms per milliliter (μg/

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mL), fibrinogen 630 mg/dL, all of which were increased. Lactic Acid Dehydrogenase (LDH) and haptoglobin were both elevated at 605 units per liter and 243 mg/dL, respectively. The patient's reticulocyte count was decreased at 0.008 cells per μL.

Non-contrast Computerized Tomography (CT) of the patient's abdomen featured non-specific hepatic nodules and splenomegaly. At this time, a peripheral blood smear was ordered, which was remarkable for 2% schistocytes without blasts. The patient underwent plasmapheresis treatment for suspected Thrombotic Thrombocytopenic Purpura (TTP) for a total of five days. The patient did not respond to therapy, as his platelets continued to oscillate between 8,000 and 12,000 μL.

After the plasmapheresis was completed, the decision was made to proceed with a bone marrow biopsy and fluorescent *in situ* hybridization, which was remarkable for a long arm deletion on chromosome 5, which supported a formal diagnosis of acute myeloid leukemia with myelodysplasia-related changes. Throughout the entire hospital course, the patient was given 11 units of packed red blood cells and 12 units of platelets for sustained anemia and thrombocytopenia, respectively. Due to the patient's age and comorbidities, the decision was made to treat him with a five-day course of decitabine, a low-intensity chemotherapy drug. On day 13 of his hospitalization, the patient and family elected for supportive care. On the morning of day 14, the patient was pronounced dead due to complications from AML and subsequent treatment.

Discussion

The case described above is an extremely rare presentation of a rare condition. This case highlights the importance of a high clinical index of suspicion for acute myeloid leukemia in patients who present with unexplained cytopenias and constitutional symptoms even when there are distracting symptoms and an absence of blasts on peripheral. Since the patient presented with the classic pentad of TTP symptoms (fever, anemia, thrombocytopenia, acute kidney injury, and altered mental status) and 2% schistocytes were seen on peripheral blood smear, diagnosis of AML was consequently delayed.

Relying on the classic presentation of TTP symptoms is unreliable, as only 20% to 30% of patients present with the pentad [3]. Moreover, the presence of schistocytes is not specific for TTP. In fact, in TTP, schistocytes typically range between 3% to 10%. [4] Schistocytes may also be seen in Disseminated Intravascular Coagulation (DIC), Hemolytic-Uremic Syndrome (HUS), and malfunctioning heart valves [4]. In our patient, increased haptoglobin, increased fibrinogen, and absence of bloody diarrhea made TTP, DIC, and HUS less likely, respectively. Moreover, the severely low reticulocyte count made malignancy or aplastic anemia much more likely. In retrospect, the patient's previously undiagnosed severe aortic stenosis was the likely etiology for the abnormal peripheral blood smear. Although the initial diagnosis of TTP was incorrect, the correct protocol was followed as plasmapheresis exchange transfusion is recommended in any patient with suspected TTP since mortality is as high as 90% without treatment [2].

Although AML is a relative rare disease, it is the most common acute leukemia in adults [5]. Non-Hispanic white males have a higher incidence than other racial and ethnic groups and the median age at diagnosis is 65 years of age [5].

The etiologies of underlying chromosomal abnormalities in most cases of AML are largely unknown [6]. The WHO 2008 classification of AML categorizes the condition into subtypes, which aids in diagnosis and prognosis [7]. Our patient was found to have a 5q deletion, which most often occurs in elderly patients with prior Myelodysplastic Syndrome (MDS) and is associated with rapid deterioration and poor prognosis [8]. Our patient's prognosis was especially poor considering he had metastatic lesions in his liver and spleen [8].

Treatment of AML is largely based on the patient's age, comorbidities, current functional status, and goals of treatment at time of diagnosis, as treatment is highly variable and may actually decrease life expectancy [9]. In patients with AML with deletions of chromosome 5q, there is insufficient data to predict the possibility of complete remission in elderly patients with comorbidities [10]. However, delaying treatment has been associated with a decreased rate of complete remission and decreased life expectancy by 3 to 5 months in select patient populations. [11-12].

Conclusion

There have been no reported cases of acute myeloid leukemia with myelodysplasia-related changes presenting as thrombocytopenic thrombotic purpura. Early diagnosis of acute myeloid in elderly patients is especially important due to the rapid progression of this disease. In summation, this case shows that acute myeloid leukemia should be under consideration in elderly patients presenting with unexplained cytopenias and constitutional symptoms, even in the absence of blasts on peripheral blood smear. It is important to diagnose acute myeloid leukemia in its early stages and manage it appropriately in order to prolong survival and increase the chances of complete remission.

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