

## Case Report

# Acute myeloid leukemia, secondary to myelodysplastic syndrome, debuting as thrombotic thrombocytopenic purpura: case report

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## ABSTRACT

We present a case of myelodysplastic syndrome (MDS) that progressed to acute myeloid leukemia (AML) with changes related to myelodysplasia that presented as thrombotic thrombocytopenic purpura (TTP). After a failure in response to plasmapheresis therapy and a poor long-term prognosis, the family opted for palliative care, the patient dying on the eleventh day of hospitalization. The case is an extremely rare presentation of a rare condition, as it is the second reported case of AML with myelodysplasia-related changes presenting as TTP, and the first reported case of TTP secondary to AML secondary to MDS.

**Keywords:** Thrombotic TTP, AML, MDS, Microangiopathic hemolytic anemia, PTT

## INTRODUCTION

Myelodysplastic syndrome (MDS) is a hematologic malignancy characterized by clonal hematopoiesis, one or more cytopenia (i.e., neutropenia, anemia and/or thrombocytopenia), and abnormal cell maturation.<sup>1</sup> MDS can be easily confused with AML because they share clinical and pathologic features; however, MDS has a lower percentage of blasts in peripheral blood and bone marrow (<20%, by definition). Patients that are diagnosed with MDS are at risk for infection, hemorrhage, symptomatic anemia, and transformation to AML, the incidence of which varies widely between subtypes of MDS.<sup>2</sup>

AML is a type of cancer arising from the clonal expansion of malignant hematopoietic precursor cells in the bone marrow in which the bone marrow produces abnormal myeloblasts, platelets, and red blood cells. Leukemic cells interfere with the production of normal blood cells.<sup>3</sup> Classically, AML patients present with symptoms related to complications of pancytopenia that include weakness and easy fatigue, infections of varying severity, and/or hemorrhagic findings such as gingival

bleeding, ecchymosis, epistaxis, or menorrhagia. Combinations of these symptoms are common.<sup>4</sup>

Thrombotic TTP is a thrombotic microangiopathy caused by greatly reduced activity of the ADAMTS13 protease that results in platelet fragmentation by un cleaved von Willebrand multimers and subsequent formation of blood clots in the entire microvasculature body.<sup>5</sup> It is an extremely rare entity (approximately 3 per million adults per year characterized by platelet-rich small-vessel thrombi causing fevers, anemia, thrombocytopenia, acute kidney injury, altered mental status, and schistocytes in the peripheral blood smear.<sup>6</sup> TTP is considered a medical emergency that is almost always fatal if proper treatment is not started immediately.<sup>7</sup> We present a patient whose clinical presentation was aligned with an atypical initial presentation (such as TTP) of AML, which evolved from an MDS with 11 months of diagnosis.

## CASE REPORT

This is a 63-year-old man, with a previous diagnosis of MDS diagnosed 11 months before the current condition, undergoing treatment with monthly cycles of azacitidine.

He presented to the emergency department with a quantified fever of up to 38.5°C, asthenia, adynamia, nausea, vomiting, edema of the lower extremities Godet +++ and altered mental status, each of which he had been present for the last 7 days. His personal pathological history included insulin-dependent diabetes mellitus, controlled systemic arterial hypertension, acute coronary syndrome secondary to atherosclerosis, as well as MDS. From the initial diagnosis of MDS to the current hospitalization, the patient was admitted 11 times to treat various complications derived from myelodysplasia, such as recurrent pneumonias, punctate subarachnoid hemorrhage, multiple transfusions of blood cell concentrates and platelet apheresis, and diarrhea associated with clostridium difficile. The patient's vital signs were reported as: temperature of 38.0 °C, heart rate of 90 bpm, respiratory rate of 12, blood pressure of 128/76 mmHg, and oxygen saturation of 94% with nasal tips at 1 L. At this time, the physical examination found an overweight and stuporous man without acute distress, generalized jaundice, hepatosplenomegaly, and disseminated petechiae in bilateral palms and bilateral lower extremities, and generalized edema (palpebral, upper extremities, ascites, testicular and lower extremities).

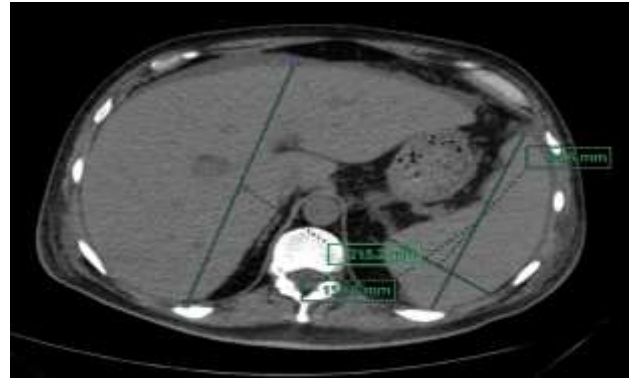
Laboratory (Table 1) the patient was bicytopenic at the expense of hemoglobin (6.3 g/dl) and platelets (14,000 µL), as well as normal leukocytes (5,600 µL). It should be mentioned that the patient's baseline leukocyte levels were between 460 and 1,390 µL, but the hematic biometry at hospital admission reported 5,600 µL. A viral and fungal panel was requested that was negative, as well as negative cultures.

**Table 1: Relevant laboratory results at hospital admission.**

Parameters (unit)	Value (reference value)
Hemoglobin (g/dl)	6.3 (13.7-16.5)
Leukocytes (µL)	5,670 (3,900-9,500)
Platelets (µL)	14,000 (149,000-368,000)
Creatinine (mg/dl)	0.73 (0.70-1.25)
Prothrombin time (seconds)	11.2 (10.3-12.8)
Partial thromboplastin time (seconds)	23.8 (20.7-34.1)
D-dimer (µg/ml)	0.41 (<0.50)
Fibrinogen (mg/dl)	380 (200-400)
Lactic acid dehydrogenase (units/L)	950 (120-246)
Reticulocytes (cells/µL)	1.10 (0.5-1.5)
ADAMTS13 activity (%)	0.5 (68-163)

Blood chemistry reported an increase in urea to 146 mg/dl, while creatinine remained at 0.73 mg/dl. Non-contrast computed tomography (CT) of the chest and abdomen showed pericardial and pleural effusion with hepatosplenomegaly (Figure 1). At that time, a bone

marrow biopsy and peripheral blood smear were requested, which reported five days later the presence of AML with myelodysplasia-related changes, as well as peripheral blood schistocytes. Since the evolution of MDS to AML was initially unknown, the patient underwent multiple plasmapheresis for suspected TTP for a total of four days. The response of this treatment was unsatisfactory, as his platelets continued to range between 14,000 and 20,000 µL.



**Figure 1: Simple abdominal tomography with evidence of hepatosplenomegaly.**

During the entire hospital course, the patient received 16 units of red blood cells and 4 platelet apheresis for sustained anemia and thrombocytopenia, respectively. On day 9 of his hospitalization, the patient and his family chose to receive palliative care. On the afternoon of the 11th hospital stay, the patient was declared dead due to complications of the TTP.

## DISCUSSION

Although the patient already had a diagnosis of MDS, the clinical presentation of this patient is rare since an evolution of the disease towards AML was not suspected, since he presented clinical and laboratory data compatible with TTP. Finally, it was confirmed that TTP was the initial manifestation of AML.

MDS encompasses a wide spectrum of laboratory manifestations that can range from cytopenia to frank pancytopenia, which the patient presented. Although anemia, thrombocytopenia, neutropenia, and fever are characteristic symptoms of MDS, it is rare for them to present with an acute change in mental status and a decrease in platelets after multiple platelet apheresis.<sup>8</sup> Using search tools such as ProQuest, Springer link, Science Direct, PubMed and Google Schools, we found that this is the second reported case of AML with myelodysplastic changes that presented with the classic pentad of TTP symptoms, schistocytes in the peripheral smear and absence of myeloblasts in the peripheral smear.<sup>9</sup>

Since the patient had been evolving for 11 months and receiving adequate azacitidine treatment, it was not

initially thought that there was an evolution towards AML. However, the sudden increase in baseline leukocyte numbers between two different hematic biometrics with a difference of 3 weeks between one and the other, led us to suspect a possible evolution of the MDS to an AML, but since the patient remained with constantly low platelet counts (less than 15,000  $\mu$ L), the bone marrow biopsy was delayed due to the high risk of bleeding, but due to the highly suggestive clinical picture of TTP, exchange transfusion by plasmapheresis was chosen, since it is recommended in suspected TTP due to a high mortality of up to 90% without treatment.<sup>10</sup>

At the time of clinical suspicion of TTP, serum ADAMTS13 measurements were taken, but the result was not released by the laboratory until the patient had died. However, at all times it was handled as a PTT. Relying on the clinical manifestations of a patient to suspect TTP is not very sensitive and specific, since only up to 30% of patients present the classic pentad.<sup>7</sup> In addition, the presence of schistocytes in peripheral blood is not exclusive to TTP, since other conditions such as disseminated intravascular coagulation, hemolytic uremic syndrome and abnormal heart valve function could produce it.<sup>11</sup> These differential diagnoses were duly ruled out.

Epidemiologically, an MDS can evolve into an AML depending on how aggressive it is. For this, the IPSS scale (International prognosis scoring system in MDS) is used, which uses three criteria (cytopenias, karyotype and blasts in bone marrow) to classify patients into 1 of 5 groups, from very low to very high-risk, according to the risk of mortality and transformation to AML.<sup>12</sup> The patient, prior to this hospitalization, had undergone two previous bone marrow biopsies, yielding an IPSS of 4 points, classifying it as intermediate risk (Interpretation: 3-year median survival with a 25% risk of transformation to AML in a period of 3.2 years).

## CONCLUSION

This is the second reported case of AML with myelodysplasia-related changes presenting as TTP, and the first reported case of TTP secondary to AML secondary to MDS. Early diagnosis with a high clinical suspicion of AML in patients with MDS is vital due to the rapid progression of this disease. In summary, this case shows that TTP should be taken into account in patients with MDS who progress to AML and who present altered mental status and decreased platelets despite multiple platelet apheresis, even in the absence of blasts in the smear of peripheral blood. In a patient who debuts as AML, appropriate treatment should be instituted to prolong survival and increase the chances of a complete remission, since its association with TTP drastically changes the short-term prognosis of patients.

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