A Rare Case of Myelodysplastic Syndrome Presenting as Thrombotic Microangiopathy

Liz Thaliath, M.D[1]; Matthew Quesenberry, M.D[2] ; John Reagan, M.D[2]

[1]*Department of Internal Medicine, Marshfield Clinic, Marshfield, WI*
[2]*Department of Hematology, Rhode Island Hospital, Brown University Health, Providence, RI*

Marshfield Clinic Health System

INTRODUCTION

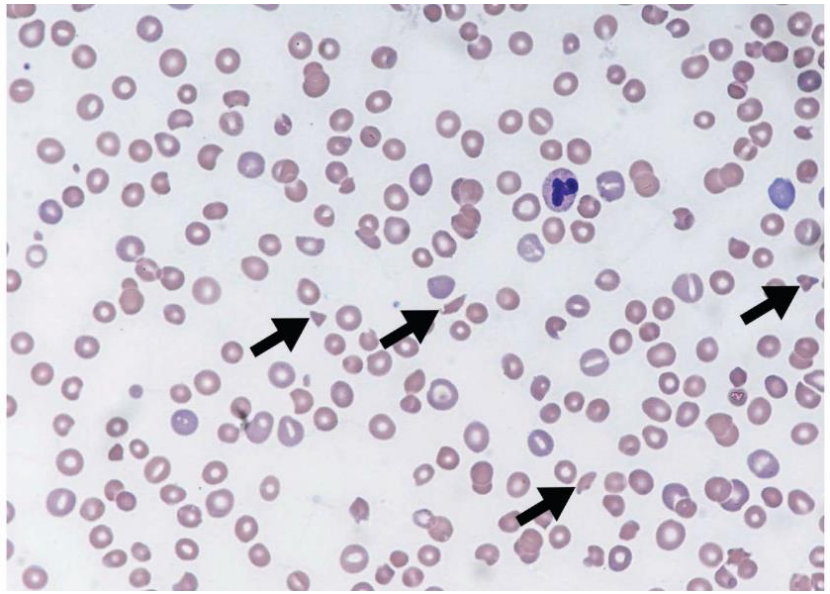
- Thrombotic microangiopathy (TMA) is characterized by microangiopathic hemolytic anemia (MAHA) and thrombocytopenia that can cause end-organ damage.
- While thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome are uncommon but still seen at academic medical centers, TMA secondary to hematologic malignancies is rare.
- Herein we present a rare case of myelodysplastic syndrome (MDS) manifesting as TMA.

CASE REPORT

- A 67-year-old female presented with worsening fatigue.
- Laboratory studies revealed anemia (hemoglobin: 7.5 g/dL), thrombocytopenia (platelet: 9×10^9/L), and markers of intravascular hemolysis, including elevated lactate dehydrogenase (LDH: 719 U/L), undetectable haptoglobin, and schistocytes on peripheral smear.
- Given high PLASMIC score and clinical suspicion for TTP, plasma exchange (PLEX) was initiated.
- However, ADAMTS13 results returned at 67%, ruling out TTP.
- Further evaluation revealed low reticulocyte percentage (1%) and normal bilirubin, findings atypical for TTP.
- Nutritional deficiencies causing hypoproliferative anemia and infectious etiologies were ruled out.
- Normal renal function and absence of a diarrheal prodrome made complement-mediated and shiga-toxin-mediated TMAs unlikely.
- Bone marrow biopsy demonstrated hypercellular marrow with erythroid predominance, dysplastic erythropoiesis, decreased granulopoiesis, and megakaryocytes with morphologic abnormalities.

CASE REPORT CONTINUED

- Flow cytometry identified 6% myeloid blasts.
- Cytogenetics revealed trisomy 17, and molecular testing identified mutations in *TP53* gene, indicating high-risk MDS with concern for early transformation toward pure erythroid leukemia.
- She was started on azacitidine 75 mg/m^2 with venetoclax for 7 days, and her platelets increased to 188×10^9/L.



The image shows features of thrombocytopenia and microangiopathic hemolysis (Wright–Giemsa stain, original magnification × 50). Arrows show red blood cell fragments (i.e., schistocytes), which are substantially reduced.
(stock image)

DISCUSSION/CONCLUSION

- While anemia and thrombocytopenia are well-documented manifestations of MDS, their association with schistocytosis and MAHA is uncommon, with only 10 such reported cases.
- Clinical overlap between MDS and primary TMAs can be substantial, particularly in the setting of anemia and thrombocytopenia.
- However, normal ADAMTS13 activity, transfusion-dependent cytopenias despite PLEX, and low initial reticulocyte count should prompt reconsideration of the diagnosis and a broader differential.
- The pathophysiological link between MDS and TMA remains speculative.
- Vasculitic changes in MDS may contribute to endothelial injury and microangiopathy.
- This case underscores the importance of considering MDS in the differential diagnosis of patients presenting with TMA.
- Bone marrow evaluation remains essential in unexplained cytopenias and hemolysis for diagnosis, as management of MDS differs significantly from those for primary TMAs.

References

Sadrzadeh, H. & Burks, E. (2020). Myelodysplastic syndrome presenting as thrombotic microangiopathy. *Blood*. 136 (20). pp. 2359–2359.

Oshima, T., Ikutomi, M., Shinohara, H., Ishiwata, J., Fukino, K., Amaki, T. and Nakamura, F., 2016. Acute myocardial infarction caused by thrombotic microangiopathy complicated with myelodysplastic syndrome. *International Heart Journal*, *57*(5), pp.634-636.

Moscoso Martínez, S.F., Jácome, E.C.P., Guevara, E. and Mattoo, V., 2017. Myelodysplastic syndrome clinically presenting with the "classic TTP pentad". *Case Reports in Hematology*, *2017*(1), p.4619406.

Jacobse, J., Sijpkens, Y.W., van't Wout, J.W., Peters, E.E. and Vlasveld, L.T., 2018. Vasculitis in myelodysplastic syndrome and chronic myelomonocytic leukemia: a report of two cases. *Journal of Hematology*, *7*(4), p.158.

Koshy, A.G. and Freed, J.A., 2020. Clinical features of vitamin B12 deficiency mimicking thrombotic microangiopathy. *British Journal of Haematology*, *191*(5).