



The Creative Clinician

Foiled By the Fragments: Masquerading Microangiopathy

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A 65-year-old woman presented to a hospital with confusion, shortness of breath, and ecchymotic skin lesions. She was afebrile. Her hemoglobin was 3.6 g/dL (normal [nl] 11-15 g/dL), platelet count was $62 \times 10^3/\text{mm}^3$ (nl $150-450 \times 10^3/\text{mm}^3$), white blood cell count was $5.9 \times 10^3/\text{mm}^3$ (nl $3.5-11 \times 10^3/\text{mm}^3$), mean corpuscular volume (MCV) was 114 fL (nl 80-99 fL), creatinine was 1.9 mg/dL (nl 0.4-1.3 mg/dL), and serum lactate dehydrogenase (LDH) was 2,200 IU/L (nl 50-175 IU/L). Based on her confusion, anemia, thrombocytopenia, and elevated serum creatinine and LDH, a diagnosis of thrombotic thrombocytopenic purpura (TTP) was made.

The patient received four units of packed red blood cells and was transferred to our hospital for urgent plasma exchange (PEX). Upon arrival, her history was unremarkable while physical examination was notable for tangential speech, conjunctival pallor, slight macroglossia, and ecchymotic areas on her extremities. Cardiopulmonary exam was normal and there was no lymphadenopathy or hepatosplenomegaly.

The patient's peripheral blood smear showed 1% to 5% schistocytes per high-power field that further suggested a microangiopathic process. However, macroovalocytes, hypersegmented neutrophils, polychromasia, and occasional teardrop cells were observed. (Figure 1). The patient received 2 units of fresh frozen plasma (FFP) to correct her coagulopathy and to partially replenish her presumptively low ADAMTS13 while a serum cobalamin level and anti-IF antibody were checked. The patient was empirically given a dose of intramuscular cyanocobalamin.

The patient's serum cobalamin level returned at 51 pg/ml (nl 211-911 pg/ml) and her anti-IF antibody was positive. After fourteen days of intramuscular cobalamin her peripheral blood smear showed resolution of megaloblastic changes and her mental status and ecchymotic areas improved.

The hematologic aberrations seen in cobalamin deficiency can include pancytopenia, the presence of hypersegmented neutrophils and macroovalocytes on peripheral blood smear, and elevated serum levels of LDH and bilirubin.¹ As seen in the present case, severe cobalamin deficiency can also present with a clinical and hematological picture similar to a microangiopathic hemolytic process. In addition, neuropsychiatric manifestations of cobalamin deficiency are marked by paresthesias, ataxia, urinary and fecal incontinence, impotence, optic atrophy, memory loss, dementia, and various psychiatric disorders including depression, hallucinations, and personality changes.¹

Schistocyte formation in cobalamin deficiency may result from increased membrane rigidity with reduced deformability and subsequent lysis as RBCs pass through the reticuloendothelial system.² The anemia of cobalamin deficiency is thought to result from a combination of lack of production and increased destruction of RBCs while thrombocytopenia is caused by a lack of production of platelets.

We believe that in cases of apparent TTP with high MCV or other data suggestive of cobalamin deficiency, serum cobalamin levels should always be checked. If a suspicion for cobalamin deficiency arises in the evaluation of TTP, empiric treatment with infusion of FFP can be used until more definitive testing is performed. PEX may be associated with serious side effects. In a nine-year cohort study of 206 consecutive patients treated for TTP, 5 of the 206 (2%) died of complications of PEX treatment. Fifty-three patients (26%) had major complications attributed to PEX treatment, including systemic infection, venous thrombosis, and hypotension requiring blood pressure support.³ With review of a pe-

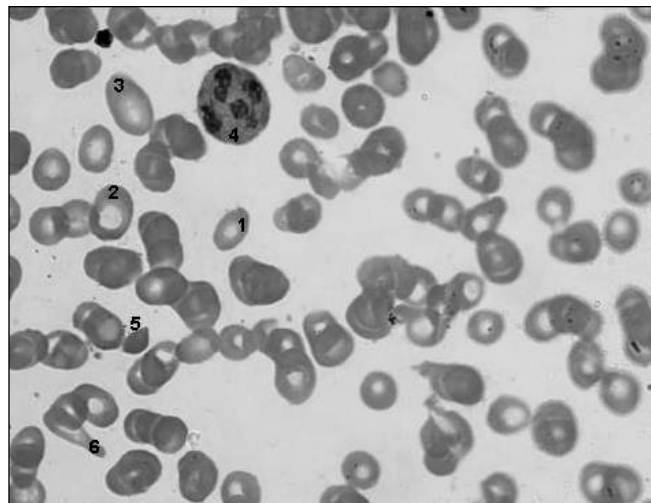


Figure 1. Peripheral blood smear of our patient with hallmarks of cobalamin deficiency. There is marked anisopoikilocytosis. Ovalocyte (1), macroovalocyte (2,3), hypersegmented neutrophil with 5 lobes (4), schistocyte (5) and teardrop cell (6).

ripheral blood smear and rapid confirmatory laboratory testing, PEX may be avoided in patients presenting with severe cobalamin deficiency mimicking TTP.

Clinicians should be aware of unusual clinical presentations of cobalamin deficiency masquerading as a serious microangiopathic hemolysis. The prompt recognition, diagnosis, and treatment of cobalamin deficiency is vital because therapy is safe, inexpensive, and corrects hematologic abnormalities while bringing about a complete or partial correction of the neuropsychiatric abnormalities in the majority of patients.

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The authors have no financial interests to disclose.

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RHODE ISLAND MEDICAL SOCIETY

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Dear Colleague,

This past summer marked a historic victory for anti-tobacco advocates. On June 22, 2009, President Obama signed into law the new Family Smoking Prevention and Tobacco Control Act giving the U.S. Food and Drug Administration (FDA) the authority to regulate tobacco products and stop the harmful practice of marketing tobacco to children. This law will help significantly reduce the number of children who start to use tobacco, the number of adults who continue to use tobacco, and the number of people who die as a result.

While this is all good news, it is evident that the Family Smoking Prevention and Tobacco Control Act cannot by itself put an end to tobacco use. Its intent is to complement, not replace, the successful work that we have been doing over the years to educate our children about the importance of being tobacco-free. Interestingly enough, in late August, major tobacco manufacturers filed suit to overturn portions of the new law, specifically the restrictions on advertising, marketing and labeling of tobacco products.

Since there is more that can be done, the Rhode Island Medical Society would welcome your support of our Tar Wars Rhode Island Program, the national tobacco-free educational program developed by the American

Academy of Family Physicians. We are looking for physician presenters to volunteer to talk with students about the dangers of tobacco use. The program involves teaching an hour-long lesson to the students (RIMS provides you all materials); and then returning to the school to judge a half-hour poster contest. The Tar Wars flyer provides further details about the Tar Wars program as well as details about the Family Smoking Prevention and Tobacco Control Act. You can also go to www.tarwars.org for more information.

If you are interested, please contact Catherine Norton at 528-3286 or cnorton@rimed.org. We anticipate school presentations to be scheduled during the months of January, February, and March 2010. We also have available for your use, "How to Present Tar Wars Guidelines."

Thank you for your support!

Sincerely,

Arthur A. Frazzano, MD
Past President
Chair, Tar Wars Rhode Island

Tar Wars, a national tobacco-free educational program developed by the American Academy of Family Physicians, is coordinated locally by the Rhode Island Medical Society, the Rhode Island Academy of Family Physicians, and the Rhode Island Chapter of the American Academy of Pediatrics.