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Muddy waters in therapeutic plasma exchange

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A 55-year-old man with severe aplastic anemia and thymoma was treated with horse anti-thymocyte globulin, cyclosporine A, and eltrombopag 150 mg daily on an IRB-approved clinical protocol. Following thymectomy, he developed progressive encephalopathy requiring mechanical ventilation. Head CT, EEG, MRI, and cerebrospinal fluid examination via lumbar puncture were unremarkable. A presumptive diagnosis of paraneoplastic syndrome was made, and a course of therapeutic plasma exchange (TPE) was initiated. In preparation for plasma exchange, the patient received transfusions of packed red cells and platelets.

On initiating TPE, the patient's plasma was noted to have a murky brown color (Figure). This alerted the apheresis nurse to check for clinical and laboratory signs of hemolysis, but no acute change in the patient's condition or hematologic indices was noted.

The unusual plasma color was attributed to the use of eltrombopag. This oral thrombopoietin receptor agonist is approved by the FDA for the treatment of chronic ITP and HCV-associated thrombocytopenia at maximum daily doses of 75 mg and 100 mg, respectively. The drug has recently been shown to increase trilineage hematopoiesis in patients with severe aplastic anemia when used in a higher dose than that approved for ITP or HCV.

Sera from patients treated with higher doses of eltrombopag (200 - 300 mg daily) have been reported to show readily apparent brownish-red discoloration, which may interfere with spectrophotometric assays¹. Eltrombopag is a diacid with carboxyl and phenolic functional groups whose color in solution varies by pH, turning reddish brown at basic pH and yellow in acidic media¹. Although citrate anticoagulant (ACD-A) itself is acidic, when added at a 1:13 ratio to blood in the extracorporeal circuit, as was done in this procedure, the pH is not significantly lowered. It is important for clinicians and laboratory personnel to be aware of this effect to avoid misinterpretation of plasma discoloration as indicative of intravascular hemolysis or severe icterus.

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Figure.