DIAGNOSTIC DILEMMA
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THE AMERICAN JOURNAL of MEDICINE®

Bruised Black and Blue: Acquired Hypoprothrombinemia

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PRESENTATION

An 80-year-old woman presented to a local hospital with 2 weeks of bleeding. She initially developed epistaxis, which was followed by diffuse ecchymoses, melena, and hematuria. Her symptoms were preceded by a pruritic rash. Other than the rash, she had been in her usual state of health. She had no anticoagulant use or prior bleeding history. Her medical history was notable for hypertension, hyperlipidemia, diastolic heart failure, and stage III chronic kidney disease. Medications included antihypertensives, a diuretic, statin, and aspirin 81 mg. Amlodipine was a new medication and simvastatin had recently been switched to atorvastatin.

ASSESSMENT

On presentation, blood pressure was 160/90 mm Hg, pulse 80 beats per minute, with the rest of her vital signs within normal limits. Examination was notable for large ecchymoses across her chest, back, and upper extremities (**Figure 1**).

Initial laboratory data revealed a prolonged prothrombin time (PT) of 34.4 (normal, 9.7-11.3) seconds, international normalized ratio of 3.5 (normal, 0.9-1.1), and acquired partial thromboplastin time (aPTT) of 81.7 (normal, 22.5-28.6) seconds. Her platelets were 167 $\times$ 10^9/L, hemoglobin was 12.2 g/dL, and white blood cell count was 9.6 $\times$ 10^9/L. Her creatinine, which was 1.6 mg/dL from a baseline of 1.4 mg/dL, subsequently peaked at 4.0 mg/dL and returned to baseline. She had elevated liver function tests with aspartate transaminase 137 IU/L, alanine transaminase 172 IU/L, and alkaline phosphatase 953 IU/L, but normal total bilirubin 0.5 mg/dL. Fibrinogen was 620 (normal, 198-507) mg/dL, D-dimer 0.62 (normal, 0.17-0.59) mg/L, and erythrocyte sedimentation rate was 72 (normal, 0-30) mm/h. Urinalysis and urine culture showed hematuria and pan-sensitive *Escherichia coli* infection. Blood cultures were negative. Review of her blood film revealed no schistocytes.

Her hospital course was marked by multiple transfusions for unremitting hematuria and melena. The excessive bleeding raised concern for disseminated intravascular coagulation and primary liver disease. However, with discontinuation of atorvastatin, her liver enzymes normalized. Conversely, treatment with vitamin K, fresh frozen plasma (FFP), cryoprecipitate, and antibiotics did not correct her coagulopathy. When the coagulopathy was further evaluated with PT and aPTT mixing studies, the PT and aPTT did not correct with mixing. Therefore, she was presumed to have an autoimmune factor inhibitor, and the local hospital initiated a hospital-hospital transfer. At the time of transfer to our center, which occurred on hospital day 7, intravenous methylprednisolone had been initiated and she had received 11 units of packed red blood cells (PRBC), 13 units of FFP, and 2 units of cryoprecipitate.

Because both PT and aPTT remained prolonged and did not correct with mixing, we suspected an inhibitor to one of the common pathway coagulation factors. These factors are I (fibrinogen), II (prothrombin), V, and X (**Figure 2**).

Factor activity assay for V was 117% (normal, 64%-109%) when checked before transfer. Therefore, factor activity assays for factor II and X were sent. Factor X was 139% (normal, 58%-145%), but factor II activity could not be quantified; however, dilution studies returned with a corrected result of 33% (normal, 72%-137%). Subsequently, a factor II inhibitor titer returned at 0.95 Bethesda Units/mL (normal, 0 BU/mL). Lupus anticoagulant panel was negative (**Figure 3**).

DIAGNOSIS

To evaluate the underlying cause of her factor inhibitor, an extensive workup was initiated. Autoimmune workup yielded a normal complement profile with no evidence of

Funding: None.
Conflict of Interest: None.
Authorship: All authors had access to the data and played a role in writing this manuscript.

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http://dx.doi.org/10.1016/j.amjmed.2015.06.011

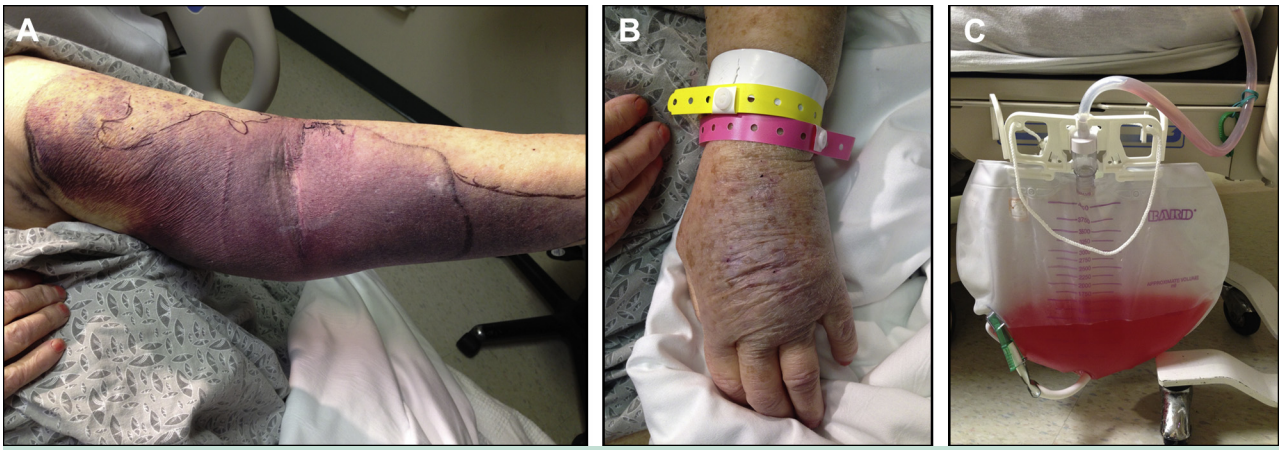

Figure 1 Ecchymosis of upper extremities and hematuria. (**A**) The patient presented with diffuse ecchymoses over her upper extremities. (**B**) She also had a hematoma over her hand. (**C**) She developed hematuria requiring continuous bladder irrigation.

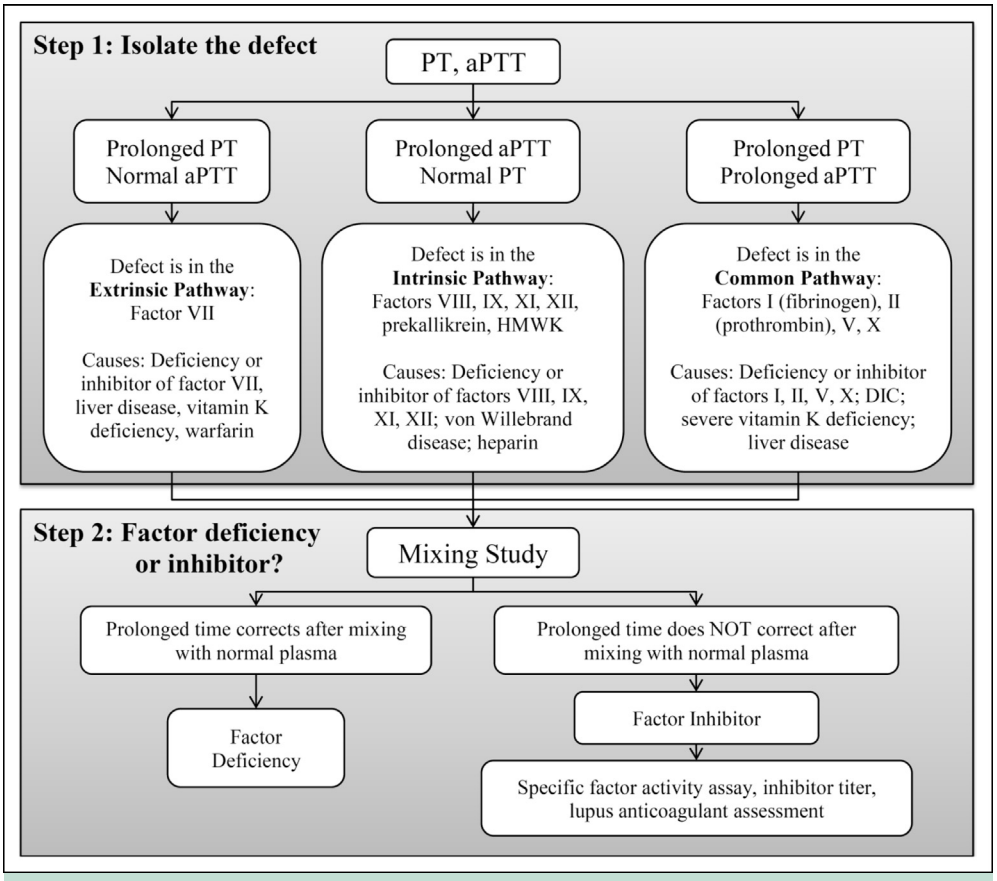

Figure 2 Approach to evaluating coagulopathy. The first step to approaching a coagulopathy is to isolate where the defect is in the coagulation pathway. A prolonged PT indicates a defect in the extrinsic pathway, and a prolonged aPTT indicates a defect in the intrinsic pathway. When both PT and aPTT are prolonged, there is a defect in the common pathway. After isolating the defect, the next step is to determine whether there is a factor deficiency or a factor inhibitor with mixing studies. If the prolonged time corrects with mixing with normal plasma, there is a factor deficiency. If the prolonged time does not correct with mixing, there is a factor inhibitor, and specific factor activity assays and inhibitor titers should be performed. aPTT = acquired partial thromboplastin time; DIC = disseminated intravascular coagulation; HMWK = high-molecular-weight kininogen; PT = prothrombin time.