An 80-year-old man with coronary artery disease and chronic obstructive pulmonary disease (COPD) was admitted to an outside hospital after a mechanical fall. On presentation to the emergency room his systolic blood pressure was found to be 86/62 mm Hg. He complained of right flank, groin, and thigh pain. On physical exam, a hematoma extending from his right groin down to his right knee was found, as well as scattered ecchymoses involving his trunk and all 4 extremities. His hemoglobin was low, at 5.6 g/dL (14-17 g/dL). A computed tomography (CT) scan revealed a right-sided retroperitoneal bleed extending from the iliopectineal fossa into his right thigh. The patient received 13 transfusions of packed red blood cells over the course of 9 days as he continued to bleed. Transfer to our facility for further workup and management ensued.

On serial testing at our institution his activated partial thromboplastin time (aPTT) was elevated at >160 seconds (normal range, 24-36 seconds). Further coagulation parameters were found as follows: platelets 182,000/μL; prothrombin time 17.6 seconds; international normalized ratio (INR) 1.4; thrombin 18 seconds; fibrinogen 778 mg/dL; and D-dimer 3866 ng/mL. Of note, the patient had not received any medications known to potentially interfere with the measured aPTT. Because the source of his bleeding was not apparent at this point, disorders of primary hemostasis, including hereditary disease states (eg, von Willebrand disease), iatrogenic disorders (eg, drug-induced), or acquired disorders, such as immune thrombocytopenia, were considered and ruled out. At this point the differential diagnoses had to be expanded, and secondary disorders of hemostasis were considered. A deficiency or decreased activity of coagulation factors was suspected. Whereas factor IX and XI deficiencies have been associated with acquired hemophilia A, the patient’s bleeding abnormality was apparent prior to initiation of antibiotic therapy.

Acquired factor VIII inhibitor levels had decreased to 13 BU and his partial thromboplastin time (PTT) was 100 seconds. The bleeding stopped 2 days after initiation of treatment. At the time of discharge, 2 weeks after presentation, factor VIII inhibitor levels had decreased to 13 BU and his partial thromboplastin time (PTT) was 100 seconds.

Discussion
Acquired factor VIII inhibitor, also called acquired hemophilia A, is a rare, potentially life-threatening bleeding disorder. It is caused by autoantibodies directed against coagulation factor VIII.1

The estimated incidence in the general population is 1 in 4 million/year. Risk factors include advanced age, pregnancy and the postpartum period, rheumatoid disease/connective tissue disease, inflammatory bowel disease, medications (especially antibiotics and psychiatric drugs), and malignancy. Both solid tumors as well as hematologic malignancies have been associated with acquired hemophilia A.2

Patients older than 85 years are more frequently affected. The annual incidence is 14.7 in 1 million in this age group. Hence, it is found rarely in young patients, but pregnancy and the postpartum period represent the exception.

Patients with acquired factor VIII inhibitor tend to bleed into the skin, soft tissue, muscle, brain, and mucous membranes. Most of the time, they present with epistaxis, retroperitoneal hematomas, or gastrointestinal bleeds, while patients with congenital factor VIII deficiency3 are more likely to bleed into the large joints. Acquired factor VIII inhibitor is associated with a high morbidity and mortality.

In the presence of an isolated elevated aPTT, once heparin has been ruled out, specific factor deficiencies and/or
inhibitors need to be considered. The inhibitor assay helps to establish the diagnosis of acquired factor VIII deficiency and allows the quantification of factor VIII inhibitor. A search for specific etiologies of acquired factor VIII inhibitors should be undertaken; however, in 50% of cases no concomitant condition is found. The differential diagnoses should be expanded within the appropriate framework and tailored to the individual patient.

Control of bleeding might be achieved by factor VIII concentrate if the bleeding is mild. However, if the hemorrhage is life-threatening, recombinant factor VII is frequently required to stop the bleeding. One has to be aware that recombinant factor VII may precipitate thromboembolic events and as such might pose a dilemma, as the degree of bleeding has to be balanced with the risk of unintended side effects. Therapy to eliminate factor VIII inhibitor is the combination of prednisone and cyclophosphamide, though monoclonal CD20 antibody (Rituximab) has become the first-line agent in the appropriate setting. Risk and benefit of therapy have to be balanced with the severity of the bleed and potential unintended side effects of immunosuppression, especially in the presence of infection.

As hospitalists, we are challenged daily by a high degree of complexities in inpatient care. Hospitalists are well trained to manage a wide variety of conditions, and coagulopathies are no exception. They are so common in the inpatient setting that every hospitalist should be familiar with the basic principles of diagnosing and managing bleeding disorders. Because of the hospitalist’s ability to promptly react, the consulting role of the hematologist can be reserved for the more unusual blood dyscrasias.

This article is intended to raise physician awareness for the discussed condition because early recognition and treatment are of paramount importance in patient outcome.

Address for correspondence and reprint requests:
Felicitas Thol, MD, Medical Center Drive, Lebanon, NH 03756; Telephone: 603-650-8380; Fax: 603-653-6110; E-mail: felicitas.thol@hitchcock.org Received 16 July 2008; revision received 12 November 2008; accepted 23 November 2008.

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