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Case Report

Anuric Acute Kidney Injury due to Bladder Tamponade in a patient with acquired Hemophilia A

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Abstract

Acquired hemophilia A is a rare, but potentially life-threatening bleeding disorder caused by autoantibodies for coagulation factor VIII. Major bleeding symptoms include subcutaneous and muscle bleeding, while hematuria is observed in less than 10% of patients. We report a case of a 49-year-old man presenting with severe and sustained hematuria without subcutaneous bleeding. He developed postrenal acute kidney injury resulting from bladder tamponade of blood clots and required temporary hemodialysis. Acquired hemophilia A was diagnosed, and he was successfully treated with recombinant factor VIIa and steroids without adverse effect including thrombotic event.

Keywords: Acquired Hemophilia A; Renal Hemorrhage; Bladder Tamponade; Post Renal Acute Kidney Injury; Tranexamic Acid; Temporary Hemodialysis; Recombinant Factor VIIa

Abbreviations:

AHA: Acquired Hemophilia A;

CT: Computed Tomography;

TA: Tranexamic Acid;

APTT: Activated Partial Thromboplastin Time;

AKI: Acute Kidney Injury;

CVC: Central Venous Catheter;

rFVIIa: Recombinant Factor VIIa;

PSL: Prednisolone;

TE: Thrombotic Events

Introduction

Acquired hemophilia A (AHA) is a rare bleeding disorder that is characterized by a deficiency of coagulation factor VIII due to the development of neutralizing autoantibodies (inhibitors) against factor VIII [1]. Spontaneous hemorrhage can occur in patients with no previous history of bleeding. Because patients with AHA often present with severe and life-threatening bleeding, an early correct diagnosis, initiation of hemostatic therapy, and eradication of inhibitors are required. The majority of patients with AHA present with subcutaneous bruising and deep soft tissue bleeding including the muscles [2]. Here we report an atypical case of AHA in a patient presenting with hematuria, but without bruising and muscle bleeding at onset. A diagnostic delay may lead to serious bleeding complications.

Case Presentation

A 49-year-old healthy Japanese man suffered from febricula and mild lumbago for about a month. When he developed hematuria in association with lower abdominal pain, he presented to urologist, and a medical examination was performed. Because no abnormal findings were detected on abdominal ultrasound, x-ray, computed tomography (CT), or cystoscopy, he was diagnosed with spontaneous passage of urinary lithiasis, and tranexamic acid (TA) and carbazochrome sodium sulfonate hydrate were prescribed. On returning home, he developed worsening right abdominal pain, and he was admitted to an emergency room. Physical examination revealed a knocking pain localized in the right costovertebral angle. No bleeding symptoms other than hematuria, including bruising, were noted. Mild hydronephrosis was detected on abdominal ultrasound. Laboratory data showed a white blood cell count of 12,170/ μ L; serum creatinine, 1.17 mg/dL; and activated partial thromboplastin time (APTT), 66.8 sec. Analgesics were prescribed, and he was allowed to return home. However, his lower abdominal pain continued to worsen despite the use of analgesia, and he presented again to the urologist three days later. His serum creatinine had increased to 8.48 mg/dL, and a severely prolonged APTT (97.9 sec) was observed. An abdominal CT revealed bilateral renal haemorrhage, urethral ectasia, and bladder tamponade (Figure 1). He was diagnosed with postrenal acute kidney injury (AKI) resulting from blood clots in the urinary system. Single-J ureteral catheter stents and urethral catheter were placed to release the obstructed urine flow

(Figure 2); however, no urine flow was noted.

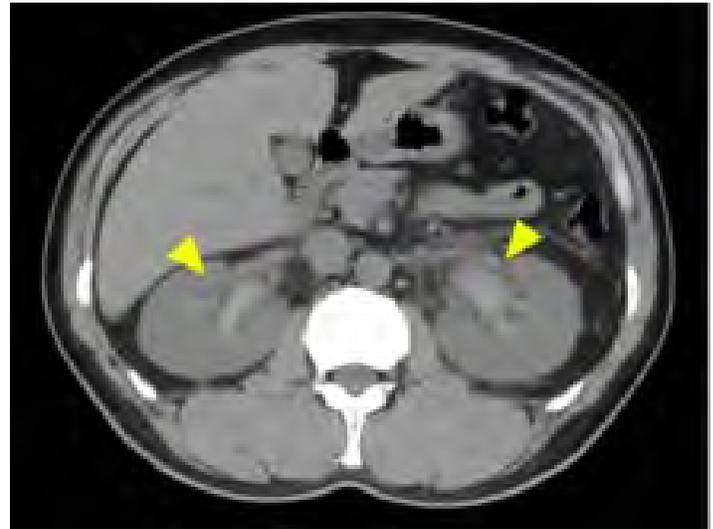


Figure 1. Abdominal CT on admission revealed bilateral renal haemorrhage and urethral ectasia (arrows).

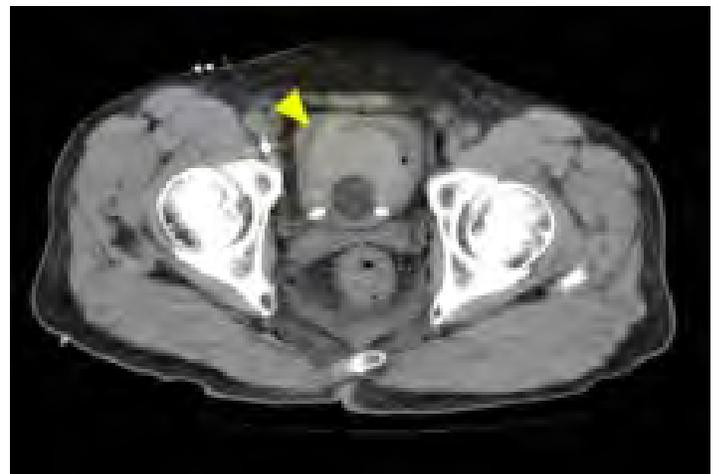


Figure 2. Bladder tamponade due to blood clots was detected on pelvic CT, and single-J ureteral catheter stents were placed (arrow).

Further investigation in our department demonstrated that the factor VIII activity level had decreased to 5% (normal range, 65–145%). In a mixing test, the APTT was not corrected with the addition of normal plasma and incubation for two hours (the APTT was 80.7 sec with a ratio of plasma to normal plasma of 50:50). The APTT was prolonged by a time-dependent inhibitor (Figure 3), and the factor VIII inhibitor level was 7.48 Bethesda units/mL. Based on the history and the laboratory findings, a diagnosis of AHA was made.

The differential diagnosis included organic urinary diseases and coagulation disorders. On imaging and cystoscopy, no organic urinary diseases, such as urinary tract tumors and hemorrhagic cystitis, were detected. A diagnosis of a lupus anticoagulant was excluded because of the severe bleeding symp-

toms and a negative test result. Another acquired coagulation inhibitor and von Willebrand disease were also ruled out because of the normal range of other coagulation factor activity and the elevated von Willebrand factor level.

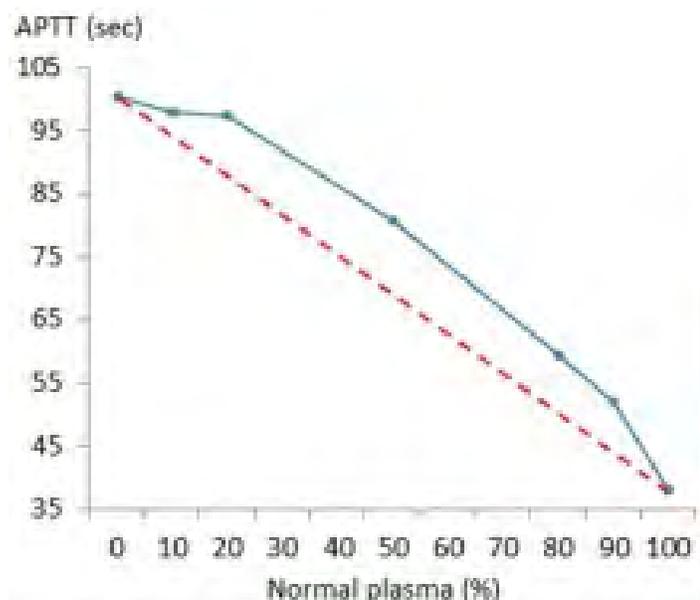


Figure 3. Cross-mixing test. Each APTT was measured by adding the indicated amount of normal plasma to the sample with a 2-hour incubation period.

The patient's bleeding symptoms increased, with multiple bruises and mild forearm swelling with severe pain and numbness. Although bleeding was observed from the catheter insertion site, we needed to place a central venous catheter (CVC) for hemodialysis. Therefore, he was started on recombinant factor VIIa (rFVIIa) at a dose of 60 µg/kg every three hours. Prednisolone (PSL) 1 mg/kg was also initiated to eradicate the factor VIII inhibitor. We were able to insert a CVC through the right femoral vein without bleeding complications. He required hemodialysis on consecutive days for uremia and an electrolyte disorder. The rFVIIa injections were continued during hemodialysis, in accordance with the same schedule. Because of the patient's severe bleeding tendency, nafamostat mesylate was used as a replacement for heparin to prevent clotting in the hemodialysis circuit, and there were no coagulation problems. His urine output recovered five days after hemodialysis was started. The transition from the oliguric to the diuretic phase was completed in seven days, and the hematuria and the clot in the urethral catheter subsequently improved. Hemodialysis was discontinued nine days later, and his creatinine eventually settled between 1.2–1.6 mg/dL. The rFVIIa was discontinued after three weeks due to confirmation of a stable hemoglobin level and absence of new bleeding.

The factor VIII inhibitor decreased to an undetectable level 18 days after the initiation of PSL 1 mg/kg, which was continued for three weeks, followed by a slow tapering and then discon-

tinuation after seven months. No association was observed with malignancies or autoimmune diseases, and the patient achieved a complete recovery of his renal function. Although we had considered the need for surgery to remove blood clots in the bladder, CT imaging revealed that the blood clots in the urinary tract had spontaneously disappeared and the Single-J ureteral catheter stents and urethral catheter were removed.

Discussion

AKI can be classified as either prerenal, intrinsic renal, or postrenal. Urethral stones, urinary tract tumors, and prostate hypertrophy are common causes of obstruction in postrenal AKI [3]. Blood clots from urinary tract hemorrhages can also cause obstructive uropathy; however, there have been few reports on postrenal AKI caused by bladder tamponade. In a retrospective study of 20 patients with bladder tamponade with blood clots at a Japanese medical center, 11 patients had malignancies (9 with bladder tumors, 1 with prostate cancer, and 1 with malignant lymphoma). All but two of the other patients had mucosal damage, such as radiation cystitis, chronic cystitis, or iatrogenic conditions. Although eight patients took oral anticoagulant agents, none of the patients had bleeding disorders [4]. Although these etiologies were assumed in the present case, AHA is the cause of bladder tamponade and postrenal AKI.

Patients with AHA typically present with subcutaneous and deep soft tissue bleeding. Mucosal haemorrhage, such as respiratory, gastrointestinal, and urinary tract bleeding, is also observed [1]. The incidence of urinary tract bleeding in patients with AHA is less than 10% [5]. Previous studies have reported that approximately 80% of patients present with subcutaneous bleeding at initial diagnosis [5], whereas in our case the patient initially demonstrated an unusual manifestation of hematuria without subcutaneous bleeding. This atypical manifestation might lead to a delay in diagnosis; thus, heightened awareness of the disease is required.

Thrombosis is a well-known complication of treatment with rFVIIa. The reported incidence of thrombotic events (TE) varies from 2.9–8.6% [6,7]. A recent review reported that a thrombin burst, which led to the formation of a stable hemostatic plug induced by rFVIIa, was thought to act at local vascular injury sites. It also described the safety of the use of rFVIIa in approved indications for the localized action [8]. However, careful attention should be paid to serious TEs, such as myocardial infarction and ischemic stroke [6]. In the present case, a CT scan showed that bleeding was widespread in the renal pelvis, ureter, and bladder. Since the source of bleeding was not apparent, we were concerned about urinary tract obstruction and dysfunction of the single-J stent due to blood clots formed by the thrombin burst. In fact, there were a large number of blood clots in the bladder and the stent in the oliguric phase. Fortunately, however, polyuria in the diuretic phase washed them out and prevented an accumulation of blood clots with-

out the need for continuous bladder irrigation. Although little has been reported on urinary tract obstruction caused by rFVIIa, there has been a case report about repeated thrombotic endotracheal occlusion in a ventilated AHA patient treated with rFVIIa [9]. In our case, the patient was treated with TA for hematuria before a diagnosis of AHA was made. TA has been widely used for the treatment of bleeding in AHA [1]; however, it has been noted that the use of TA for hematuria can lead to the retention of clots in the ureters and bladder [10]. Further studies are required to investigate the possibility of urinary tract obstruction following hemostatic therapy with rFVIIa and TA.

The cause of bilateral renal hemorrhage is not known. In the present case, trauma (including a contusion), renal disease, and urinary tract diseases were not detected. There have been two case reports of bilateral renal bleeding due to AHA [11,12]. However, in our case the cause of the renal hemorrhage was unknown. AHA is a rare bleeding disorder, but a sudden onset of critical and life-threatening bleeding can occur, even in healthy persons. Clinicians need to suspect a diagnosis of AHA when there is severe, prolonged, and atypical bleeding. Early diagnosis could provide patients with appropriate hemostatic therapy, thereby avoiding a fatal bleeding event.

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