CASE REPORT

Retroperitoneal Hematoma in a Patient with Advanced Chronic Kidney Disease Receiving Warfarin Therapy

Takashi Maruyama¹, Masanori Abe¹, Tetsuya Furukawa¹, Shinichiro Kobayashi¹, Yoshinori Yoshida¹, Hiroko Noda², Kazuyoshi Okada¹ and Masayoshi Soma³

Abstract

A 73-year-old man with chronic kidney disease stage G5 was admitted to our hospital because of a worsening kidney dysfunction. He had undergone prosthetic valve replacement of the mitral valve 5 years previously and was currently taking warfarin. He showed excessive anticoagulation on admission, with a prothrombin time-international normalized ratio (PT-INR) of 3.91. The use of warfarin was ceased and PT-INR decreased to 2.1. Since the patient would need renal replacement therapy, he underwent arteriovenous fistula surgery for hemodialysis access on day 16. However, on day 18, he suddenly complained of lumbago and went into shock. His blood pressure dropped to 73/49 mmHg, and the hemoglobin level fell to 4.9 g/dL. Computed tomography revealed a huge retroperitoneal hematoma. Emergent lumbar artery embolization was performed on two consecutive days; however, the bleeding persisted, with subsequent development of abdominal compartment syndrome with impaired respiratory and cardiovascular function, and the patient died. Autopsy revealed a hematoma measuring 30×20×20 cm involving the psoas muscle and external iliac artery; the hematoma was covered with fibrous tissue instead of muscle. The psoas muscle is supplied by the internal iliac artery; however, a collapsed artery could not be confirmed in our patient. The closest major artery to the hematoma was located at the intersection of the psoas muscle and the external iliac artery. All arteries showed severe atherosclerosis. In patients with advanced chronic kidney disease, anticoagulant therapy should be administered carefully, and the etiology of retroperitoneal hematoma should be further investigated.

Key words: anticoagulant therapy, retroperitoneal hematoma, chronic kidney disease, hemodialysis, warfarin


Introduction

The incidence of retroperitoneal hematoma—a rare clinical entity with various etiologies—continues to increase because of complications related to interventional procedures. Spontaneous retroperitoneal bleeding is a distinctive clinical entity that can occur in the absence of a specific underlying pathology or trauma (1). Its symptoms and natural history range from slight pain to femoral neuropathy or precipitous shock and cardiovascular collapse. Patient survival often depends on rapid and accurate diagnosis, as the bleeding may be insidious and initially unrecognized. Retroperitoneal hematoma represents one of the most serious and potentially lethal complications of anticoagulation therapy and can cause anemia, with devastating consequences (2). Therefore, it is crucial to be aware of and recognize retroperitoneal hematoma. We herein report a case of spontaneous retroperitoneal hematoma occurring in an elderly man with chronic kidney disease (CKD) stage G5 who had undergone prosthetic valve replacement of the mitral valve and was taking warfarin.

Case Report

A 73-year-old man was referred to our hospital because...
of a 1-week history of lower limb edema, shortness of breath, and loss of appetite. He had undergone mitral valve replacement with a mechanical valve 5 years previously, and at the same time, he had been diagnosed with CKD due to nephrosclerosis. He was admitted to our hospital due to a worsening kidney dysfunction. On admission, his vital parameters were as follows: temperature, 36.4°C; blood pressure, 144/91 mmHg; heart rate, 94 beats per minute (regular); respiratory rate, 20 breaths per minute; and body weight, 61.2 kg. Physical examination revealed signs of anemia in the palpebral conjunctiva, edema of the lower limbs, and clear consciousness. Chest radiography indicated cardiomegaly with a cardiothoracic ratio of 63% and mild bilateral pleural effusion. Abdominal computed tomography (CT) scan findings showed atrophy of the bilateral kidneys but no findings indicating post-renal failure (Fig. 1a). Ultrasonography also revealed thinning of the bilateral renal cortices and multiple cysts in the bilateral kidneys. Based on the laboratory findings presented in Table, we diagnosed CKD stage G5, hyperkalemia, metabolic acidosis, and anemia. Although urinary protein excretion was 1.81 g/day, the serum albumin level was low, possibly due to malnutrition. On admission, because of excessive anticoagulation and an elevated prothrombin time-international normalized ratio (PT-INR) of 3.91, the administration of warfarin potassium was ceased, and therapy with oral sodium bicarbonate and intravenous furosemide was initiated. Moreover, the patient received a transfusion of 560 mL of red cell concentrate over a 48-hour period.

Subsequently, the excessive anticoagulation improved (PT-INR, 2.1), and the patient produced >1,000 mL urine per day. On day 5 of hospitalization, he was breathing more easily. The O2 level in a blood gas analysis, cardiomegaly, and the mild bilateral pleural effusion noted on radiography had all improved. With regard to anemia, the results of gastroscopy performed on day 2 were normal, and a fecal occult blood test was negative. Although his symptoms had improved, renal replacement therapy would be needed in the future, as kidney dysfunction persisted. Therefore, on day 16, the patient underwent arteriovenous fistula surgery in preparation for hemodialysis access. His blood pressure ranged from 130/85 to 120/75 mmHg after admission. However, on day 18, he suddenly complained of lumbago and the blood pressure dropped to 73/49 mmHg and the hemoglobin level decreased to 4.9 g/dL. Based on the results of the previous examinations, we suspected that the anemia was not due to gastrointestinal bleeding. Therefore, we performed systemic CT to determine the cause of anemia; this revealed a huge hematoma in the left retroperitoneum (Fig. 1b), which was the likely cause of both the anemia and lumbago. Emergency lumbar artery embolization was performed on the same day (Fig. 2a). On day 19, the kidney function worsened, and anuria occurred due to hypovolemic shock; therefore, hemodialysis was initiated. However, because the patient’s blood pressure decreased during hemodialysis, CT was repeated, thus revealing that the hematoma had increased in size. Subsequently, emergency intercostal artery embolization was performed a second time (Fig. 2b).

Thereafter, the patient was treated with therapeutic doses of intravenous heparin. The activated partial thromboplastin
time ratio was 1.3, no sudden deterioration in anemia was noted, the blood pressure was stable, and the size of the hematoma did not increase. However, the anemia gradually worsened, and the patient was administered packed red blood cell transfusions. Overall, the total transfusion of red blood cells amounted to 5,600 mL. Maintenance hemodialysis was performed thrice weekly since the anuria persisted. However, the patient subsequently developed disseminated intravascular coagulopathy, and platelet counts decreased sharply. Furthermore, pneumonia occurred on day 40. Although the huge, persistent hematoma was treated conservatively, it led to abdominal compartment syndrome and affected both the digestive and respiratory systems. On day 52, sepsis caused by *Escherichia coli* was diagnosed. The hematoma pressed against the left diaphragm, causing type II respiratory failure, which was treated by bilevel positive airway pressure (Fig. 1c, d). The size of the hematoma did not decrease by conservative therapy. The patient’s condition gradually worsened, and hemodialysis was stopped on day 73 because of hemodynamic instability. The patient died on day 80 of hospitalization.

An autopsy was performed; the findings are shown in Fig. 3. The size of the hematoma was 30×20×20 cm. Its outer surface was covered with fibrous tissue instead of muscle, and new and old clots were intermingled in the hematoma, which involved the psoas muscles and external iliac artery (Fig. 3a, b). The coils used for arterial embolization were found inside the hematoma; however, the fifth lumbar and twelfth intercostal arteries could not be observed macroscopically since they were tiny and friable. The psoas muscle is supplied by the internal iliac artery, but no collapsed artery could not be identified in our patient. Further-

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**Table.** Laboratory Findings on Admission.

<table>
<thead>
<tr>
<th>Peripheral blood</th>
<th>Blood chemistry</th>
<th>Blood gas analysis (room air)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 5,900/μL</td>
<td>Total protein 5.4 g/dL</td>
<td>pH 7.404</td>
</tr>
<tr>
<td>RBC 276×10⁶/μL</td>
<td>Serum albumin 2.2 g/dL</td>
<td>pCO₂ 28.9 mmol/L</td>
</tr>
<tr>
<td>Hemoglobin 8.7 g/dL</td>
<td>BUN 71.5 mg/dL</td>
<td>PO₂ 52.8 mmol/L</td>
</tr>
<tr>
<td>Hematocrit 28.4%</td>
<td>Creatinine 5.96 mg/dL</td>
<td>HCO₃⁻ 18.4 mmol/L</td>
</tr>
<tr>
<td>Platelet 23.3×10⁵/μL</td>
<td>eGFR 8.45 mL/min/1.73 m²</td>
<td>Base excess -6.5 mmol/L</td>
</tr>
<tr>
<td>Blood coagulation</td>
<td>T-Bil 0.34 mg/dL</td>
<td></td>
</tr>
<tr>
<td>PT % 32.8%</td>
<td>ALT 13 IU</td>
<td>pH 5.5</td>
</tr>
<tr>
<td>PT-INR 3.91</td>
<td>ALP 228 IU</td>
<td>Protein 1+</td>
</tr>
<tr>
<td>APTT ratio 1.60</td>
<td>LDH 364 IU</td>
<td>Occult blood 1+</td>
</tr>
<tr>
<td>Fibrinogen 556 mg/dL</td>
<td>CPK 322 IU</td>
<td>Glucose –</td>
</tr>
<tr>
<td>D-dimer 1.0 μg/mL</td>
<td>ATP 139 mEq/L</td>
<td>Sediment –</td>
</tr>
<tr>
<td>AT-III 110%</td>
<td>Potassium 5.6 mEq/L</td>
<td>Red blood cell 1-4/HF</td>
</tr>
<tr>
<td>ALP</td>
<td>Chloride 108 mEq/L</td>
<td>White blood cell 1-4/HF</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Calcium 7.1 mg/dL</td>
<td></td>
</tr>
<tr>
<td>D-dimer</td>
<td>Phosphate 4.7 mg/dL</td>
<td></td>
</tr>
<tr>
<td>AT-III</td>
<td>CRP 2.19 mg/dL</td>
<td>Protein excretion 1.81 g/day</td>
</tr>
</tbody>
</table>


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**Figure 2.** The arrow indicates the sites of bleeding in (a) the fifth lumbar artery and (b) the twelfth intercostal artery.
more, no collapse or aneurysm was evident in either the aorta or its major branches. The closest major artery to the hematoma was located at the intersection of the psoas muscle and the external iliac artery, and all arteries showed severe atherosclerosis. Microscopically, the hematoma in adipose tissue showed intermingling of new and old bleeding (Fig. 3c, d). No signs of gastrointestinal bleeding were evident.

**Discussion**

In clinical medicine, gastrointestinal hemorrhage frequently causes sudden anemia. In the present case, however, the sudden anemia was the result of a retroperitoneal hematoma. In cases of a sudden onset of anemia, it is therefore important to perform a CT examination of the sites where pain is reported. Retroperitoneal hematoma is a well-recognized but relatively rare condition, with an incidence of 0.1% in a series of 2012 patients (3). Retroperitoneal hemorrhage is most frequently seen as a complication of femoral artery catheterization and pelvic or lumbar trauma. Although it may rarely be caused by the rupture of renal or mesenteric aneurysms or ovarian artery aneurysms, bleeding can also occur due to underlying causes in any of the retroperitoneal structures, such as the pancreas, adrenal glands, or kidneys as well as a complication of any retroperitoneal surgery (4-7). However, it can also happen spontaneously, without any obvious precipitating factors, namely, so-called spontaneous retroperitoneal hematoma. This is most commonly seen in patients receiving anticoagulation therapy, those with bleeding abnormalities, elderly individuals, and patients on hemodialysis (8-11); its incidence has been reported to range from 0.6-6.6% among patients undergoing therapeutic anticoagulation (3, 12). In general, patients maintained on chronic hemodialysis have an increased incidence of spontaneous bleeding in various parts of the body, especially if they are receiving heparin or warfarin (13).

Hemorrhagic complications and cerebral hemorrhage are frequently encountered in patients with advanced CKD (14, 15), which are caused by various abnormalities such as low blood vitamin K levels, excess warfarin administration, anemia, and platelet dysfunction. Therefore, the Japanese Society for Dialysis Therapy (JSDT) guidelines...
agulopathy was considered to be absent. In addition, when arterial embolization had been performed without any problems, congenital coagulopathy was considered to be present, although these could not be identified histologically. Qanadli et al. reported that spontaneous bleeding starts at the microvascular level, and large vessels are stretched or ruptured as the hematoma enlarges. Others have suggested that anticoagulation-induced immune microangiopathy may be responsible, and unrecognized minor trauma in the microcirculation in the presence of anticoagulants may lead to hemorrhage (19). However, some authors have suspected that unrecognized trauma, such as minor trauma in sports and vomiting or coughing, may initiate blood loss which continues unabated when clotting factors are absent or depleted. Although such minor trauma is a recognized inciting factor in hemophilia-related spontaneous retroperitoneal bleeds (20, 21), it could not be specifically identified in our patient. Based on the present autopsy findings, the following pathogenesis of our patient was considered. Anticoagulant therapy was administered because he had undergone mitral valve replacement with a mechanical valve. The fifth lumbar artery and some blood vessels branching from the external iliac artery collapsed because they had been rendered friable and prone to rupture due to atherosclerosis, vasculopathy, and uremia; thus, the hematoma formed close to the iliosos muscle. Because of the timing of development and variation in the size of the hematoma, multiple bleeding sites, including the twelfth intercostal artery, were considered to be present, although these could not be identified during autopsy. The anticoagulation therapy had to be continued because of the patient’s medical history; however, because of the high number of blood vessels feeding the hematoma, effective hemostasis could not be achieved despite performing arterial embolization. Based on the CT findings, the hematoma was initially thought to be an iliosos muscle hematoma. However, the autopsy revealed no abnormalities in the vessels feeding the psoas muscle, and the outer surface of the hematoma was covered with fibrous tissue and not muscle. Consequently, the mass was diagnosed to be a retroperitoneal hematoma.

The treatment of retroperitoneal hematoma remains controversial. It is recommended that all retroperitoneal hemorrhage be treated conservatively, as it is believed that open surgery may disturb the tamponade effect of the retroperitoneum (22). However, there are no specific guidelines to indicate the optimal time to intervene with endovascular or open surgery to stop the bleeding. Therefore, early recognition of retroperitoneal hematoma can enable prompt and appropriate therapy, including endovascular and antimicrobial treatment, and may minimize the sequelae associated with this disorder. Despite performing these treatments in this patient, the high number of arteries feeding the hematoma made it impossible to treat it effectively or to improve the patient’s chances for survival by suppressing disease progression.

In summary, despite providing otherwise appropriate treatment for anticoagulation and not finding any obvious arterial deformities, we experienced a fatal case of retroperitoneal hematoma in an elderly man with CKD stage G5. In patients with advanced CKD, anticoagulant therapy should be administered carefully, and the cause of retroperitoneal hematoma should be further investigated.

Written informed consent was obtained from the patient’s family for publication of this case report and any accompanying images.

Author’s disclosure of potential Conflicts of Interest (COI). Masanori Abe: Honoraria, Daiichi Sankyo, Kyowa Hakko Kirin, Otsuka Pharmaceutical.

Acknowledgement We thank Dr. Keishin Sunagawa for the pathology report.

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