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Patient: Male, 54-year-old
Final Diagnosis: Giant right renal artery aneurysm
Symptoms: Bilateral leg edema
Medication: —
Clinical Procedure: —
Specialty: Hematology • Radiology • Urology

Objective: Rare coexistence of disease or pathology

Background: Classical hemophilia, or hemophilia A, is an X-linked recessive genetic disorder characterized by deficiency in clotting factor VIII. Renal artery aneurysms (RAAs) are also rare and are defined as a focal dilatation of the renal artery that exceeds 1.5 cm in diameter. These 2 rare conditions – giant RAA and hemophilia A – were simultaneously observed in our patient. This report presents a male patient with hemophilia A with a 10-cm aneurysm of the right renal artery, which was treated with transarterial coil embolization and factor VIII infusion. The giant RAA was an incidental finding and was suspected after the abdominal ultrasound (US).

Case Report: We present the case of a 10-cm right RAA in a 54-year-old man with hemophilia A. The patient had a congenital severe coagulation factor VIII deficiency (hemophilia A). He presented at a routine hematologist visit with an atypical symptom of severe symmetrical leg edema. Laboratory tests showed increased levels of creatinine and proteinuria. Investigations proceeded with computed tomography (CT) and digital subtraction angiography (DSA). Endovascular coiling of the aneurysm was performed with perioperative recombinant coagulation factor VIII substitution, and the recovery was uneventful. At 6-year follow-up there are no signs of proteinuria, and kidney function was stable.

Conclusions: We present a case of renal artery aneurysm effectively treated by endovascular embolization, showing the importance of managing patients with hemophilia A according to a guidelines-based multidisciplinary approach and ensuring the lowest possible risk of peri- and intraoperative complications by using minimally-invasive treatments.

Keywords: Aneurysm • Endovascular Procedures • Hemophilia A

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Background

Classical hemophilia, or hemophilia A, is an X-linked recessive genetic disorder characterized by deficiency in clotting factor VIII [1,2]. It is classified according to clotting factor VIII level in the blood. There are 3 severity stages: mild (clotting factor VIII more than 5%), moderate (factor VIII 1-5%), and severe (factor VIII <1%) [1-3]. The typical clinical sign of hemophilia is bleeding, which is often spontaneous [1-3]. The most common sites are muscles and joints [2]. The highest-risk group for bleeding is patients with severe hemophilia [2]. Hemophilia patients are treated with clotting factor administration [2,3]. The regimen and dosage of clotting factor depend on the severity stage of the disease, type of bleeding, and procedure type. It is very important to make a factor substitution plan before the surgical treatment or procedure [2,4,5]. According to Fijnvandraart et al, factor VIII concentrations should be raised to 0.80-1.00 International Units/milliliter (IU/mL) immediately before commencing surgery and maintained above 0.50 IU/mL for between 5 days and 14 days after surgery, depending on the surgical site and type of surgical procedure [2].

Renal artery aneurysms (RAA) are rare and are defined as a focal dilatation of the renal artery that exceeds 1.5 cm in diameter [6,7]. If the size of the RAA is more than 5 cm, it is defined as giant [8-11]. Most documented giant RAAs are 5-12 cm, with only a few severe hemophiliac patient case reports in the literature [7,12-17]. In the case of RAA, the defect is localized in internal elastic tissue of the artery and affects all 3 layers of the arterial wall [18]. Etiological factors may include arterial hypertension, atherosclerosis, fibromuscular dysplasia, vasculitis, trauma, or congenital defects [7,18,19]. According to Rundback, RAAs are classified into 3 groups: saccular, fusiform, and intralobar; the most common type is saccular and the most commonly affected site is the right kidney [18,19].

The prevalence of RAA is 0.1-1% in the general population and is detected in less than 10% [20]. The first case report of RAA was published in 1770 by Rouppe [6]. Most RAAs are asymptomatic, with the diagnosis being made incidentally by an abdominal ultrasound (US) or computed tomography (CT) screening for other pathologies [21,22]. Giant RAAs are even more rare, with few cases described in the literature [7]. Despite this, in very rare cases it can present as an emergency due to a rupture with severe pain syndrome and critical bleeding [13,18,19].

RAA in a hemophiliac has been reported once before, by G. Das in 1984 [9]. In recent years, new strategies for the management of RAAs have been developed with a minimally-invasive approach [22]. Nowadays, diagnosis is usually made by angiography, followed by endovascular treatment as the method of choice [13,23].

This report is of 54-year-old man with hemophilia A presenting with a 10-cm right RAA managed with endovascular coil embolization and factor VIII infusion and followed up for 6 years.

Case Report

A 54-year-old White man (non-smoker, no substance abuse) with congenital severe coagulation factor VIII deficiency (hemophilia A) presented to the hematologist in a routine visit in June 2015.

The patient had been diagnosed with severe hemophilia A in childhood. Initially, he was treated with on-demand fresh frozen plasma (FFP) transfusions, and FFP transfusions were later replaced by cryoprecipitate. The treatment was continued with plasma-derived factor derivate, followed by prophylactic treatment with plasma-derived factor concentrates, but he now uses recombinant factor VIII (NovoEight). He developed lower- and upper-extremity arthropathies as hemophilia A complications. He was using recombinant coagulation factor VIII substitution 2000 International Units (IU) (Novo Eight) in a prophylactic regimen. There had been no spontaneous bleeding episodes since 2013. The patient has never developed inhibitors to factor VIII. The patient also had comorbidities: latent viral hepatitis C and primary arterial hypertension.

He presented in June 2015 with lower-leg edema, which had been progressing for a few weeks.

The patient was referred for laboratory and imaging investigations. Analysis of urine and biochemistry was performed. The 24-hour urine analysis showed proteinuria at 8.06 g/l (normal range <0.12 g/l), slightly decreased urine specific gravity 1.010 (normal range 1.015-1.030), and erythrocytes in the urine sediment. Despite changes in the urine, the creatinine level (76 mmol/L) and glomerular filtration rate (GFR) (115 ml/min) were normal. Hypoalbuminemia and increased erythrocyte sedimentation rate – 62 mm/h (normal range 0-5 mm/h) – were found. Laboratory tests for multiple myeloma were negative.

The abdominal US examination described normal-size kidneys, but showed multiple unilateral renal cysts in the right kidney, the largest being 10 cm in diameter. According to the results of the abdominal US, the differential diagnosis consisted of renal cancer, atypical renal cyst, and renal hematoma. Color Doppler US revealed blood flow within this structure, suggesting the diagnosis of RAA. One of the previous abdominal US examinations, performed on the patient at the age of 39 years, demonstrated initial changes in the right kidney and a suspicion of small RAA, but it was not followed up for an unknown reason. There are no other medical records of abdominal US which could confirm RAA at a younger age.

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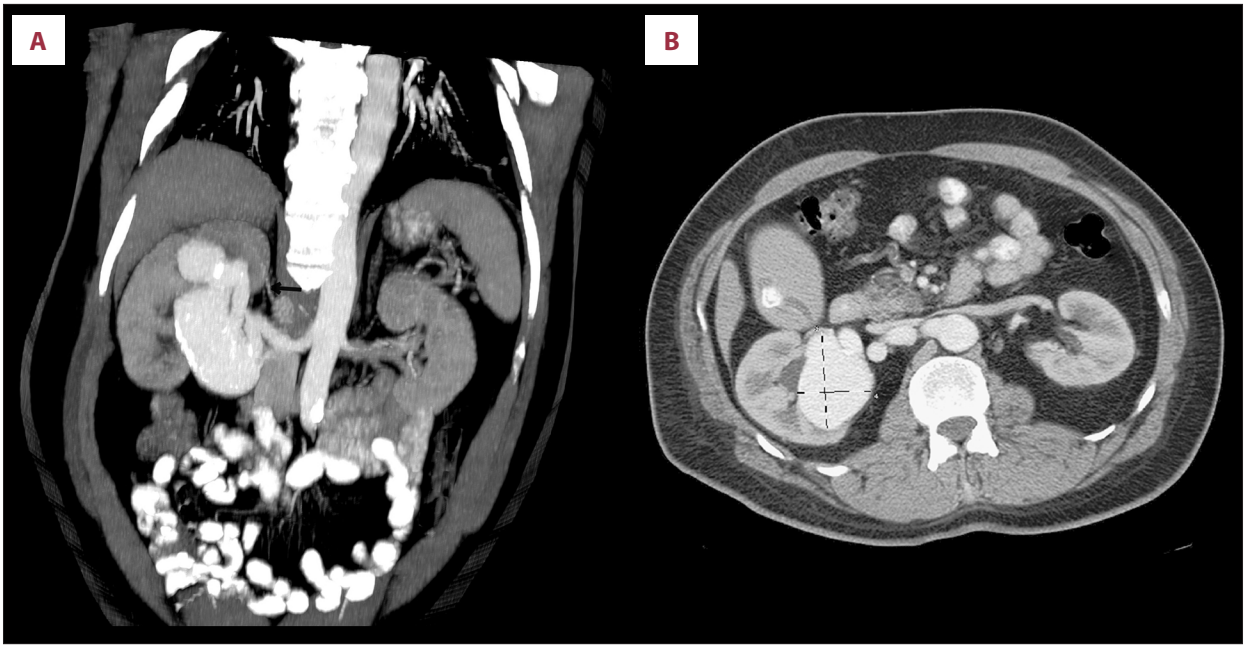

Figure 1. (**A, B**) CT/CTA showing a giant multi-saccular right RAA (5.3×6.7×10.2 cm) extending in the renal pelvis and an accessory artery (arrow) from the aorta to the upper pole of the right kidney.

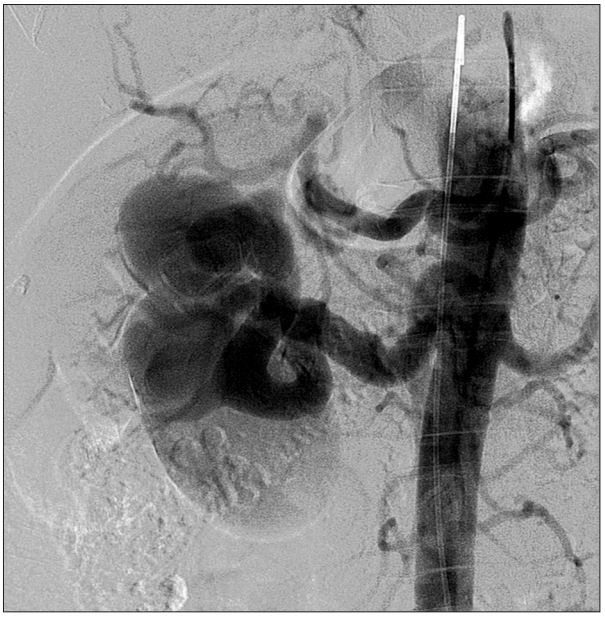

Figure 2. DSA showing a large multi-saccular aneurysm of the right renal artery with an accessory artery to the upper pole of the right kidney.

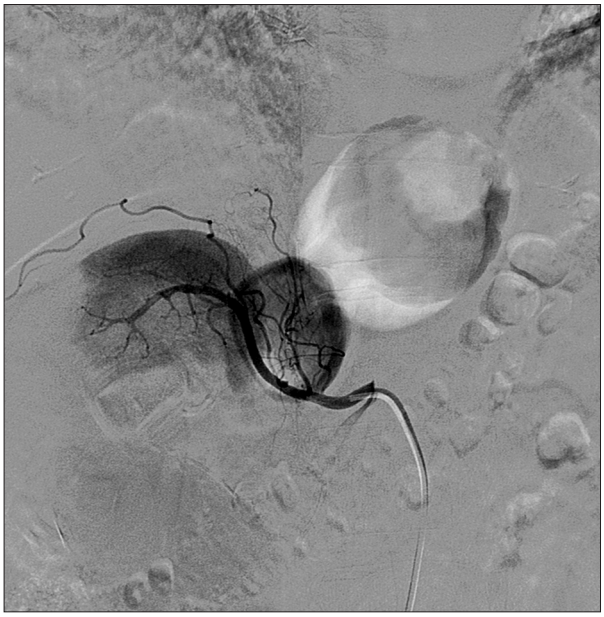

Figure 3. Super-selective renal accessory artery DSA, showing partial renal parenchymal perfusion in an upper pole.

Afterwards, an abdominal CT was performed. The CT with intravenous contrast injection revealed a dysplastic, elongated right renal artery with a multi-saccular aneurysm (5.3×6.7×10.2 cm) extending to the renal sinus (**Figure 1A, 1B**). There was also an accessory artery from the aorta to the upper pole of the right kidney (**Figure 1A, 1B**).

Based on the nephrologist's recommendations, a renal scintigraphy was performed. It showed delayed excretion and filtration in the right kidney and delayed filtration in the left kidney. There were typical signs of chronic kidney disease.

An additional abdominal and selective renal DSA was performed to specify the diagnosis. A giant multi-saccular 10-cm

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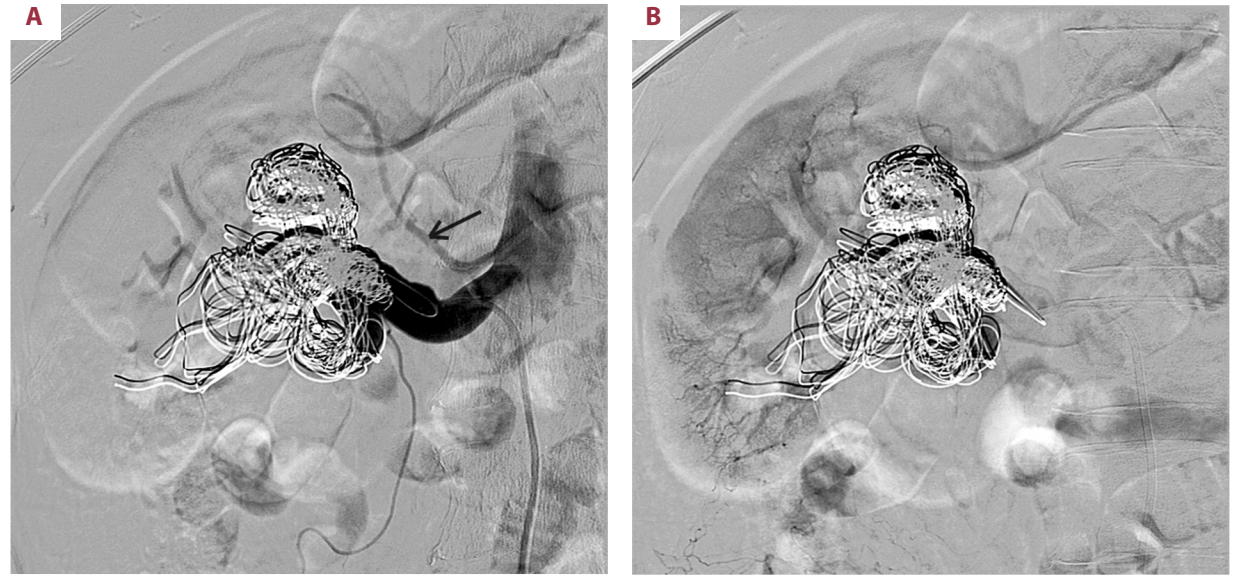

Figure 4. (**A, B**) A final intraoperative DSA showing the complete occlusion of the RAA filled with coils and a preserved right upper pole accessory artery (arrow) with a good contrast enhancement of renal parenchyma in the upper and middle part.

aneurysm of the dysplastic right renal artery was confirmed and significantly reduced flow to the renal parenchyma was found in a late venous phase. An accessory artery to the upper pole was also confirmed with the perfusion of the upper 1/3 of the right kidney (**Figures 2, 3**).

After a multidisciplinary evaluation with the participation of an interventional radiologist, urologist, and hematologist, the decision was in favor of minimally-invasive treatment with a nephron-sparing approach. One month later, endovascular coiling of the aneurysm was performed via a right transfemoral approach under local anesthesia. The right renal artery was selectively catheterized with a Vista Brite Tip® IG 6 Fr renal guiding catheter (Cordis Corporation, Hialeah, FL, USA) and the RAA was super-selectively catheterized with a PX Slim (Penumbra, Inc., Alameda, CA, USA) microcatheter. Embolization of the aneurism was followed by occlusion of the parent artery, performed using a combination of 7 detachable large-volume Ruby™ coils (Penumbra, Inc., Alameda, CA, USA), 13 Tornado® embolization coils (Cook Medical, Bloomington, IN, USA), and 9 Nester® embolization coils (Cook Medical, Bloomington, IN, USA). The final intraoperative DSA confirmed the complete absence of flow in the aneurism and no signs of intraprocedural bleeding. The accessory artery of the upper pole was preserved (**Figure 4A, 4B**). Perioperative prophylaxis of bleeding was performed with an additional dose of recombinant coagulation factor VIII on the day of the operation and for the following 3 days. Afterwards, the patient continued hemophilia A treatment without changes.

In the postoperative period, we expected severe pain syndrome and extensive kidney infarction. But, despite the prognosis, the patient felt only slight discomfort in the right side, and there were no indications for active postoperative pain relief. This could probably be explained by a long period of pre-existing decrease in blood flow in the renal parenchyma due to the hemodynamic priority of the aneurysm and the relatively more significant role of the accessory renal artery in the blood supply to the right kidney.

The postoperative period was without any complications. The leg edema was gradually decreasing. Kidney function remained normal. The patient was discharged on the 7th postoperative day. Continued treatment with recombinant factor VIII in schedule 2000 IU 3 times a week was prescribed.

After 4 months, a follow-up CT and computed tomography angiography (CTA) were performed. They showed a completely thrombosed right RAA, no coil misplacement or migration, and a fully patent upper-pole artery (**Figure 5A, 5B**). The function of the kidney was preserved, as seen by the contrast excretion in the CT urography (**Figure 6**).

The hematologist visit was on 13 January 2022, 6 years after the surgery. There were no concerns about leg edema or pain. Urine analysis was normal, but the function of the kidneys was slightly decreased due to arterial hypertension and the patient's age. Renal scintigraphy and abdominal CT did not show any new pathological findings. At 6-year follow-up, the success rate was 100%.

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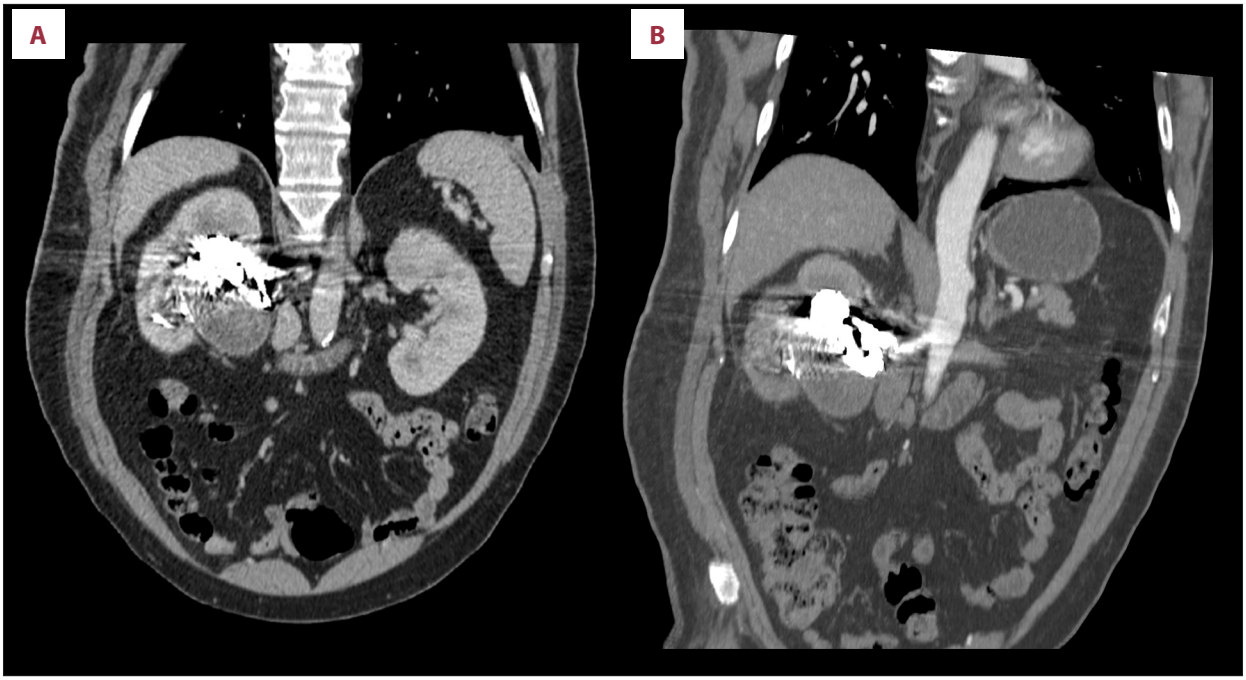

Figure 5. (**A, B**) Four-month follow-up abdominal CT/CTA showing coil mass and complete occlusion of the RAA and the preserved right kidney parenchymal perfusion.

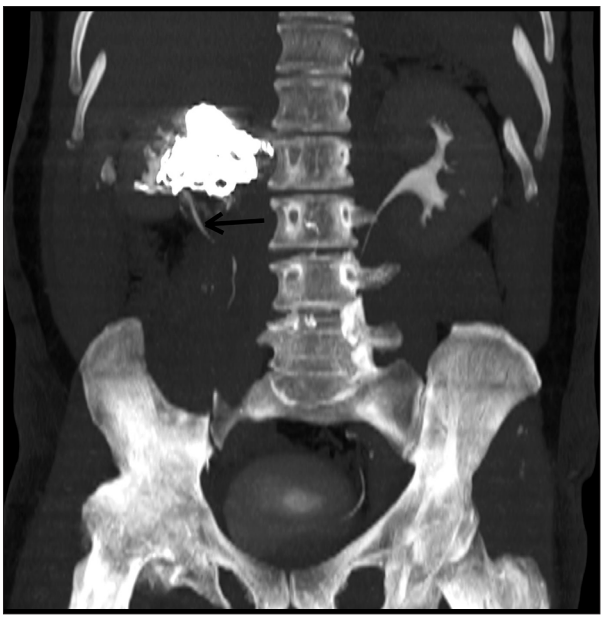

Figure 6. Four-month follow-up abdominal CT/CTA showing contrast excretion in the right ureter (arrow).

Discussion

This report is of 54-year-old man with hemophilia A presenting with a 10-cm right RAA managed with endovascular coil embolization and factor VIII infusion.

An unusual RAA presentation in combination with hemophilia A is shown in this case report. Typically, RAA presents with abdominal pain, hematuria, and uncontrollable hypertension, or there are no symptoms at all. The main patient concern was leg edema, which could be provoked by changed kidney function, hypoalbuminemia, hypertension, and an RAA compression effect to the kidney.

RAA symptoms appear more commonly when it becomes larger. RAA enlargement is unpredictable, but complications can appear as they enlarge [13,18,22]. Complications of RAA include rupture, thrombosis of the parent artery, hypertension, and arteriovenous fistulae formation [22,24]. However, most RAAs are asymptomatic and are usually incidental findings [19,21].

The role of imaging in RAA is very important. The combination of Gray-scale US and color Doppler US can raise the suspicion of the existence of an RAA, but using angiography it is 100% confirmed [22]. In diagnostic imaging, CTA or MRA are the criterion standard for final diagnosis of a pseudo-aneurism or true aneurysm of this size. DSA should be reserved for ambiguous findings and for cases when mini-invasive treatment is intended [11,18,19,22]. Our patient underwent abdominal US and showing suspicious changes; afterwards, CT, CTA, and DSA were performed and the diagnosis was confirmed.

There are different treatment tactics in RAA. Most of the RAAs are followed up by US and patient's symptoms. There are 2 main treatment options: open surgical repair and endovascular

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techniques [18,19,22] Indications for surgical or endovascular treatment are: RAA size >2.0-2.5cm, interval enlargement, renovascular hypertension, pain, hematuria, intrarenal thromboemboli, and lesions in women in childbearing age [18,19]. Open surgical repair has been the traditional standard of care for years in RAAs; however, endovascular treatment techniques have proven to be effective, with lower morbidity. There are studies showing decreased complication rates and hospitalization times. According to Cappucii et al, endovascular treatment is safe in visceral artery aneurysms and pseudoaneurysms, with few long-term complications and successful therapeutic treatment [9]. Our patient had congenital coagulation factor VIII deficiency – severe hemophilia A. Our team avoided open surgical treatment due to an unacceptably high risk of major bleeding and postsurgical complications. In this case, endovascular treatment was the method of choice due to very high bleeding risk. The aim was to preserve as much renal parenchyma as possible, taking into account the possibilities to preserve the accessory artery to the upper pole of the right kidney. Endovascular treatment is associated with a significant reduction of blood loss during minimally-invasive operations, with reduction in the requirement for blood transfusions and shorter hospital stay [15-17]. With the development of endovascular treatment technics, embolization of RAAs has become the method of choice for treating RAAs, with the preservation of renal parenchyma, as described by Gutta et al [8]. According to literature reviews, in surgical treatment, it is recommended to add coagulation factor VIII to the treatment plan in patients with hemophilia for 14 days before open surgery, during the surgery, and in the postoperative period every 12 hours for a few days [2,3,4,16], which increases the cost of treatment but reduces the bleeding risk. Our patient received just 3 extra injections of recombinant factor VIII.

Such a combination of 2 rare pathologies – RAA and haemophilia – has been described once in the literature, in 1984 in a 42-year-old man with mild hemophilia and bilateral renal artery malformations. There were major complications, including retroperitoneal haematomas, kidney rupture, and severe postoperative complications such as kidney failure [8]. Our literature search showed that the combination of aortal aneurysm and hemophilia is more common, with 6 reported hemophiliac patients: 5 patients with hemophilia A and 1 patient with hemophilia B [13,14,21-25]. Open surgery or less invasive methods were used, depending on the availability of the method and time when the surgery was performed [13,21-25].

Conclusions

Thus, there are only few published reports on the treatment of these 2 simultaneous diseases – renal aneurysm and hemophilia. Our case report shows the atypical presentation of RAA and demonstrates that an endovascular approach is effective and safe for patients with a high risk of bleeding (eg, coagulopathies) and RAA. Our patient underwent endovascular treatment with no complications and with excellent outcome.

This report has presented a case of renal artery aneurysm effectively managed by endovascular coil embolization and highlights the importance of managing patients with hemophilia A according to a guidelines-based multidisciplinary approach. However, unfortunately, the scarcity of relevant reports in the literature creates difficulties in decision-making and are treatments are still selected on an individual basis in accordance with the experience of the particular medical team.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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