Case Report

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Wunderlich Syndrome: Early Misdiagnosis with Acute Renal Colic During COVID-19 Pandemic

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ABSTRACT

Wunderlich syndrome, also known as the spontaneous non-traumatic retroperitoneal hemorrhage, is an uncommon condition characterized by acute, spontaneous, non-traumatic renal hemorrhage into the subcapsular or perirenal spaces. The majority of the cases are caused by renal cell carcinoma or renal angiomyolipoma. Other causes are arteriovenous malformation, cystic renal disease, and anticoagulation medications. The classic presentation is "Lenk's triad" of acute flank pain, palpable flank mass, and hypovolemia. The diagnosis is based on clinical suspicion and confirmed by a CT scan, which is the preferred imaging modality. Due to the rarity of these cases and the wide range of clinical manifestations, the treatment is divergent ranging from conservative management to nephrectomy. Herein, we present a case of massive right renal hemorrhage caused by warfarin toxicity that was initially misdiagnosed as acute renal colic due to the patient's refusal to refer to the clinic during Corona Virus Disease- 19 era and was later managed with a right nephrectomy.

Keywords: Wunderlich syndrome; Acute renal colic; Nephrectomy; COVID-19; Renal cell carcinoma.

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Introduction

Wunderlich syndrome, or spontaneous non-traumatic retroperitoneal bleeding, is a rare condition. The majority of cases are caused by renal cell carcinoma or renal angiomyolipoma. Other causes are arteriovenous malformation, cystic renal disease, and anticoagulation medications [1, 2]. Due to the rarity of these cases and the wide range of clinical manifestations, the treatment options range from conservative care to nephrectomy. Herein, we present a case of massive right renal hemorrhage caused by warfarin toxicity that was initially misdiagnosed as acute renal colic due to not referring to the clinic with the fear of Corona Virus Disease-19 (COVID-19), which was later managed with a right nephrectomy.

Case Presentation

A 71-year-old woman with a history of mitral valve replacement and atrial fibrillation (AF) who was on warfarin experienced right abrupt onset flank pain radiating to external genitalia, as well as nausea and vomiting. She declined to be visited in the clinic due to the COVID-19 outbreak and asked for a phone consultation instead. She had minor urination problems, but no gross hematuria, or fever. Considering her previous history of renal stones and the pattern of her pain, we prescribed painkillers and requested a renal ultrasound, and urinalysis with the impression of acute renal colic. After two days of follow-up, and phone calls, the patient's pain was aggravating and she felt a heavy sensation on her right flank. Urinalysis was positive for blood, and the renal ultrasound showed a hypoechoic structure with a maximum diameter of 140×54 mm, and inferomedial extension of 87×48 mm. These findings were highly suggestive of a partially small size right kidney with an extrinsic impression caused by a real mass or a similar lesion that covered the entire kidney. Due to the bizarre shape of the right kidney and non-conclusive ultrasonography, we requested the patient be referred to Shiraz Central Hospital for further evaluation. On the day of admission, the patient looked ill with pale conjunctivae. Her pulse rate was 120 beats per minute and irregular (AF), and her blood pressure (BP) was 100/60 mmHg. A tense and tender mass was palpated in the right flank and upper quadrant of the abdomen, extending to the lower quadrant. Her laboratory data demonstrated a drop in hemoglobin (Hb) to 6.6 g/dL (baseline was 12 g/dL). The platelet count was normal (239000/µl), but the prothrombin time (PT) was 56.0 seconds with an international normalized ratio (INR) of more than 6. The level of blood urea nitrogen (BUN) and creatinine were 40 mg/dL and 2.82 mg / dL, respectively. Urine microscopy revealed trace blood with 3-5 red blood cells per high-power field of the microscope. Due to warfarin toxicity, the patient was admitted with an impression of retroperitoneal hematoma. A non-enhanced computed tomography (CT) scan of the abdomen and pelvic cavity disclosed an inhomogeneous lesion along the superolateral border of the right kidney, which seemed to be engulfing the entire kidney with perinephric fat stranding.

In the first days of admission, the Hb level was adjusted to 10 mg/dL by blood transfusion. Moreover, we administered the patient several bags of fresh frozen plasma (FFP) to treat the coagulopathy and prevent further bleeding. On the fifth day of hospitalization, the creatinine level dropped to 1.7 mg/dL, and an enhanced abdominopelvic CT scan was performed, which showed a partially enhancing small-size kidney engulfed by a heterogenous lesion causing mass effect surrounded by scattered non-enhancing septa (Figure 1). On the sixth day of hospitalization, the Hb level dropped to 8 mg/dL with aggravation of flank pain and flank fullness, which was in favor of rebleeding. Therefore, the patient was transferred to the operating room, and through a right incision, we entered the abdominal cavity. A massive hematoma in the retroperitoneum was detected, pushing the liver upward and the ascending and transverse colon anteriorly (Figure 2). The right colon was medialized and we entered the retroperitoneal space. The hematoma was confined to the Gerota's fascia with extension into the pelvic cavity but not pulsatile. After ligation of the renal pedicle, the right kidney, and Gerota's fascia was removed, the bleeders were controlled and a Jackson- Pratt surgical drain was inserted into the retroperitoneum. The postoperative course was rather uneventful, and the oozing from the retroperitoneum was not significant. A few days later, the patient was discharged in a good condition with a creatinine level of 1.8 mg/dL and INR of 2.5.

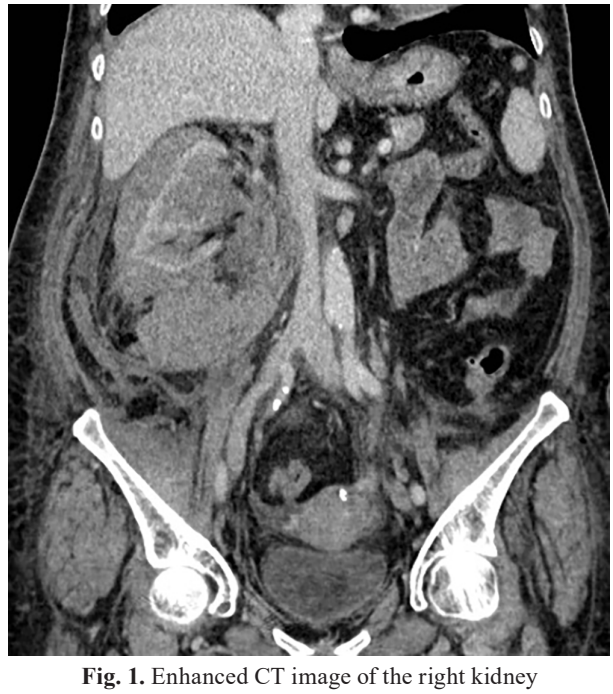

Fig. 1. Enhanced CT image of the right kidney

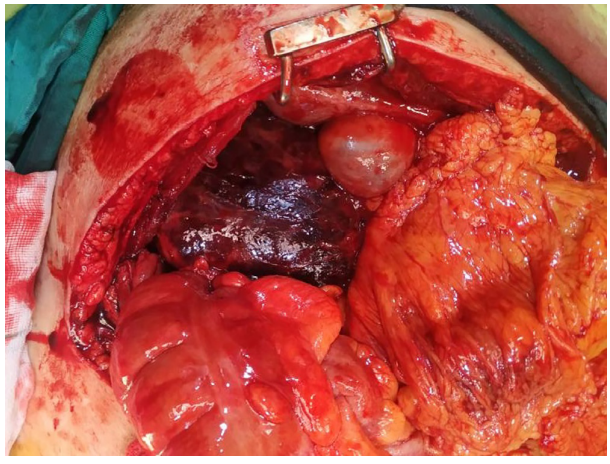

Fig. 2. Huge hematoma surrounding the right kidney

A gross evaluation of the kidney revealed extensive hemorrhage and blood clots in the renal parenchyma and perinephric fat (Figure 3). A microscopic examination was in favor of chronic pyelonephritis with hemorrhage and vascular congestion (Figure 4). Since renal cell carcinoma (RCC) is the most prevalent cause of spontaneous renal hemorrhage, we invited another pathologist to review the slides and utilized immunohistochemistry (IHC) markers to rule out renal malignancy; however, reevaluation of the case confirmed the initial diagnosis.

Discussion

Wunderlich syndrome, which was first described in 1856, is a rare condition marked by acute, spontaneous, non-traumatic renal hemorrhage into the subcapsular or perirenal spaces [3]. The majority of cases are caused by renal cell carcinoma or renal angiomyolipoma. Arteriovenous malformation, cystic renal disease, and anticoagulation medications are some of the other causes [1, 2]. The classic presentation is "Lenk's triad" of acute flank pain, palpable flank mass, and hypovolemia. The diagnosis is made based on clinical suspicion and is confirmed by a CT scan, which is the preferred imaging modality. The treatment depends on the severity of the disease and hemodynamic stability, available radiologic equipment, and the surgeon's experience, which can range from conservative management to angioembolization or nephrectomy [1, 4].

Our case presented with "Lenk's triad" but was initially misdiagnosed with acute renal colic, since we were unable to perform a physical examination because the patient refused to be admitted due to the fear of COVID-19. Moreover, she had previously experienced renal colic related to stone disease. We decided to perform a nephrectomy based on the CT scan finding, which revealed severe hemorrhage that has made the kidney non-functional, as well as the patient's hypovolemia and continuous blood loss.

In the present case, the cause of Wunderlich syndrome was warfarin toxicity. The patient was on warfarin due metallic heart valve and had declined

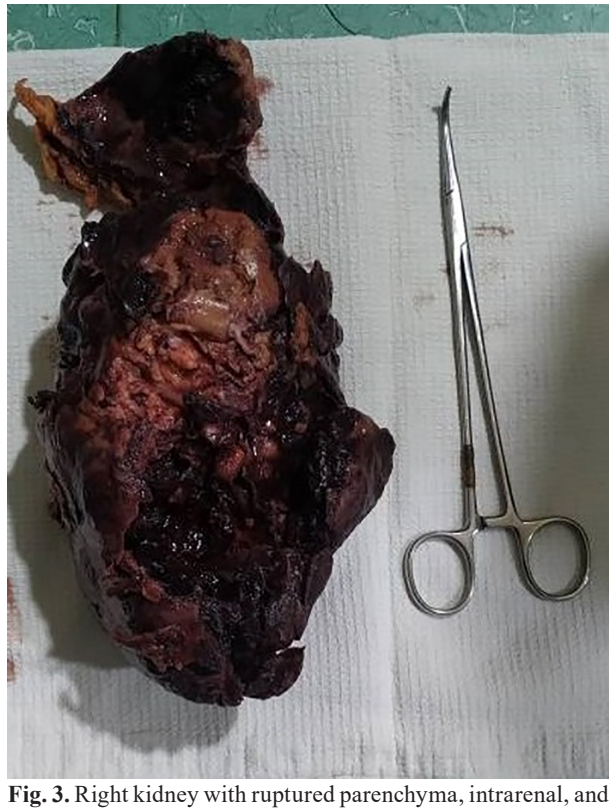

Fig. 3. Right kidney with ruptured parenchyma, intrarenal, and perirenal hemorrhage

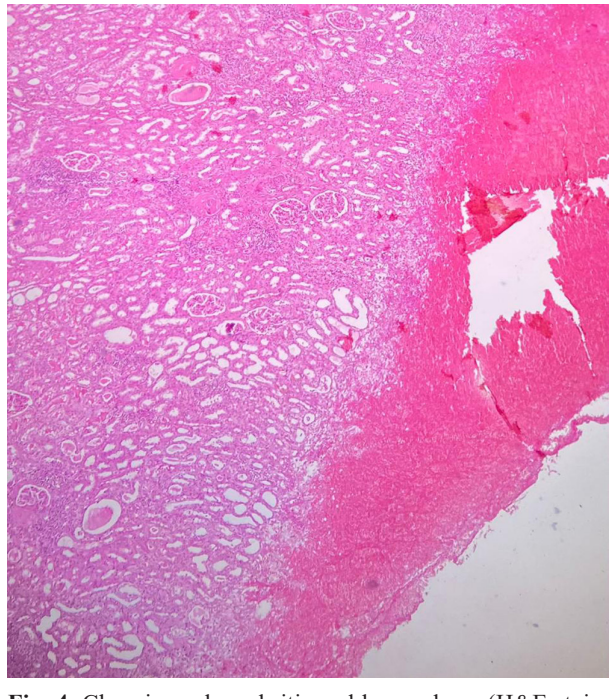

Fig. 4. Chronic pyelonephritis and hemorrhage (H&E stain, ×40)

to get her PT and INR checked regularly due to the COVID-19 pandemic. Since the kidney is protected in the retroperitoneal space, it is a rare place for spontaneous hemorrhage despite warfarin toxicity. Therefore, the first etiology was an undiagnosed RCC which presented with spontaneous bleeding in the setting of warfarin toxicity.

The excised kidney demonstrated histopathologic signs of chronic pyelonephritis. With suspicion of

RCC which is the most prevalent cause of spontaneous renal hemorrhage, we asked another pathologist to reevaluate the slides and also run IHC markers on the excised kidney; however, reassessment and IHC markers were all negative for malignancy.

Chronic pyelonephritis in our patient confirmed the findings of a study by Brodsky *et al.,* which found a relationship between the acute increase in PT/INR and deterioration of renal function in warfarin-treated patients. They indicated that obstruction of renal tubules by red blood cells was the mechanism for repeated acute kidney injury and subsequent chronic renal disease [5]. Our patient had been on blood thinners for eight years and repeated microscopic hemorrhage and clot formation in renal tubules could be a cause of chronic pyelonephritis.

Conclusion

Although anticoagulation is a rare cause of Wunderlich syndrome, clinicians should have a high index of suspicion for renal hemorrhage in patients who are using blood thinners and have abrupt onset acute flank pain. We can also propose that chronic pyelonephritis might be a risk factor for spontaneous renal hemorrhage in the context of warfarin toxicity. However, further research is required to support this notion.

Declaration

Ethics approval and consent to participate: Written informed consent was obtained from the patient. This study was approved by the ethics committee of Shiraz University of Medical Sciences (https://ethics.research.ac.ir/IR.SUMS.REC.1401.057).

Consent for publication: Written informed consent was obtained from the patient.

Conflict of Interest: None declared.

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Authors' Contribution: RM: Managed the patient, Study design and conception, data acquisition, manuscript drafting, and revision. AA: Study design and conception, data acquisition, manuscript drafting, and revision. MR: managed the patient. SN: Managed the patient. MS: Histopathological analysis. AM: Histopathological analysis. SHH: Interpretation of radiological images.

Acknowledgments: Not applicable.

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