

# Wunderlich Syndrome: Urological Emergency of Renal Hemorrhage

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## ABSTRACT

Wunderlich syndrome is a urological emergency characterized by spontaneous renal bleeding into the subcapsular and perirenal spaces or resulting in retroperitoneal hemorrhage. Renal neoplasms are the most common causes, with renal cell carcinoma and angiomyolipoma being the most common malignant and benign neoplasms respectively. Metastatic cancer-associated renal bleeding is very rarely identified. In most cases, bleeding occurs from a renal etiology may be the first manifestation of the disease. Computerized tomography is the best imaging method to establish the diagnosis and in some cases the etiology and is the examination of choice for risk assessment prior to surgical exploration and radical nephrectomy. Angiography and selective renal arterial embolization are emerging as effective modalities, which are often useful in the diagnosis and treatment in the acute phase of the hemorrhage in order to control bleeding.

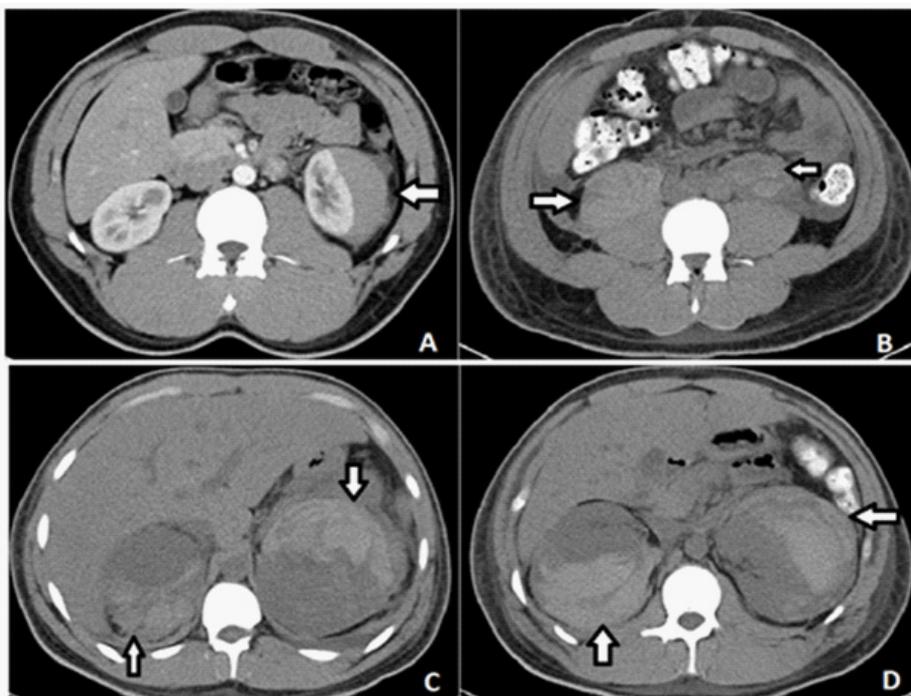
## INTRODUCTION

First described by Wunderlich in 1856, spontaneous, nontraumatic, renal bleeding with hematoma contained in the subcapsular and/or perirenal spaces within the Gerota's fascia could

result in the development of acute renal failure with anuria [1].The clinical features of Wunderlich syndrome (WS) can be varied and nonspecific. The classical manifestations defined as the Lenk's triad present with acute onset of flank pain, palpable tender mass and hemodynamic deterioration due to hypovolemic shock. It can be fatal if not timely recognized and treated promptly [2].

## Etiology

A wide spectrum of neoplastic and noneplastic renal pathologies may result in WS. Seventy percent of WS are due to benign causes, including neoplasm, vascular disease, and infection [3]. Renal neoplasms are the most common cause for WS, with renal cell carcinoma being the most common malignant neoplasm, whereas angiomyolipoma is the most common benign neoplasm. The renal angiomyolipoma and renal cell carcinoma constitute 60%~70% of cases. Other causative conditions of WS include vascular causes, such as vasculitis (polyarteritis nodosa being the most common cause), renal artery aneurysms, arteriovenous malformations and fistulas, and venous thrombosis, as well as non-vascular causes, for example,cystic renal diseases, renal infections, calculus disease, nephritis, and coagulation disorders or clotting dyscrasia [4-5]. Cross-sectional imaging findings help in the detection of the subcapsular, perinephric and/or retroperitoneal hemorrhage and may identify underlying etiology (Figure 1). Angiography may demonstrate contrast blush indicating renal intraparenchy malarterial hemorrhage [5].



**Figure 1:** Computerized tomographic images of the abdomen are showing subcapsular hematoma (A), hemoretroperitoneum (B) and bilateral perirenal hematoma (C and D), as being indicated by arrows.

## Renal cell carcinoma

Spontaneous disruption or hemorrhage of the kidney may rarely occur in renal cell carcinoma as WS. Underlying malignancy may be missed on initial CT scan until occurrence of WS [6-7]. Old age is associated with risk for renal cell carcinoma in the patients with WS [8].

## Angiomyolipoma

Renal angiomyolipoma, a benign mesenchymal tumor composed of smooth muscle cells, blood vessels and fat elements, is associated with a tendency to rupture and sometimes results in massive retroperitoneal hemorrhage. The bleeding tendency is related to the irregular, aneurysmal, tortuous blood vessels that compose the tumor [9-11]. Inferior vena cava fatty thrombus may complicate renal angiomyolipoma [12].

The greatest risks for bleeding are tumor size and grade of the vascular component of the tumor, especially where a diameter more than 4 cm [13]. Small renal angiomyolipomas are asymptomatic and usually require no therapy, although follow-up is recommended in order to follow its growth [14]. Because the patient is stable and the tumor is not malignant, treatment is conservative. Follow-up imaging may reveal the full recovery of kidney function and the resolution of the hematoma [15].

Larger or symptomatic lesions can be electively embolized and/or resected with a partial nephrectomy. WS with retroperitoneal hemorrhage frequently requires emergency embolization, as retroperitoneal bleeding can lead to severe complications and increase morbidity [16]. The hemodynamically stable patients could be conservatively treated with selective transarterial embolization. Nephrectomy is limited for the patients hemodynamically unstable or in case of failed embolization. It might require emergency embolization of the bleeding angiomyolipoma, and elective embolization of a contralateral lesion could be undergone if bilateral angiomyolipomas are detected. Bilateral renal angiomyolipomas are rare and usually associated with tuberous sclerosis, however, a very rare case of bilateral renal angiomyolipomas could occur in an individual without tuberous sclerosis [15, 17].

## Pregnancy-associated

Angiomyolipoma is a rare benign tumor of kidney which demonstrates rapid growth during pregnancy due to hormonal stimulation, most commonly leading to rupture in third trimester or even rarely at 10th week of gestation. The latter had pseudo-aneurysm formation with extra-tumor rupture during pregnancy. The active bleeding could expand to perinephric hematoma during early days of conservative management. Counseling and consent for continuing or aborting the pregnancy is of utmost importance for best possible outcome for patient and fetus [18-19].

## Tuberous sclerosis-associated

Renal angiomyolipoma is a rare benign tumor that can occur sporadically, or in association

with tuberous sclerosis. Angiomyolipomas in tuberous sclerosis are usually bilateral and multicentric in the kidney and liver [20-23].

## Other tumors

Other renal tumors, such as leiomyosarcoma of primary or metastatic origin, Ewing sarcoma and metastatic adenocarcinoma [24-27], may present with features of WS and radical nephrectomy might be urgently performed owing to suspicion of renal cell carcinoma. Renal leiomyosarcomas are the most common histological subtype of renal sarcomas, accounting for approximately 50-60% of the reported cases. These tumors are usually peripherally located and appear to arise from either the renal capsule or smooth muscle tissue in the renal pelvic wall [28].

## CHORIOCARCINOMA SYNDROME

Choriocarcinoma syndrome is known as a lethal complication of tumor hemorrhage at the site of metastasis from mixed germ cell tumor with component of choriocarcinoma [29]. Testicular germ cell tumors represent the most common malignancy among young men with testicular mass. Clinician should also know the signs and symptoms of choriocarcinoma syndrome, characterized by bleeding from metastatic sites, which represents a medical emergency and is associated with high morbidity and mortality [30-31]. Choriocarcinoma is the most aggressive type of germ cell tumor with elevated human chorionic gonadotropin and characteristically metastasizes to the lungs, liver, bone and/or brain [32]. Choriocarcinoma syndrome consists of hemorrhagic manifestations of metastases in germ cell cancer containing choriocarcinoma elements, which usually occurs before and during the onset of systemic treatment with chemotherapy. It should be suspected in patients with hemorrhage in tumor metastases [33]. Spontaneous renal hemorrhage secondary to metastatic choriocarcinoma, a presentation of WS as a component of choriocarcinoma syndrome, is rarely reported [34-35].

## Vasculitis

Vascular causes of WS are infrequent, and the most frequent vasculitis is resulting from polyarteritis nodosa [36-40]. Polyarteritis nodosa is a systemic vasculitis of medium and small-sized arteries associated with aneurysm formation. Multiple microaneurysms could be detected in the kidneys, pancreas, liver and spleen [39]. The renal and superior mesenteric arterial aneurysms secondary to polyarteritis nodosa may be complicated by rupture and hemorrhage as features of WS [41]. The development of WS in a patient with polyarteritis nodosa may be triggered by the influenza infections [39]. Spontaneous bilateral renal hemorrhage as the initial manifestation of polyarteritis nodosa is rare, and it can be associated with delays in diagnosis and treatment [37]. Other vasculitides, such as lupus-related vasculitis, may also present as WS [38]. Vasculitis-related WS could be treated successfully with glucocorticoids and cytotoxic agents without surgical intervention [36]. Prognosis of untreated polyarteritis nodosa is very poor with 13% of 5-year survival rate. Therefore, early recognition of disease and proper treatment with immune suppressors will prevent catastrophic complications and improves survival [42].

## Anticoagulant and end-stage renal disease

Oral anticoagulant therapy has been responsible for a few cases of WS [43-45]. Spontaneous nontraumatic rupture of the kidney is an extremely uncommon condition in patients on hemodialysis, who are predisposed to bleeding diathesis in the setting of platelet dysfunction and endothelial abnormalities [45-49]. Chronic kidney disease, a known cause of coagulopathy, is also associated with WS [50].

## Miscellaneous medical conditions

Urolithiasis, severe hypertension, and jogging could be responsible for a few cases [51-53]. Some patients had no significant medical conditions [54].

## MANAGEMENT

The abdominal CT scan is the most accurate diagnostic method for detection of WS. CT scanning is highly recommended to achieve a definitive diagnosis and to determine the approach to follow, trying to use conservative surgery whenever possible, or treating the disease with open nephrectomy. The management of WS includes a conservative approach in the hemodynamically stable patients and active treatment in the unstable patients. Active treatment includes surgery or angioembolization. Open surgical management is necessary in patients with haemodynamic instability and is the preferred approach in most cases if angioembolization is not available [55, 56].

## Radical nephrectomy

For spontaneous bleeding in the kidney due to rupture with large retroperitoneal hemorrhage or malignant tumors diagnosed on initial CT, with well function of contralateral kidney, radical nephrectomy is usually required [6, 7, 57]. In a retrospective study of 26 patients with 28 events of WS in Korea, twelve patients (46%) underwent exploration and total nephrectomy [8].

## Laparoscopic nephrectomy

Laparoscopic exploration for undergoing radical nephrectomy and partial nephrectomy could achieve results similar to those with open renal exploration.

Nonetheless, renal hemorrhage extending outside of the renal capsule is technically challenging as association with more adhesions than subcapsular renal hemorrhage. Thus a central renal lesion of bleeding is more achievable by laparoscopic nephrectomy [58-60].

## Partial nephrectomy

The nephron sparing surgery with partial nephrectomy is a rather conservative surgery to treat WS. Robotic-assisted laparoscopic partial nephrectomy or with a Da Vinci S is an established minimal access treatment that has been effectively used for a ruptured renal angiomyolipoma [12, 61, 62].

## Selective embolization

There are some scenarios to avoid surgery in the WS when the patient's general conditions are not fully stabilized due to the presence of malignant neoplasm, or if the renal hemorrhages are thought to be benign, and thus embolization may be an appropriately initial modality [63]. Conservative treatment with selective embolization and a periodic follow-up often achieve a successful outcome [2]. Renal angiogram could demonstrate active extravasation of some renal arterial branches. Renal arteriography with embolization is an important therapeutic method to control the bleeding and to avoid surgery. Selected post-embolization image should demonstrate absence of contrast blush with no flow of contrast into the bleeding site of the kidney [64, 65]. But embolization with the intention of delayed surgery may affect the overall resectability of the tumor, as more difficult resection due to adherence in the later stage [6].

The patients with chronic kidney disease or in long-term hemodialysis may have elevated risk of bleeding-related complications, which can also be considered one of the possible risk factors for development of WS. Selective renal arterial embolization is useful and safe for active renal bleeding in most of these cases [66]. Renal angiography not only helps in diagnosis of the underlying cause in select cases but also allows conservative control of active bleeding, like selective pseudoaneurysm embolization, which can avoid unnecessary emergent radical surgery [67].

## Infectious complication

WS with perirenal or subcapsular hematomas might progress into a complication of urosepsis or perinephric abscess if WS is managed conservatively. Repeated imaging and minimally invasive management with timely percutaneous drainage could achieve successful outcome [54].

## CONCLUSION

Wunderlich syndrome (WS) is rare but understanding the variety of disease etiologies will aid in decision making and improve outcomes for patients. A clinically characteristic triad of WS includes acute flank pain, a palpable flank mass and hypovolemic shock. WS could manifest other symptoms or complications with hematuria, urinary tract infections or renal failure. An early diagnosis and timely treatment are important in cases of WS to prevent life-threatening events. The abdominal CT scan is the most accurate diagnostic method for detection of the presence of WS. An early or immediate exploratory surgery is favored in treating WS for patients with hemodynamic instability, which is a surgical emergency. However, the surgical risk increases in patients with renal angiomyolipoma larger than 4cm and during pregnancy. These high risk patients could be conservatively treated with selective transarterial embolization. Open nephrectomy is reserved for the patients hemodynamically unstable or in case of failed embolization.

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