



## Original Contribution

## Spontaneous perirenal hemorrhage (Wunderlich syndrome): An analysis of 28 cases



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## ABSTRACT

**Introduction:** This study aimed to analyze the characteristics, etiology, and treatment of a series of patients with spontaneous perirenal hemorrhage (Wunderlich syndrome [WS]).

**Methods:** We retrospectively reviewed the records of 26 patients hospitalized for WS in a tertiary urological center between 2011 and 2018. All patients were evaluated for perirenal hemorrhage observed on computed tomography (CT) in the emergency department. Clinical variables (age, underlying diseases, symptoms, shock, and hospitalization period), laboratory test results, and radiological and pathological results were reviewed.

**Results:** The series included 28 events from 26 patients with a mean follow-up period of  $20.2 \pm 18.0$  months. Flank pain was most common symptoms (92%). Twelve patients (46%) had visible renal lesions and associated hematoma and 14 only showed perirenal hematoma. In six patients with shock (systolic blood pressure  $< 90$  mm Hg), 2 underwent emergency angioembolization. Twelve patients (46%) underwent exploration and total nephrectomy. In the final diagnosis, 4 cases of renal cell carcinoma, 3 of angiomyolipoma, 4 of simple renal cyst, 2 of acquired cystic kidney disease, 4 of sarcoma or other malignancy, 4 of chronic pyelonephritis, and 5 of idiopathic WS were observed. Patient age was associated with prediction of renal cell carcinoma in the patients with WS.

**Conclusion:** Renal masses are the main cause of WS, and CT is the diagnostic procedure of choice. Old age is a possible risk factor for renal cell carcinoma in etiology of WS. Surgical treatment is preferred in patients diagnosed with renal malignancy and in cases of hemodynamic instability.

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## 1. Introduction

Wunderlich syndrome (WS) is a life-threatening emergency medical condition that refers to a spontaneous nontraumatic bleeding confined to the perinephric space [1]. WS is classically characterized by Lenk's triad: acute flank pain, flank mass, and hypovolemic shock. However, the clinical symptoms vary and are nonspecific [2].

The etiology of WS is varied. The syndrome can result from either renal (tumors, vascular disease, and inflammatory disease) or extrarenal (adrenal disease, abdominal aortic aneurysms, etc.) causes [3]. Many urologists believe that because of the high likelihood of an underlying malignancy, exploratory surgery, or nephrectomy is necessary in patients with WS [3]. However, WS is a very rare condition, and the

cause of the disease, treatment, and disease research process have rarely been published.

Thus, we aimed to investigate the demographics, medical causes, and management of a series of patients diagnosed with WS.

## 2. Materials and methods

This study was approved by the Institutional Review Board of our hospital.

We performed a retrospective review of a series of patients diagnosed with spontaneous retroperitoneal hemorrhage in our department between 2011 and 2018. In all cases, the patients presented with back pain of sudden onset and the diagnosis was based on the results of the computed tomography (CT) performed in the emergency department.

The main criterion to diagnose WS on CT is bleeding in the subcapsular or perirenal space ( $>60$  Hounsfield units [4]).

We analyzed patients' demographic data, past medical history, length of hospital stay, information regarding symptoms and physical examination, laboratory data, imaging studies, and data from pathological studies.

**Abbreviations:** WS, Wunderlich syndrome; CT, computed tomography; HR, hazard ratio; AML, angiomyolipoma; RCC, renal cell carcinoma; ACKD, acquired cystic kidney disease; MRI, magnetic resonance imaging.

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All values are expressed as mean  $\pm$  standard deviation and proportions for continuous and categorical variables, respectively. Multivariate logistic regression analysis was conducted to examine the hazard ratio (HR) and 95% confidence interval of the association between malignancy and variables. SPSS 20.0 software (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. Differences were considered statistically significant if *p*-values were  $<0.05$ .

### 3. Results

The series included 28 events from 26 patients. A patient with tuberous sclerosis complex has 3 events of WS. The study participants included 12 women (46%) and 14 men (54%), with a mean age of  $48.1 \pm 17.8$  years. As regards history of previous disease, 9 (35%) patients had hypertension and 8 (31%) had diabetes mellitus. Six (23%) patients had chronic kidney disease requiring dialysis.

Twenty-four (92%) patients experienced flank pain, which included 8 patients with left-sided pain, 15 with right-sided, and 1 with bilateral pain. Fever was observed in 5 patients (19%).

Microscopic hematuria above 5–9 red blood cells per high-power field was observed in 10 patients, and gross hematuria was observed in 2 patients. Six dialysis patients were unable to undergo urinalysis in the emergency department (Table 1).

On radiologic evaluation, 12 patients (46%) had visible renal lesions and associated hematoma, and 14 showed only perirenal hematoma.

After identifying the underlying cause, all patients with suspected malignancy underwent definitive surgical treatment. Five patients had definitive findings of angiomyolipoma (AML) on CT and did not undergo surgery. One patient showed possible AML or renal cell carcinoma (RCC) according to the radiologist's reading. However, surgical exploration showed renal cyst rupture (Table 2).

In 6 patients with shock (systolic blood pressure  $< 90$  mm Hg), 2 underwent emergency angioembolization. One patient underwent delayed angioembolization for treatment of AML.

Twelve (46%) patients underwent exploration and total nephrectomy. No patient experienced perioperative complications. On

**Table 1**  
Clinical characteristics and laboratory test results of patients with Wunderlich syndrome.

	No. (percentage) Mean $\pm$ SD
Age (y)	48.1 $\pm$ 17.8
Performed exploration or nephrectomy	12 (46%)
Duration from admission to exploration (d)	4.0 $\pm$ 3.0
Performed angioembolization	3 (12%)
Follow-up duration (mo)	20.2 $\pm$ 18.0
Sex	
Male	14 (54%)
Female	12 (46%)
Underlying diseases	
Hypertension	9 (35%)
Diabetes	8 (31%)
Chronic kidney disease (dialysis)	6 (23%)
Tuberous sclerosis	1 (4%)
Symptoms and signs	
Fever	5 (19%)
Flank pain	24 (92%)
Gross hematuria	2 (8%)
Microscopic hematuria ( $>5$ –9/HPF)	10 (39%)
Shock (systolic blood pressure $< 90$ mm Hg)	6 (23%)
Laboratory data	
Hemoglobin	10.5 $\pm$ 2.8
WBC ( $\times 10^3/\mu\text{L}$ , peak level)	11.81 $\pm$ 3.79
ANC ( $\times 10^3/\mu\text{L}$ , peak level)	9.57 $\pm$ 3.61
Platelets	217.7 $\pm$ 76.7
PT (s)	14.0 $\pm$ 1.2
aPTT (s)	35.9 $\pm$ 8.3
CRP (mg/L, peak level)	26.4 $\pm$ 48.2

HPF: high-power field, WBC: white blood cells, ANC: absolute neutrophil count, PT: prothrombin time, aPTT: activated partial thromboplastin time, CRP: C-reactive protein.

**Table 2**  
Radiologic findings of patients with Wunderlich syndrome.

	No. (percentage)
Visible tumor in radiologic study	12 (46%)
Laterality	
Left	5
Right	6
Bilateral	1
Location	
Upper	3
Mid	4
Lower	3
Huge	2
First impression from radiologic study	26
AML	6 (23%)
RCC	5 (19%)
ACKD	2 (8%)
Simple renal cyst	2 (8%)
Sarcoma	1 (4%)
Hematoma or hemorrhage only	10 (38%)

AML: angiomyolipoma, RCC: renal cell carcinoma, ACKD: acquired cystic kidney disease.

pathologic evaluation of 13 patients (12 by exploration and 1 by renal biopsy), pathological studies showed 3 cases of RCC (1 associated with polycystic kidney disease), 2 of simple renal cyst, 1 of acquired cystic kidney disease (ACKD), 2 of sarcoma [5], 1 of lymphoma, 1 of malignant perivascular epithelioid cell tumor, and 3 of chronic pyelonephritis.

In the final diagnosis that synthesized radiologic or pathologic reports, 4 cases of RCC, 3 of AML, 4 of simple renal cyst, 2 of ACKD, 2 of sarcoma, and 4 of chronic pyelonephritis were observed (Table 3).

With a mean follow-up period of  $20.2 \pm 18.0$  months, 4 patients died upon admission due to WS or related renal malignancy, and 1 died due to other reasons. None of the remaining patients experienced recurrence of the treated disease, with the exception of 1 patient with tuberous sclerosis and multiple AMLs.

In the logistic regression analysis of the predictors of RCC and AML, patient age was found to be the only significant predictor (HR = 0.294, *p* = 0.016).

### 4. Discussion

WS is a spontaneous, nontraumatic, subcapsular, perirenal hemorrhage. In 1856, Wunderlich was the first to describe a condition of spontaneous renal bleeding with dissection of blood into the subcapsular and/or perinephric spaces [4]. The classic clinical triad includes unilateral flank pain, general malaise with hypovolemic shock, and a palpable lumbar mass (Lenk's triad) [6]. However, the presence of all three symptoms is uncommon, occurring in only 20% of cases. [7]

A meta-analysis of WS showed that 83% of the patients presented with acute onset of flank pain, 19% had hematuria, and 11% had symptoms and signs of hypovolemic shock [8].

According to our analysis, flank pain was observed in 92% of patients, gross hematuria was observed in 8%, and microscopic hematuria was observed in 39%. Unstable vital signs resulting from shock were present

**Table 3**  
Final diagnosis of patients with Wunderlich syndrome.

	No. (percentage)
RCC	4 (15%)
AML	3 (12%)
Chronic pyelonephritis	4 (15%)
Simple renal cyst	4 (15%)
ACKD	2 (8%)
Idiopathic	5 (19%)
Sarcoma	2 (8%)
PEComa	1 (4%)
Lymphoma	1 (4%)

RCC: renal cell carcinoma, AML: angiomyolipoma, ACKD: acquired cystic kidney disease, PEComa: perivascular epithelioid cell tumor.

in 23% of patients. The reason for such findings is that the hospital in which the study was performed is a tertiary hospital and treats patients with more severe cases.

The etiology of WS is varied, with renal causes being the most common: AML, RCC, renal artery aneurysm, hydronephrosis, or calyceal rupture. Extrarenal causes include pheochromocytoma, adrenal myelolipoma, retroperitoneal tumors, and systemic diseases such as coagulopathies and vasculitis [3]. Zhang et al. [8] reviewed 165 patients with WS between 1985 and 1999. Renal neoplasm was the most common cause of WS, with AML being the most common neoplasm. Although this article is a very important research about the etiology of WS, only a few researches have also extensively studied on the causes of WS.

The results of our examinations were quite similar. Renal neoplasm was the most common cause of WS, observed in 43% of patients. RCC was also discovered in patients with acquired cystic kidney diseases; therefore, in cases in which CT suggests any suspicious findings, a surgical exploration is indicated.

The majority of patients with WS visit the emergency department because of the abrupt onset of flank pain. Ultrasound, CT scan, and magnetic resonance imaging (MRI) can be used to detect bleeding and identify the underlying cause [9]. CT is preferred for the initial imaging workup [10]. This modality is the examination of choice and provides information about the etiology, as well as the severity of the associated disease, demonstrating the presence of perirenal hematoma with a sensitivity of 92%–100% [10,11]. When fat density is observed in the renal parenchyma, the existence of AML may be presumed and conservative treatment implemented [4].

However, the initial CT may miss the presence of RCC in up to 60% of cases [12]. Zagoria et al. [10] revealed that CT combined with MRI allows accurate diagnosis of spontaneous perinephric hemorrhage, but the underlying pathological condition is often undetectable in the acute phase due to the presence of perinephric blood. In addition, in cases in which the mass that caused the bleeding cannot be confirmed, arteriography can be used to diagnose or treat certain patients.

In the current study, 6 patients experienced hypovolemic shock. Among these patients, 5 recovered after receiving conservative hydration therapy and transfusion. However, one patient experienced the stabilization of vital signs following urgent angioembolization, and nephrectomy was therefore performed for RCC [13]. Shock was relatively common finding on WS, however, surgical exploration is not absolutely necessary in all shock cases.

Definitive treatment for WS will depend on the clinical condition and underlying cause of the patient; possible therapeutic options include conservative therapy, angioembolization, nephron-sparing surgery, or radical nephrectomy.

In cases in which AML, the most frequent cause, is clearly observed on CT, patients may be managed with conservative therapy. However, since the initial CT sometimes misses renal masses requiring surgical treatment, close follow-up, and imaging studies are required.

AML occurs more frequently among women than among men [14]. However, in cases when AML was accompanied by WS, gender had no significant predictive value as a risk factor of the disease. In the aspect of risk factor of RCC in WS, patient age was found to be a significant predictor of RCC (HR = 0.294,  $p = 0.016$ ). Since the number of cases in the current study was quite small, these findings must be carefully interpreted. However, these results appear to be significant.

In cases of RCC, the surgical approach is determined based on the preference of the surgeon. However, since port-site metastasis develops following laparoscopic partial nephrectomy in certain patients with WS [15], a retroperitoneal approach is recommended to prevent peritoneal seeding in selected patients.

This study has some limitations. First, it was performed at a single center and included a small sample size. Second, the number of cases in which the final pathology was confirmed through surgical exploration was low (50%). However, in limited cases in which AML was clearly observed on CT or the lesion was unidentified yet the vital signs were stable, patients were managed with conservative therapy and a close follow-up was performed to avoid missing RCC.

Despite these limitations, this study is considered significant as WS is a disease that occurs very infrequently; therefore, the preexisting studies are mostly case reports or small-scale reports based on the data from approximately 10–20 patients. In a recent systematic review of WS [16], only 102 cases were examined in 79 publications; systematic review is insufficient method in studying this syndrome. Therefore, the 28 cases evaluated in this study are highly significant. This study can be used as a reference for future treatment of patients with WS. Further studies performed in other centers and including larger sample sizes will be beneficial.

## 5. Conclusions

Renal masses are the main cause of WS, and CT is the diagnostic procedure of choice. Old age is a possible risk factor of RCC, which is among the etiologic factors of WS. Surgical treatment is preferred in patients with diagnosed renal malignancy and in cases of hemodynamic instability.

## Declarations of interest

The authors declare no competing financial interests.

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