



## Wunderlich syndrome associated with warfarin use

### Síndrome de Wunderlich asociado al uso de Warfarina

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#### SUMMARY

**Introduction:** Wunderlich syndrome is described as spontaneous or non-traumatic renal hemorrhage. It is a rare and frequently fatal condition.

**Objective:** To present a case of Wunderlich syndrome associated with the use of oral anticoagulants.

**Clinical case:** A 77-year-old male patient with a personal history of hypertension, ischemic heart disease and atrial fibrillation treated with warfarin, without adequate

control. He comes to the emergency room with a colicky right lumbar pain that has lasted two days and has radiated to the right flank, iliac fossa and hemiscrotum, associated with hematuria, sweating and chills, with no fever, and marked weakness and general malaise. He denies any history of trauma or other urinary symptoms. Signs of hypovolemia associated with the pain are present.

Complementary tests were indicated, where a retroperitoneal hematoma was found in relation to Wunderlich syndrome. A

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conservative approach was maintained and, as the general condition deteriorated, it was decided to perform emergency surgical treatment, where, when approaching the retroperitoneum area, a perirenal hematoma was found in relation to the lower pole of the right kidney. Right nephrectomy was performed. The histological study did not define an anatomical cause.

**Conclusions:** Wunderlich syndrome is a rare condition, but can be fatal if not treated promptly. Treatment depends on the patient's hemodynamic status.

**Keywords:** oral anticoagulant; nephrectomy; hematuria.

## RESUMEN

**Introducción:** El Síndrome de Wunderlich se describe como la hemorragia renal espontánea o de origen no traumático. Es una entidad poco frecuente y con frecuencia mortal.

**Objetivo:** Presentar un caso de síndrome de Wunderlich asociado al uso de anticoagulantes orales.

**Caso clínico:** Paciente masculino de 77 años de edad, con antecedentes patológicos personales de hipertensión arterial, cardiopatía isquémica y fibrilación auricular tratada con warfarina, sin control adecuado. Acude a cuerpo de guardia por presentar dolor lumbar derecho a tipo cólico, de dos días de evolución con irradiación a flanco,

fosa iliaca y hemiescrotos derechos, asociado a hematuria, sudoraciones y escalofríos, sin constatar fiebre, y marcado decaimiento y malestar general. Niega antecedente de trauma y otros síntomas urinarios. Se constatan signos de hipovolemia asociado al dolor.

Se indican complementarios donde se constata hematoma retroperitoneal en relación con un síndrome de Wunderlich. Se mantuvo una conducta conservadora y al presentar deterioro del estado general se decide realizar tratamiento quirúrgico de urgencia donde, al abordar la zona de retroperitoneo, se constató un hematoma perirrenal en relación con el polo inferior del

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riñón derecho. Se realizó nefrectomía derecha. En el estudio histológico no se definió causa anatómica.

El tratamiento depende del estado hemodinámico del paciente.

**Conclusiones:** El síndrome de Wunderlich es una entidad poco frecuente, pero puede ser mortal si no se trata de manera oportuna.

**Palabras clave:** anticoagulante oral; nefrectomía; hematuria

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## INTRODUCTION

Spontaneous subcapsular or perirenal hemorrhage of non-traumatic etiology is a rare condition that causes a sudden collection of blood in the renal cell. Hemoperitoneum is exceptional. The hemorrhage is self-limited by the resistance of the perirenal tissue. <sup>(1)</sup>

Spontaneous retroperitoneal hemorrhage was subtly described in 1700 by Bonet. In 1856 the German physician Carl August Wunderlich made a detailed description of this condition as an acute spontaneous hemorrhagic vascular disorder of the kidney, with the presence of a hematoma dissecting the subcapsular and perirenal spaces and named it as “spontaneous apoplexy of the renal capsule”. In 1910 Coenen described 13 cases. <sup>(2)</sup>

In 2002, Zhang et al. reported the etiology of spontaneous renal hemorrhage in a meta-analysis of 47 publications in which they collected 165 cases. In 61 % the etiology was neoplastic, 48 (31 %) patients had angiomyolipoma, renal cell carcinoma was found in 43 (30 %), renal vascular diseases in 28 (17 %) and other diverse causes such as: infections, periarteritis nodosa, use of anticoagulants or antiplatelet agents in 15 % and in 7 % of the cases studied the etiology was idiopathic. Murad reported that angioliopomas larger than 4 cm have a 25 % chance of presenting as Wunderlich syndrome. <sup>(2)</sup>

The literature reports 300 cases worldwide, most of which are reports of isolated cases diagnosed by urologists; rarely by emergency services, almost always they are patients treated for malignant

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neoplasms of renal cells that are complicated or debut as a non-traumatic spontaneous renal hemorrhage. The presence of hemoperitoneum is exceptional because the hemorrhage is limited by the resistance of the perirenal tissue. <sup>(2)</sup>

Two articles have been published in Cuba presenting three cases of this pathology, both related to tumoral causes. <sup>(3, 4)</sup> The aim of this paper is to present a case of Wunderlich syndrome associated with the use of oral anticoagulants.

## CLINICAL CASE

77-year-old male patient with a history of high blood pressure, ischemic heart disease, and atrial fibrillation treated with warfarin (without regular INR monitoring). He came to the emergency room with a crampy right lower back pain that had been developing for two days and was radiating to the flank, iliac fossa, and right hemiscrotum, associated with total light red hematuria without clots, nausea, sweating, chills (without fever), asthenia, and general malaise. He denied a history of trauma or other urinary symptoms. He was admitted to the Internal Medicine emergency service and the following tests were performed:

Leukogram: 12, 9 x 10<sup>9</sup>/L

Neutrophils: 75, 6

Hb: 11, 9 g/dl

Hematocrit: 34, 9 %

Platelets: 179 x 10<sup>9</sup>/L

INR: 8

Blood glucose: 14, 2 mmol/L

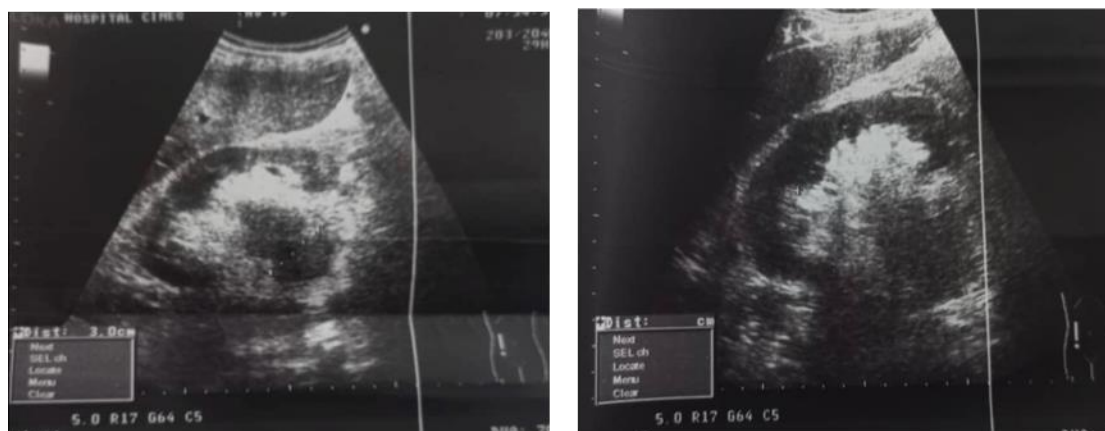
**Abdominal ultrasound (Figure 1):** enlarged, heterogeneous right kidney with increased echogenicity of its parenchyma. A poorly defined, heterogeneous hypoechoic image is observed towards the middle part, which appears to be related to the 3.0 cm dilated renal pelvis, with dense content inside, without visible cause.

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**Fig. 1.** Abdominal ultrasound

Given the suspicion of renal colic of obstructive cause, the decision was made to consult the Urology department. The physical examination revealed: fascia and gait of a sick, sweaty patient; hypocolored skin and mucous membranes, heart rate: 77 bpm; BP: 100/60 mm/Hg; FR: 23 bpm S02: 96 %.

His abdomen presented visible volume increase in the right flank, iliac fossa and lumbar fossa region, with pain on palpation of these areas and a hematoma of approximately 4 cm in diameter in the right flank region, with a purplish-greenish color (although the patient denied a history of trauma at that level). Figure 2



**Fig. 2.** Hematoma in the right flank region. Grey Turner sign

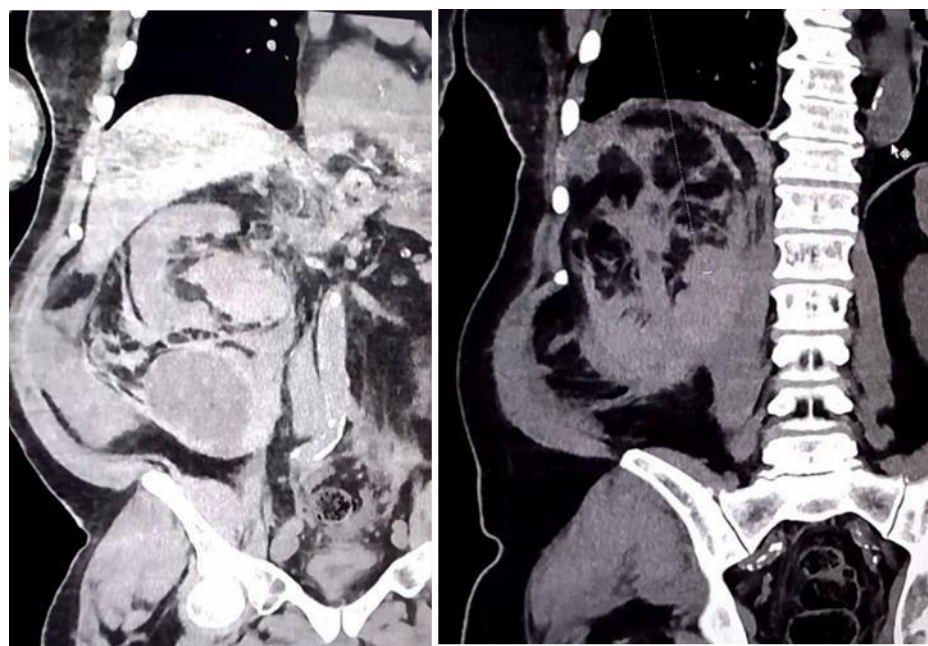
A simple CT scan of the abdomen was performed, which showed a retroperitoneal hematoma in relation to the lower pole of the left kidney and hypodense images in the renal pelvis that seemed to be related to the hematoma, and at that level they described a secondary level of <http://revcimeq.sld.cu/index.php/imq> [revinmedquir@infomed.sld.cu](mailto:revinmedquir@infomed.sld.cu)

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erythrocyte sedimentation with variable density around 21 HU. Thickening of the perirenal peritoneum and a small pleural effusion on that side were also observed. Figure 3



**Fig. 3.** Computed axial tomography of the abdomen, coronal section

The patient was admitted with a diagnosis of retroperitoneal hematoma and suspected Wunderlich syndrome. Conservative treatment was initially indicated:

- Absolute rest.
- Hydration and transfusion of fresh plasma.
- Administration of vitamin K and antibiotics.

Despite having them prescribed, during the night the patient did not take his antihypertensive medications and presented BP figures of 170/100 mmHg, with deterioration of the general condition, which motivated the change in therapeutic behavior.

The following preoperative tests were performed urgently: hemoglobin 5 g/dl; hematocrit: 15 %, INR: 5. The patient's INR was stabilized and a radical right nephrectomy was performed by laparotomy. Figure 4

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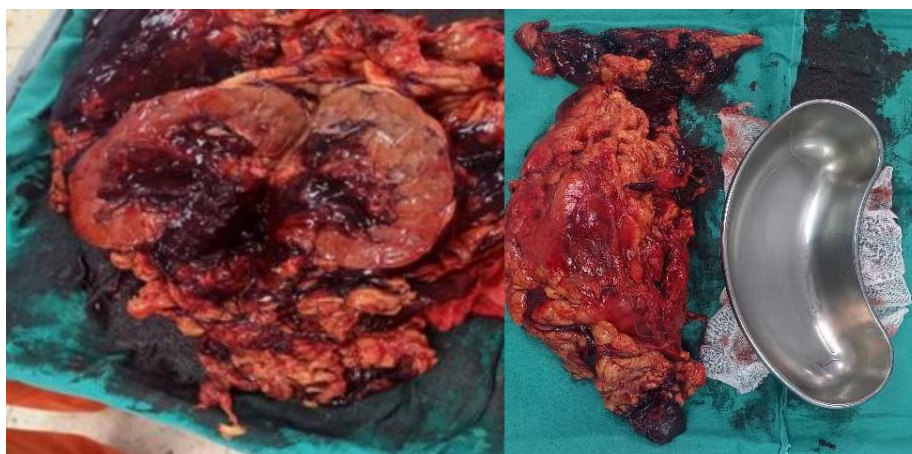
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During surgery, a retroperitoneal hematoma was found in close relation to the lower pole of the right kidney, the latter being enlarged. Approximately 3500 ml of blood was aspirated and the organ was removed. Compromise of the perirenal fat and the excretory system was evident. Hemostasis was performed and the organ was closed in layers.

The histological study did not corroborate tumor, or another anatomical cause of spontaneous rupture, so it was concluded that it was Wunderlich syndrome, related to warfarin without adequate control.



**Fig. 4.**Kidney removed

The patient had a six-day stay in the intensive care unit, it was necessary to improve therenal function and ventilatory mechanics (he had a medium-sized right pleural effusion). 1000 ml of red blood cells and 500 ml of plasma were transfused to replace the lost volume, and the hemoglobin level was raised to 10 g/dl.

Thenor being transferred to the operating room, he presented septicemia as a postoperative complication and required antibiotic treatment, with favorable evolution. He was discharged after 22 days, with follow-up by outpatient clinic.

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## COMMENTS

The spontaneous perirenal or subcapsular renal hemorrhage of non-traumatic cause (Wunderlich syndrome) is defined as a rare but potentially fatal condition. Approximately 300 cases are reported in the literature consulted. In Cuba, the authors found two publications of cases associated with this disease. <sup>(3, 4)</sup>

The origin is varied, 50 % of cases present as a tumoral disease (adenocarcinoma followed by angiomyolipoma). Other less frequent causes are: hydronephrosis, blood dyscrasias, treatment with anticoagulants, systemic diseases or rupture of renal cysts. <sup>(5)</sup>

In the patient who presented, there was no evidence of any other risk factor for the disease, except for the uncontrolled use of oral anticoagulants, since the patient presented with an open INR due to the continued use of warfarin. The anatomopathological study confirmed that there was no anatomical cause, so it was concluded that it was a spontaneous retroperitoneal hematoma (Wunderlich syndrome) associated with the use of oral anticoagulants. This entity has an incidence of approximately 15 % of the total reported cases.

In clinical practice, Wunderlich syndrome can present in various forms: from nonspecific low back pain to acute surgical abdomen. Lenk's triad is present in only 20 % of cases and includes intense lumbar or flank pain, hypovolemic shock and palpable retroperitoneal tumor. <sup>(6)</sup>

Diagnosis can be difficult and is based on clinical signs and symptoms, additional examinations (ultrasound, computed axial tomography and arteriography). The imaging technique that best helps to define the diagnosis and etiology of this syndrome is computed axial tomography. <sup>(7)</sup>

Therapeutic options are surgery or therapeutic embolization; however, in cases where no signs of malignancy are detected on CT scan, nor active bleeding on arteriography, conservative treatment with follow-up and imaging tests every three months may be indicated. <sup>(7)</sup>

It is suggested that the initial treatment in cases of retroperitoneal hematoma be conservative whenever the patient's condition allows it, but it has been shown that in the case of

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hemodynamic instability, surgical treatment becomes the fundamental pillar and radical nephrectomy is performed.<sup>(1, 2)</sup>

Nephrectomy can be performed through a laparotomy incision, especially in those patients who maintain hemodynamic instability or who present a decrease in hemoglobin and hematocrit levels in a short period of time. In recent decades, with the development of minimally invasive techniques, other ways have been incorporated for performing the procedure, such as laparoscopic nephrectomy and robot-assisted nephrectomy, with the disadvantage that well-trained personnel are needed in these procedures, as well as the instruments to perform them.<sup>(4)</sup> In untreated cases, mortality is 100 %, especially when surgical treatment is not performed; while in patients who undergo surgery, mortality is reduced to 40-50 %.<sup>(3)</sup>

Conservative treatment should be the initial approach in these cases, provided the patient's hemodynamic status allows it. Otherwise, surgical treatment is required, which almost always consists of performing radical nephrectomy.

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### Conflicts of interest

The authors report no conflicts of interest.

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