

# Wunderlich syndrome as a rare complication of polyarteritis nodosa: a case report

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## SUMMARY

Spontaneous subcapsular and perirenal hemorrhage, known as Wunderlich syndrome (WS), is a rare clinical manifestation of polyarteritis nodosa (PAN). We report a case of a 48-year-old male with a history of recurrent episodes of leg muscle tenderness and dysesthesia, bilateral flank pain, painful nodular skin lesions in the lower limbs, weight loss, and difficult-to-control arterial hypertension. The abdominopelvic computed tomography angiography showed a large left perirenal hematoma, leading to the patient's admission to the intensive care unit. After the exclusion of infectious or neoplastic foci, the patient was diagnosed with PAN and started intravenous methylprednisolone pulses with a good response. Since WS is a rare initial clinical manifestation of PAN, an early diagnosis and aggressive treatment will significantly improve clinical outcomes.

**Key words:** Wunderlich syndrome, polyarteritis nodosa, spontaneous perirenal hematoma, retroperitoneal hemorrhage, computed tomography.

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## INTRODUCTION

Polyarteritis nodosa (PAN) is a rare form of necrotizing systemic vasculitis that primarily affects medium-sized vessels and is characterized by a broad spectrum of clinical presentations (1). Thus, a high level of suspicion is needed for its diagnosis. Renal involvement is the most common complication of PAN and usually presents with arterial hypertension, hematuria, proteinuria, and renal insufficiency (2). Spontaneous subcapsular and perirenal hemorrhage, known as Wunderlich syndrome (WS), is rare in PAN, and its diagnosis can be confused with acute pyelonephritis or trauma, resulting in delayed diagnosis and treatment. Thus, a case of WS in PAN is being reported for its rarity and complexity of diagnosis.

## CASE REPORT

A 48-year-old male smoker (27 pack-years) presented with a history of recurrent epi-

sodes of leg muscle tenderness and dysesthesia, bilateral flank pain, painful nodular skin lesions in the lower limbs, and weight loss of 10 kg with 1 year of evolution. Furthermore, the patient reported a recent onset of difficult-to-control arterial hypertension, despite being treated with perindopril, indapamide, and amlodipine. On several visits to the emergency department, he was diagnosed with acute pyelonephritis. In the last visit, the patient additionally reported abdominal and chest pain with refractory hypertension. There were no arthralgias, fever, mucocutaneous changes, respiratory, or genitourinary manifestations. At physical examination, the patient was pale, hypertensive (252/145 mmHg), and presented with a diffusely distended abdomen that was painful during deep palpation. On investigation, he had hypochromic microcytic anemia [hemoglobin (Hb) 7.5 g/dL], elevation of C-reactive protein [(CRP) 120 mg/L], erythrocyte sedimentation rate (105

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**Table I** - Laboratory findings before and after high-dose corticosteroid therapy.

Laboratory findings	Before treatment	After treatment	Reference range
Hemoglobin (g/dL)	7.5	12.9	13.0-18.0
WBCs ( $\times 10^9/L$ )	11.8	24.0	4.0-11.0
Platelets ( $\times 10^9/L$ )	491	254	150-400
ESR (mm/1 <sup>st</sup> hour)	107	3	0-15
Albumin (g/L)	30.8	33.3	38-51
AST (U/L)	48	31	10-37
ALT (U/L)	57	62	10-37
GGT (U/L)	31	50	10-49
ALP (U/L)	63	66	30-120
Creatinine (mg/dL)	1.5	1.6	0.67-1.17
Urea	57	63	10-50
CRP (mg/L)	120	2.2	<3

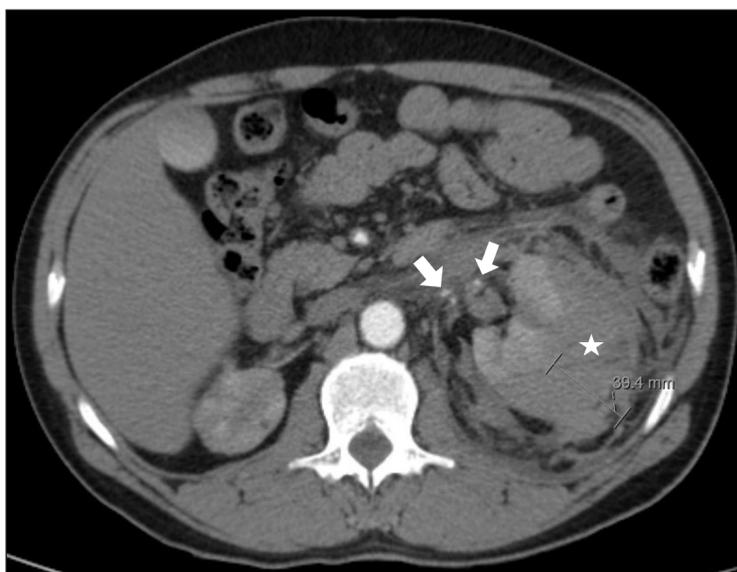
WBCs, white blood cells; ESR, erythrocyte sedimentation rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT,  $\gamma$ -glutamyl transferase; ALP, alkaline phosphatase; CRP, C-reactive protein.

mm/first hour), and creatinine 1.5 mg/dL (Table I). An abdominopelvic computed tomography angiography (CTA) showed a large left perirenal hematoma with a small active hemorrhagic focus and images suggestive of pseudoaneurysms measuring 6 mm with no image of neoplasm or infectious focus (Figure 1).

The patient was admitted to the intensive

care unit and received a transfusion of one unit of packed red blood cells. An arteriography, after 24 hours, documented an irregularity in the contours of the renal artery without evident active hemorrhage foci. After hemodynamic stabilization, he was referred to the urology service, where he completed seven days of antibiotic therapy with ceftriaxone.

However, due to the persistence of pain complaints, high blood pressure being difficult to control, and persistent elevation of inflammatory parameters with no infectious or neoplastic foci, the patient was transferred to the rheumatology service for further study. In our service, the patient remained with mild pain and controlled blood pressure with amlodipine, metoprolol, and lisinopril. The laboratory analysis revealed stabilization of Hb (9.7 g/dL) and a persistent elevation of CRP (100 mg/L) and creatinine (1.7 mg/dL). Platelets, hepatic parameters, and muscle enzymes were normal. The 24-hour urine collection revealed mild proteinuria (0.46 mg/24 hours). Further evaluation revealed normal protein electrophoresis and complement; negative serologies for hepatitis B, hepatitis C, and human immunodeficiency virus; and negative blood and urine cultures. Rheumatoid factor, antinuclear antibodies, extractable nuclear antigen antibodies, and antineuro-

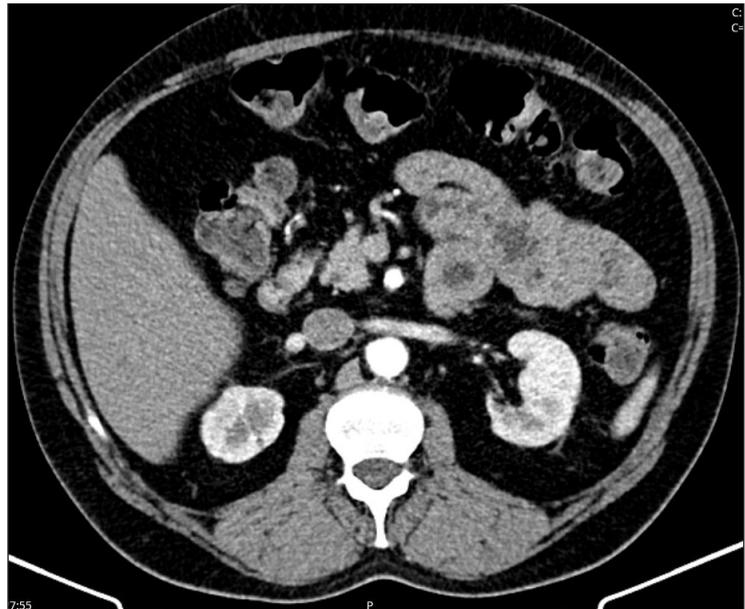


**Figure 1** - Abdominopelvic computed tomography angiography showing a large left perirenal hematoma with a small active hemorrhagic focus (asterisk) and images suggestive of pseudoaneurysms (arrows).

phil cytoplasmic antibodies were negative. The lower limb electromyogram was normal. A lower limb biopsy of the soleus nerve and muscle showed muscle with unspecific changes in the neurogenic profile. Excluding neoplasia and infection according to the American College of Rheumatology (ACR) criteria (3), the patient was classified with PAN and started intravenous methylprednisolone pulses (1000 mg/day for three days). By the second cycle of methylprednisolone, the clinical and analytical (complete blood count and inflammatory parameters) improvement was significant (Table I). After discharge, the patient was referred to the outpatient department of rheumatology with prednisolone 0.5 mg/kg/day and started monthly intravenous doses of cyclophosphamide (0.6 g/m<sup>2</sup>) with gradual and analytical improvement. The CTA reassessment reported a significant reduction in the size of peri-renal hematoma, with no active hemorrhage (Figure 2).

## DISCUSSION

Firstly described in 1856 by Carl Wunderlich, WS is a rare life-threatening condition characterized by acute non-traumatic subcapsular and perirenal hematomas (4). The classic clinical features of WS, represented by Lenk's triad, include acute flank pain, a palpable flank mass, and hypovolemic shock (5). This triad is clearly not manifested in this patient; however, it is crucial to note that the diagnostic sensitivity is low. Neoplasms, specifically renal angiomyolipoma and renal cell carcinoma, constitute the predominant underlying pathology in up to 60% of cases. CTA is the preferred imaging method with a sensitivity of 100% for detecting perirenal hemorrhage and identifying neoplasms as well as pathological changes in surrounding tissues (6). In our case, abdominopelvic CTA confirmed the diagnosis, showing a large left perirenal hematoma with an active hemorrhagic focus with no underlying neoplasia, which is the more common etiology. The second CTA reassessment reported a significant reduction in the size of the hematoma, with no active hemorrhage. Indeed, non-invasive



**Figure 2** - Abdominopelvic computed tomography angiography reassessment showing a significant reduction in the size of peri-renal hematoma, with no evidence of active hemorrhage.

techniques, namely CTA or magnetic resonance angiography, are becoming increasingly important for the diagnosis and evaluation of the response to the treatment of PAN. In this case, angiography was performed because it eventually could reveal vascular lesions not seen on CTA. A renal biopsy was not performed due to its hemorrhagic risk.

A spontaneous subcapsular and perirenal hemorrhage usually requires an urgent arterial embolization, and in severe cases, surgical intervention may be necessary. In our patient, an arteriography conducted after 24 hours revealed that the retroperitoneal hemorrhage ceased spontaneously. The subsequent treatment options depend on the etiology of WS. The most common etiologies of WS are renal neoplasms, with angiomyolipoma being the primary cause, followed by renal cell carcinoma (7). Vascular diseases were the second most important cause, with PAN accounting for 17% of cases (6).

PAN is a rare form of necrotizing systemic vasculitis that typically affects medium and small arteries. The true prevalence is unknown, though previous research reported that its incidence rises with age, with a peak

in the fifth decade and a slight male predominance. Most cases of PAN are idiopathic; however, secondary causes have been described, such as hepatitis B and hepatitis C infections, malignancies, and connective tissue diseases.

PAN had a broad spectrum of nonspecific clinical manifestations, namely systemic symptoms and multiorgan involvement, with the kidneys and skin being the most common organs involved. Vascular manifestations, such as aneurysms of the visceral arteries and thrombosis associated with rupture and hemorrhage, may occur. The inflammatory parameters are elevated; however, there is no specific diagnostic test for the diagnosis of PAN, and it is not associated with antineutrophil cytoplasmic antibodies.

This patient was classified with PAN according to the ACR criteria, with a sensitivity of 82% and a specificity of 87% (six criteria): tenderness of leg muscles; loss of body weight over 4 kg; development of diastolic hypertension (145 mmHg); elevation of creatinine (1.7 mg/dL); neuropathy (lower limb biopsy showed muscle with changes in the neurogenic profile); and abdominopelvic CTA showed images suggestive of pseudoaneurysms. Pseudoaneurysms are usually associated with vascular injuries, and PAN is a vasculitis that affects medium-sized arteries. While the formation of true aneurysms is a more prominent feature of PAN, in severe cases, especially when there is significant involvement of blood vessels, vascular complications such as pseudoaneurysms are rarely described (8). In the context of PAN, these complications can occur when chronic inflammation affects the integrity of the arterial wall. It is important to note that PAN can have a variety of clinical manifestations, and the severity and extent of vascular complications can vary.

The treatment for PAN varies based on the severity of the disease. In cases of active, severe disease presenting with renal insufficiency or symptomatic aneurysms, as in this case, the induction treatment should be pulse intravenous or high-dose oral glucocorticoid therapy with cyclophosphamide.

The optimal duration of glucocorticoid therapy is not well established; however, longer tapering is recommended. Due to its toxicity, cyclophosphamide therapy should generally be limited to three/six months per course. Once disease remission has been achieved, immune modulators such as azathioprine or methotrexate are recommended (9). Untreated PAN has a poor prognosis. Nevertheless, an early diagnosis and aggressive treatment of PAN will significantly improve survival from 13% to 80% at five years of follow-up (10).

## ■ CONCLUSIONS

WS in PAN is a rare life-threatening complication whose diagnosis can be a complex challenge. Thus, a high index of clinical suspicion is needed to obtain an early and accurate diagnosis, thereby preventing serious complications.

## Contributions

All the authors made a substantial intellectual contribution, read and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

## Conflict of interest

The authors declare that they have no competing interests, and all authors confirm accuracy.

## Ethics approval and consent to participate:

Not applicable.

## Patient consent for publication

Obtained.

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## Availability of data and materials

All data are available from the corresponding author upon request.

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