Acta Biomed 2023; Vol. 94, N. 3: e2023073 DOI: 10.23750/abm.v94i3.14087

Case report

Hypovolemic shock due to Wunderlich syndrome (spontaneous renal haemorrhage): a case report and literature review

Andrea Vercelli[1], Laura Pagani[1*], Konstantinos Christodoulakis[2], Gennaro Marcello[2], Marcello Petrini[3], Emanuele Michieletti[3], Chiara Celaschi[4], Gianfranco Cervellin[5], Erika Poggiali[1]*

[1] Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy; [2] Urology Unit, Guglielmo da Saliceto Hospital, Piacenza, Italy; [3] Radiology Unit, Department of Radiological Functions, Guglielmo da Saliceto Hospital, Piacenza, Italy; [4] Anatomical Pathology Unit, Guglielmo da Saliceto Hospital, Piacenza, Italy; [5] Academy of Emergency Medicine and Care, Pavia, Italy. * the authors equally contributed to this work.

Abstract. Wunderlich syndrome (WS) or spontaneous renal haemorrhage is a rare and life-threatening condition often leading to haemorrhagic shock. WS is characterized by an acute onset of non-traumatic subcapsular and perirenal haematoma formation due to several causes, including neoplasms, cystic rupture, vasculitis, coagulopathies, and infections. The classical presentation includes acute flank or abdominal pain, a palpable flank mass and hypovolemic shock (Lenk's triad). Nausea, vomiting, fever, and haematuria can also be present. Computed tomography angiography is mandatory to localize the source of haemorrhage. Super-selective embolization can be performed to stop bleeding, while surgery is reserved to haemodynamic unstable patients and neoplastic cases. We describe a case of WS in a 79-year-old male patient, who rapidly developed hypovolemic shock requiring urgent nephrectomy. (www.actabiomedica.it)

Key words: Wunderlich syndrome, Lenk's triad, flank pain, renal haemorrhage, haemorrhagic shock, hypovolemic shock, acute renal injury

Introduction

Wunderlich syndrome (WS) is a rare life-threatening condition defined as a spontaneous, atraumatic, subcapsular, perirenal haemorrhage (1), that can rapidly cause hypovolemic shock and death (2). The classical presentation is the Lenk's triad, that includes sudden-onset flank pain, a palpable flank mass and hypovolemic shock (3), even if most of the patients complain of non-specific symptoms, such as nausea, vomiting and fever. Haematuria represents a fickle feature (4). The most common causes of WS are renal angiomyolipoma and renal cell carcinoma (5). Some cases can be due to vascular diseases, infections, coagulopathies, and cyst rupture, or remain idiopathic (6). We present a case of WS in a 79-year-old male patient, who rapidly developed hypovolemic shock requiring urgent total nephrectomy.

Case Report

A 79-year-old man presented to our emergency department complaining of sudden-onset severe right-sided flank pain radiated to mid back and associated with hypotension (90/50 mmHg) and vomiting. No history of trauma was reported. His past medical

history was unremarkable. His medications included cardioaspirin (100 mg day) in primary prevention, and citalopram for depression. On presentation he was apyretic, pale with dry mucous membranes, and confused. Blood pressure was 60/40 mmHg, heart rate 68 beat/minute, peripheral oxygen saturation 94% while breathing in room ambient air. His abdomen was distended and painful in the right flank and right lower abdominal quadrant on palpation. Point-of-care ultrasound (POCUS) displayed normal abdominal aorta diameter, inferior vena cava collapse with normal cardiac ejection fraction, no pericardial and/or pleural effusion, no free abdominal fluid. The right kidney could not be correctly displayed.

Table 1 shows the laboratory results. Blood count documented a slight normochromic normocytic anaemia (Hb 12.4 g/dL, MCV 96 fL, MCH 31.4 pg) with increased leukocytes (15.600/mm^3) and normal C-reactive protein and procalcitonin. D-dimer and troponin I were elevated (6172 ng/mL and 34.8 pg/mL, respectively). Serum creatinine and blood urea nitrogen resulted slightly increased (1.27 mg/dL and 51 mg/dL) with normal electrolytes. Liver function, creatine-kinase, lactate dehydrogenase and coagulation time were all in the normal range. A RT-PCR nasopharyngeal swab for SARS CoV2 was negative. Arterial blood gas analysis showed increased lactates (12 mmol/L, normal value 0-10) with normal pH (7.44).

A urine catheter was placed excluding gross haematuria. Supportive therapy, including crystalloids (1000 cc i.v.) and two units of packed red blood cells (PRBC), was immediately administered in the emergency room. The patient underwent a full-body contrast-enhanced computed tomography (CT), that excluded an aortic dissection and revealed a laceration in the inferior pole of the right kidney for about 17 mm, with a coarse subcapsular haematoma (5 x 3 cm) extended in the retroperitoneum till the right iliac fossa (Figure 1), that presented arterial spillage of contrast medium, which increased in the venous phase (Figure 2). The left kidney was normal with multiple small stones in the upper and lower middle calyx groups and a further stone (7 x 3 mm) at the third distal of the ureter, without hydronephrosis. The chest CT scan excluded pneumoniae or tumors. As such, a diagnosis of WS was done. In presence of

Table 1. Patient's laboratory findings at admission, after surgery and at discharge.

	At admission	After surgery	At discharge
WBC (4-10 x 10^9/L)	**15.6**	8.1	4.7
Neutrophil Count (2-8 x 10^9/L)	**13.8**	6.2	2.8
RBC (4.3-5.7 x 10^6/L)	**3.95**	**2.95**	**3.30**
Hb (13.2-17.3 g/dL)	**12.4**	**8.9**	**10.0**
Hct (39-49%)	**37.9**	**27.6**	**29.2**
MCV (82-98 fL)	96	93.6	88.5
MCH (27-32 pg)	31.4	30.2	30.3
PLT Count (150-450 x 10^9/L)	183	155	154
D-dimer (0-500 ng/mL)	**6172**	ND	ND
HS Troponin (< 20 pg/mL)	**34.8**	ND	ND
Creatinine (0.6-1.2 mg/dL)	**1.27**	**2.78**	**1.26**
BUN (10-50 mg/dL)	**51**	**107**	**73**
Potassium (3.5-5.0 mEq/L)	4.0	3.7	4.5
Sodium (135-146 mEq/L)	141	144	139
CK (0-172 U/L)	128	101	ND
LDH (0-248 U/L)	231	186	ND
C-reactive protein (< 0.5 mg/dL)	0.49	**19.7**	0.5
PCT (< 0.5 ng/mL)	0.3	0.4	0.03

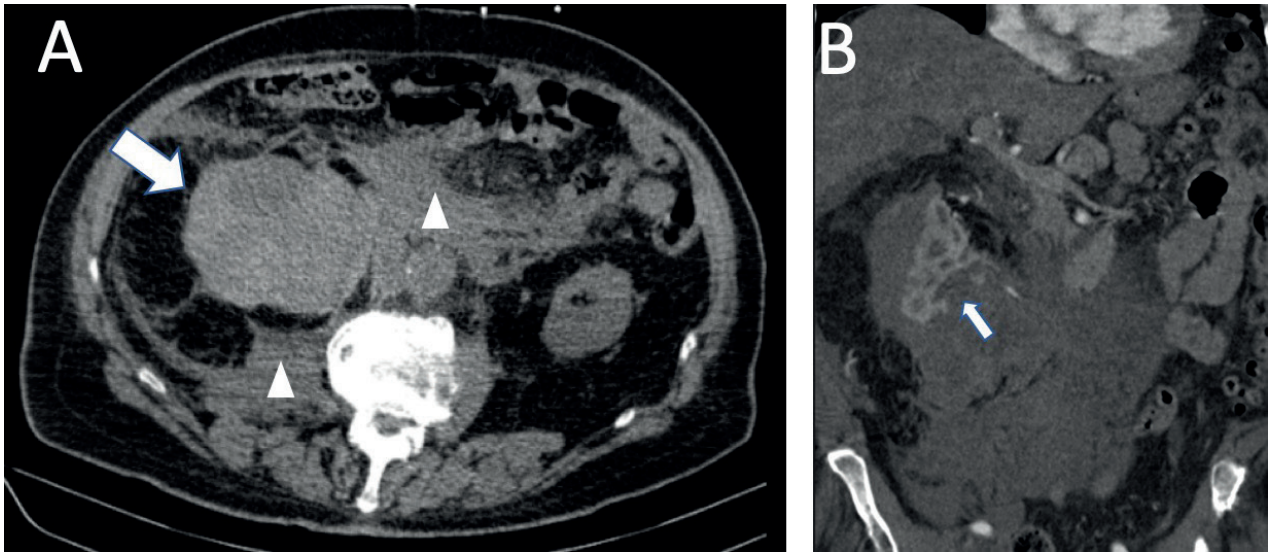

Figure 1. CT non-contrast image of a large subcapsular right renal haematoma (arrow in A) extending into the retroperitoneal space (arrowheads) with a large parenchymal laceration showed in the venous phase in the coronal multiplanar reconstruction (arrow in B).

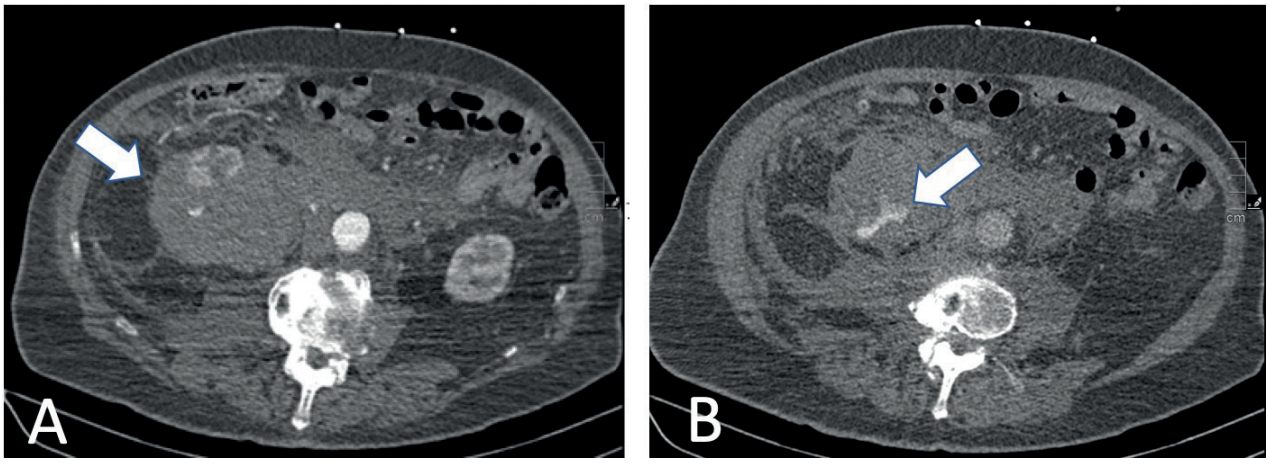

Figure 2. Contrast CT showing the large subcapsular right renal haematoma with blush of contrast in the arterial phase (arrow in A), increasing in the venous phase (arrow in B), consistent with active bleeding.

active bleeding and haemodynamic instability, a right total nephrectomy was immediately performed. After surgery, his haemoglobin dropped from 12.4 g/dL to 8.9 g/dL, and creatinine increased from 1.27 mg/dL to 2.78 mg/dL with normal electrolytes, that ameliorated with i.v. hydration and 1 unit of PRBC. The histopathological examination ruled out neoplasms and reported numerous simple cysts (maximum diameter 0.8 cm) and multiple papillary adenomas (maximum diameter 0.6 cm) with chronic inflammation of the renal parenchyma. Post-operatory evolution was complicated by a COVID-19 pneumonia with respiratory failure requiring low-flow oxygen (4 L/min by nasal cannula) and oral steroid therapy for 14 days (methylprednisolone 16 mg once daily). Oral iron supplementation (ferrous sulphate iron 325 mg one tablet daily) and erythropoietin (5000 U sc twice per week) were administered for the treatment of anaemia and renal failure. The patient was discharged after 25 days of hospitalization in good clinical condition, with no need of oxygen, and a stage 3 chronic renal failure. A nephrological and urological follow-up was planned.

WBC, white blood cells; RBC, red blood cells; Hb, haemoglobin; Hct, haematocrit; MCV, mean cell volume; MCH, mean cell haemoglobin; PLT, HS, high-sensitive; BUN, blood urea nitrogen; CK, creatine-kinase; LDH, lactate dehydrogenase; PCT, procalcitonin. Normal range values are in brackets, altered values in bold. ND, not done.

Discussion

Spontaneous renal haematoma was first described by Théophile Bonet in his "*Sepulchretum, sive anatomia pratica ex cadaveribus morbo denatis*" (1679), and later classified as a syndrome by Carl Reinhold August Wunderlich in 1856. Since the first description, an increasing number of cases have been reported in literature, but still today WS represents a challenge for the emergency physicians for its insidious clinical presentation and the lack of treatment guidelines. Early recognition and diagnosis of WS are crucial to avoid fatal complications, including death and multiple organ failure, and to establish a proper management, which significantly reduces the mortality rate.

Neoplasms including renal angiomyolipoma (AML) and renal cell carcinoma (RCC) are the most common cause of WS up to 60 - 65% of cases (1) followed by vascular diseases such as polyarteritis nodosa, renal artery aneurysms, and pseudoaneurysms (20 - 30%) (5, 7). AMLs are the commonest benign neoplasms liable for WS, clinically asymptomatic in most cases, even if the bigger ones (> 4 cm) could be at high risk of bleeding (8). RCC represents the most common malignant etiology of WS, causing up to 30 - 35% of cases of WS. Old age is a possible risk factor for renal cell carcinoma causing WS (9). Other neoplasms that can cause WS include metastases, sarcomas, adenomas, oncocytomas, and transitional cell carcinomas (6).

Uncommon causes are hydronephrosis and cystic rupture (5 - 10%) (10), being the infections even rarer (11), including renal abscesses, acute pyelonephritis, emphysematous pyelonephritis, and xanthogranulomatous pyelonephritis. Two cases of WS have been reported in COVID19 patients (12, 13). Other rare causes of WS include haematological disorders, such as haemophilia and blood dyscrasias, anticoagulation therapy, and post-puerperal status (9). Only a case of WS following a Russell's viper bite has been reported in a 22-year-old Indian male (14). Some cases remain idiopathic or unknown, probably due to rupture of small cysts or small extrarenal vessel, infection, inflammation or passed calculi (15). High risk pre-existing clinical conditions for WS are haemodialysis, diabetes mellitus, hypertension, end-stage renal disease, history of urinary tract infections, especially pyelonephritis, and renal cystic disease (6).

The diagnosis can be difficult due to the broad spectrum of clinical manifestations, and the suspicious of WS must always be confirmed by imaging. The clinical presentation can widely vary, depending on the amount of the bleeding. The classical Lenk's triad is present in only 20% of cases (9); 83% of the patients have acute flank or abdominal pain, 19% present with haematuria (gross or microscopic), and 11% have hypovolemic shock (16).

Prognosis depends on the prompt diagnosis since spontaneous retroperitoneal haemorrhage is a lethal condition when not timely detected (17). The differential diagnosis includes rupture of an abdominal aortic aneurysm, visceral aneurysms, or other visceral bleeding. Some cases may be misdiagnosed as renal colic.

POCUS is often the initial imaging, especially in the emergency department, but findings have to be confirmed with contrast-enhanced CT, that represents the gold standard technique when WS or a retroperitoneal haemorrhage is suspected (18). Emergent abdominal CT scan is mandatory if the patient presents haemodynamic instability with hypotension to identify the cause of haemorrhage and active bleeding (4), revealing the presence of perirenal haematoma with a sensitivity of 92 – 100% (9).

The management of WS can be very difficult, particularly in anticoagulated patients since very few cases have been reported in literature (19-22). Treatment depends on the clinical condition of the patient, considering the presence of active bleeding as well as the patient's haemodynamic status (9). In haemodynamically stable patients, treatment is conservative and based on early volume resuscitation with intravenous fluids and blood transfusion, immediate reversal of anticoagulation, pain control and antibiotics, associated

with serial POCUS and/or abdomen CT scan used for follow-up (23). When active extravasation is detected on imaging, angiography and selective embolization are the preferred approach to stop acute and potential life-threatening haemorrhage and preserve the renal parenchyma (1, 24, 25), while partial or radical nephrectomy should be reserved for neoplastic causes or refractory bleeding, due to its high morbidity and mortality (9, 26). In our case, WS could be associated with the spontaneous rupture of renal cysts. Our patient required emergency surgical intervention because of his haemodynamic instability, and he had a favourable post-operative outcome.

Conclusions

WS represents a real challenge for the emergency clinicians, requiring a prompt diagnosis and treatment to avoid a fatal outcome. Haemodynamic instability until hypovolemic shock render WS a life-threatening condition. Our case highlights the importance of a timely diagnosis and treatment to improve patient outcome.

Contributions: AV and LP collected details of the case and drafted the manuscript. LP, KC, GM, MP, EM and CC cared for the patient. GC and EP critically revised the manuscript. All authors approved the final version and stated the integrity of the whole work.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Funding: This work was not supported by any grant.

Availability of data and materials: All data underlying the findings are fully available.

Ethics approval and consent to participate: As this was a descriptive case report and data was collected without patient identifiers, ethics approval was not required under our hospital's Institutional Review Board guidelines.

References

1. Katabathina VS, Katre R, Prasad SR, Surabhi VR, Shanbhogue AK, Sunnapwar A. Wunderlich syndrome: cross-sectional imaging review. J Comput Assist Tomogr 2011;35(4):425-433. doi: 10.1097/RCT.0b013e3182203c5e.
2. Medda M, Picozzi SC, Bozzini G, Carmignani L. Wunderlich's syndrome and hemorrhagic shock. J Emerg Trauma Shock 2009;2(3):203-205. doi: 10.4103/0974-2700.55346.
3. Lenk R. Uber Massenblutungen in das Nirenlager. Dtsch Zeits Chir. 1909;102:222.
4. Parmar N, Langdon J, Kaliannan K, Mathur M, Guo Y, Mahalingam S. Wunderlich Syndrome: Wonder What It Is. Curr Probl Diagn Radiol 2022;51(2):270-281. doi: 10.1067/j.cpradiol.2020.12.002.
5. Zhang JQ, Fielding JR, Zou KH. Etiology of spontaneous perirenal hemorrhage: a meta-analysis. J Urol 2002; 167(4): 1593-1596. doi:10.1097/00005392-200204000-00006.
6. Albi G, del Campo L, Tagarro D. Wunderlich's syndrome: causes, diagnosis and radiological management. Clin Radiol 2002;57(9):840-845.
7. Chung R, Chawla A, Peh WC. Clinics in diagnostic imaging (178). Wunderlich syndrome and pseudoaneurysm. Singapore Med J 2017;58(6):289-293. doi:10.11622/smedj.2017049.
8. Ramirez-Limon DA, Gonzaga-Carlos N, Angulo-Lozano JC, Miranda-Symes O, Virgen-Gutierrez F. Wunderlich Syndrome Associated With Angiomyolipomas. Cureus 2022;14(4):e23861. doi:10.7759/cureus.23861.
9. Kim JW, Kim JY, Ahn ST, et al. Spontaneous perirenal hemorrhage (Wunderlich syndrome): An analysis of 28 cases. Am J Emerg Med 2019;37(1):45-47. doi:10.1016/j.ajem.2018.04.045.
10. Mariolis-Sapsakos T, Nannou E, Angelis S, Filippou D. Wunderlich Syndrome: Spontaneous Cystic Rupture on Account of Acquired Kidney Atrophy. Cureus 2022;14(10):e30386. doi:10.7759/cureus.30386.
11. García-Chairez LR, Montelongo-Rodríguez FA, Moreno-Arquieta IA, Ayala MM, Gutierrez-González A. Unusual Presentation of Wunderlich Syndrome. Ochsner J 2022; 22(3):273-276. doi:10.31486/toj.21.0120.
12. Prawira M, Pramod SV, Wijayanti Z. Wunderlich syndrome in a COVID-19 patient with poor outcome. Urol Case Rep 2022;45:102267. doi:10.1016/j.eucr.2022.102267.
13. Presicce F, Martini M, Minisola F, Falavolti C, Filianoti A. Wunderlich syndrome, an unexpected urological complication in a patient with coronavirus disease 2019 (COVID-19): A case report. Curr Urol 2022;16(2):74-76. doi:10.1097/CU9.0000000000000100.
14. Senthilkumaran S, Miller SW, Williams HF, et al. Development of Wunderlich syndrome following a Russell's viper bite. Toxicon 2022;215:11-16. doi:10.1016/j.toxicon.2022.06.004.
15. Simkins A, Maiti A, Cherian SV. Wunderlich Syndrome. Am J Med 2017;130(5):e217-e218. doi:10.1016/j.amjmed.

2016.11.031.
16. Dhanapal V, Ramachandran R, Radhan P, Vivekanandan B, Jeevanandham B, Jacob P. The many facets of Wunderlich syndrome: A multidetector computed tomography based review. Int J Contemp Med 2019;41:A88–A93.
17. Kaleta F, Sankhyan P, Sahebazamani M. Wunderlich syndrome: a case of hypovolemic hemorrhagic shock. Chest 2020;158 (4 Supplement):A1024. doi: 10.1016/j.chest.2020.08.951.
18. Baishya RK, Dhawan DR, Sabnis RB, Desai MR. Spontaneous subcapsular renal hematoma: A case report and review of literature. Urol Ann 2011; 3(1): 44-46. 10.4103/0974-7796.75852.
19. Mabjeesh NJ, Matzkin H. Spontaneous subcapsular renal hematoma secondary to anticoagulant therapy. J Urol 2001;165(4):1201.
20. Ferrando F, Budía A, Mira Y, Vayá A, Aznar J. Spontaneous renal subcapsular hematoma in an anticoagulated patient. Clin Appl Thromb Hemost 2006;12(1):89-92.
21. Giovini M, Poggiali E, Zocchi P, Bianchi E, Antonucci E, Barbera M. A Case of Spontaneous Renal Haemorrhage (Wunderlich Syndrome) in an Anticoagulated Patient. Eur J Case Rep Intern Med 2022;9(4):003269. Published 2022 Apr 1. doi:10.12890/2022_003269.
22. Maltês S, Carvalho Gouveia C, Serrazina F, Rebelo M. Life-Threatening Wunderlich Syndrome Associated with Apixaban and the Complexity of Anticoagulation Management in Bleeding Patients: A Case Report [published online ahead of print, 2022 Jul 8]. Acta Med Port 2022;10.20344/amp.16941. doi:10.20344/amp.16941.
23. Chan YC, Morales JP, Reidy JF, Taylor PR. Management of spontaneous and iatrogenic retroperitoneal haemorrhage: conservative management, endovascular intervention or open surgery? Int J Clin Pract 2008;62(10):1604-13.
24. Paparella MT, Eusebi L, Gangai I, Bartelli F, Guglielmi G. Wunderlich syndrome: a rare case in a young woman. Acta Biomed 2021;92(S1):e2021113. Published 2021 Oct 6. doi:10.23750/abm.v92iS1.11185.
25. Jain V, Ganpule A, Vyas J, et al. Management of non-neoplastic renal hemorrhage by transarterial embolization. Urology 2009;74(3):522-526. doi:10.1016/j.urology.2008.11.062.
26. Ahn T, Roberts MJ, Navaratnam A, Chung E, Wood S. Changing etiology and management patterns for spontaneous renal hemorrhage: a systematic review of contemporary series. Int Urol Nephrol 2017; 49(11):1897-1905.

Correspondence:
Received: 28 November 2022
Accepted: 28 December 2022
Erika Poggiali, M.D.
Emergency Department, Guglielmo da Saliceto Hospital, Via Taverna 49, Piacenza, Italy
e-mail: poggiali.erika@gmail.com