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A RARE CAUSE OF SPONTANEOUS PERIRENAL HEMORRHAGE: REVISITING WUNDERLICH SYNDROME.

CAUSA RARA DE HEMORRAGIA PERIRRENAL ESPONTÁNEA: REVISIÓN DEL SÍNDROME DE WUNDERLICH.

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ABSTRACT
Wunderlich syndrome (WS),defined as spontaneousnon-traumatic renal or perirenal hemorrhage is a rare but potentially life-threatening condition first described by Carl Reinhold August Wunderlich in 1856. The common underlying causes include Primary renal neoplasms, vascular lesions, and coagulopathies. Contrast-enhanced computed tomography (CT) remains the standard imaging modality forclinical evaluation and histopathologic examination confirms the underlying etiology, informinglong-term management and prognostication. Therapeutic options include conservative management, selective arterial embolization, and surgery depending on hemodynamic stability and underlying cause with minimally invasive interventions becoming the standard of care. Integrating radiologic, surgical, and histopathologic insights is crucial for timely diagnosis and optimal outcomes.This case report adds to the body of literature on this rare clinical entity and highlights clinicopathological features, etiologic mechanisms, diagnostic approaches, and management strategies of WS in a patient with a left adrenal mass.

RESUMEN
El síndrome de Wunderlich (SW), definido como hemorragia renal o perirrenal espontánea no traumática, es una entidad poco frecuente pero potencialmente mortal descrita por primera vezpor Carl Reinhold August Wunderlich en 1856. Las causassubyacentesmáshabitualesincluyenneoplasiasrenalesprimarias, lesiones vasculares y coagulopatías. La tomografía computarizada (TC) con contraste continúa siendo la técnica de imagen de referencia para la evaluación clínica, mientras que el estudio histopatológico confirma la etiología y orienta el manejo y el pronóstico a largo plazo.

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Las opciones terapéuticas comprenden manejo conservador, embolización arterial selectiva y tratamiento quirúrgico, según la estabilidad hemodinámica y la causa de base, con técnicas mínimamente invasivas que se han convertido en el estándar de atención. La integración de los hallazgos radiológicos, quirúrgicos e histopatológicos es esencial para un diagnóstico oportuno y resultados óptimos. Este caso contribuye a la literatura sobre esta infrecuente entidad clínica y subraya las características clínico-patológicas, los mecanismos etiológicos, las estrategias diagnósticas y las opciones de tratamiento del SW en un paciente con una masa suprarrenal izquierda.

Keywords: Wunderlich syndrome (WS), Peri-renal hemorrhage, Angiomyelolipoma (AML), renalcell carcinoma (RCC), Computed Tomography (CT).

Palabras clave:Síndrome de Wunderlich (SW), hemorragiaperirrenal, angiomiolipoma (AML), carcinoma de célulasrenales (CCR), tomografíacomputarizada (TC)

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INTRODUCTION

Wunderlich syndrome (WS), also known as spontaneous renal hemorrhage, is defined as bleeding into the subcapsular or perirenal space without antecedent trauma.[1]It presents as a medical emergency with significant diagnostic and therapeutic challenges that bridge multiple specialties, including and not limited to urology, radiology, and pathology.[2] The syndrome most frequently arises secondary to solid renal masses including renal angiomyolipoma (AML) and renal cell carcinoma (RCC), but can also occur in patients with coagulopathies, vascular disease and adrenal tumors.[3,4]

Angiomyolipoma, a benign mesenchymal tumor composed of smooth muscle, fat, and dysmorphic vessels, accounts for nearly half of all WS cases.[5]Thedelicate vessels in AML lack elastic tissue, rendering them susceptible to aneurysmal dilation and rupture.[6] In contrast, RCC-related hemorrhage typically results from tumor necrosis, vascular invasion, or fragile neovascularization.[7] Other pathophysiological mechanisms involved in the emergence of WS may include cyst rupture, vasculitis and hypertensive vascular injury.[8] Idiopathic WS, though rare, may reflect microvascular fragility or unrecognized cystic pathology within the Kidneys.Rare cases have been seen in pregnancy however the underlying cause was attributed to AML.[9]

The common presentation in WS is acute flank pain, a palpable mass, and hypovolemic shock—a triad known as Lenk's triad, which classically occurs in less than 20% of cases.[10]Owing to the rarity of the disease, a diagnosis can be missed even in patient's presenting with features of the classical triad.[11] This underscores the need for a high index of suspicion of WS and standardized robust diagnostic algorithms for WS which currently do not exist.

Imaging via CT scan is a highly accurate first choice method for identifying and localizing renal and perirenal hemorrhage however an underlying etiology may not always be identified on imaging alone. CT scan imaging is also useful in guiding percutaneous drainage of the hematoma and follow-up examinations, providing details on the evolution of the hematoma. Typical CT findings in WS vary with the stage of the hematoma and include avascular isoechoic to hyperechoic fluid collections in the acute bleeding or hypoechoic to anechoic fluid collections with septations and heterogeneity in the subacute and chronic hematomas. Color Doppler ultrasound Scan is an affordable option for the identification of active bleeding while magnetic Resonance Imaging (MRI) can differentiate subacute hematomas from neoplastic lesions. CT scan may also identify a well-defined lipid rich mass in AML or an enhancing tumor mass with calcification in RCC. While CT scan is the preferred imaging modality, US scan and MRI are also useful and multimodality evaluation is often superior in comparison to single modality imaging [12,13]

Because radiological assessment does not always provide diagnostic information and clinical lesions may share overlapping imaging characteristics, Histopathologic confirmation is essential, especially where there is high suspicion for malignancy. The diagnostic material may be a large surgical resection of affected organs or identified masses but where minimally invasive clinical interventions are opted, TRU-CUT biopsies can be utilized reliably in specific situations.[14,15]

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Histopathological analysis remains indispensable for accurately identifying the cause of WS, by providing essential information about the nature of any underlying lesions and differentiating benign from malignant causes. In AML, histological sections demonstrate triphasic morphology comprising smooth muscle bundles, mature adipose tissue, and thick-walled vessels lacking elastic lamina.[16] Immunohistochemically, AML cells express HMB-45 and Melan-A, distinguishing them from RCC. RCC-associated WS exhibits malignant epithelial cells with cytoplasmic clearing or granular eosinophilia, often with necrosis and hemorrhage.[17]RCC variants may contain hemosiderin-laden macrophages and areas of cystic degeneration.

In rare instances, retroperitoneal hemorrhage arises from adrenal tumors or cysts which have ruptured and elicit secondary tissue changes.[18] However only a few of these cases have been classified as WS arising from primary adrenal lesions.[3,19]

Management of WS is not standardized and largely depends on hemodynamic stability of the patient, extent of hemorrhage, and underlying etiology. Conservative treatment is reserved for stable patients with small, self-limiting hematomas.[5,11] Selective arterial embolization has emerged as the preferred first-line intervention for ongoing hemorrhage, achieving hemostasis while preserving renal function.[20] Surgery, such as partial or radical nephrectomy, is indicated when embolization fails or where malignancy is suspected. Prognosis largely depends on the underlying cause; AML-related WS generally carries an excellent prognosis, whereas RCC-related cases have variable outcomes. A recent series reported survival rates exceeding 90% with appropriate multidisciplinary management.[5]

CASE

We present a case of a 66-year-old male who presented with postprandial abdominal heaviness and symptoms of reflux esophagitis. The patient volunteered history of being a former smoker, with 41 pack years. He reported a history of tonsillectomy in childhood and was only using atorvastatin at the time of presentation with no prior or recent use of anticoagulants. There was no history of any known allergies or trauma reported by the patient.

Abdominal CT ***(Figure 1)***showed a left adrenal mass measuring slightly over 7cm in widest diameter, with some internal areas of calcification. Adjacent to this mass was a small old retroperitoneal hematoma. The rest of the abdominal organs were normal on imaging.

On examination he had a soft and depressible abdomen with tender hepatomegaly noted.
He was admitted urgently due to abdominal pain, perspiration, and mild coldness of the extremities. He underwent surgery a few hours later for what was clinically diagnosed as an adrenal tumor. The patient was stable post-operatively and did not require any further intervention. We followed him up for 2 months.

The macroscopic details of the resected specimen are seen in***Figure 2.***The histopathology description follows in ***Figure 3.***

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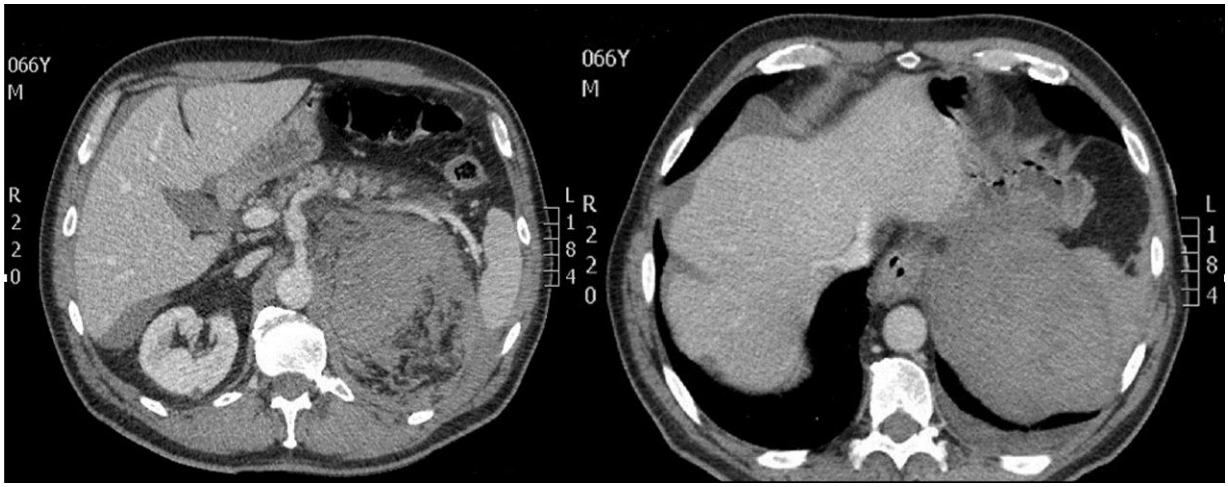

FIGURE 1. Left adrenal mass measuring approximately 7.2 x 6.3cm with internal calcification.
Adjacent to this mass superiorly is a higher density area likely corresponding to a residual encapsulated hematoma, measuring 8cm in its greatest axis in contact with the spleen.
No free intraperitoneal fluid observed. Liver, gall-bladder, biliary tract, Kidneys, Pancreas and Spleen show no significant findings.

FIGURE-2. The specimen submitted for histopathology was an irregular cystic-solid mass of tissue measuring 62 x 57 x 49mm with a total weight of 52g and rubbery in consistency. The surface was variegated with yellow-brown areas distinct from normal fat. The cavity of the mass was formed by a

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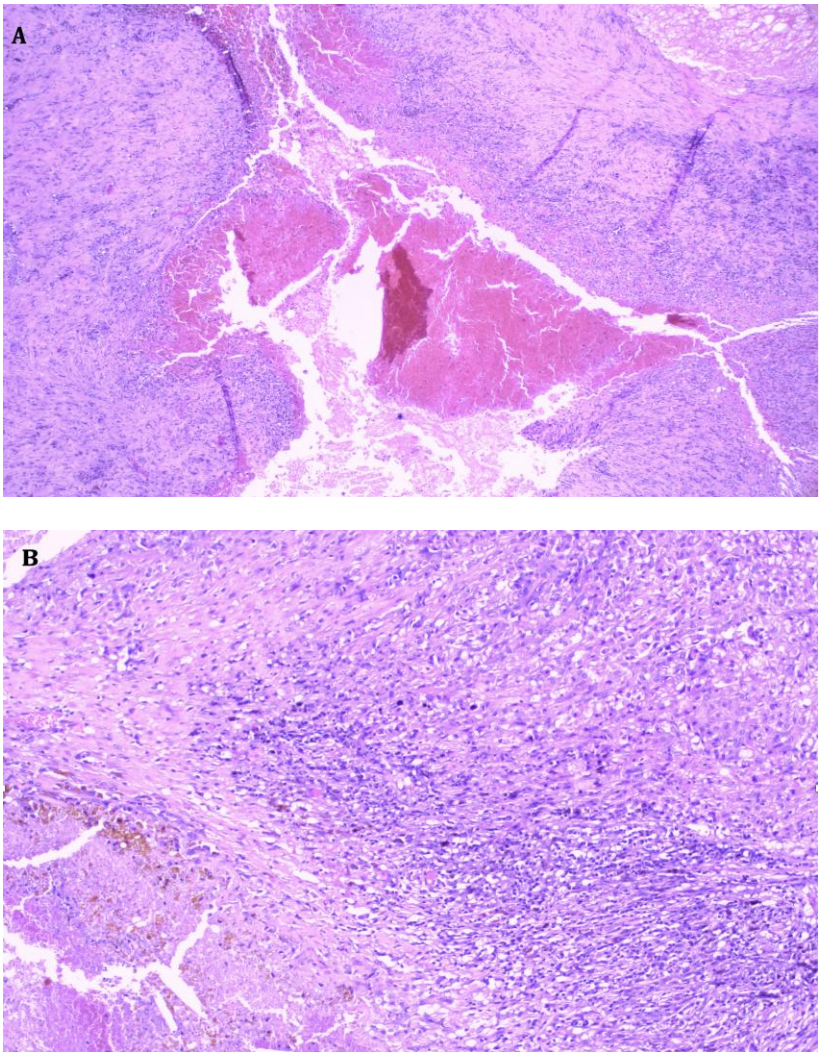
large hematoma with a prominent tract identified along the area with the probe. No single neoplastic nodule was identified.



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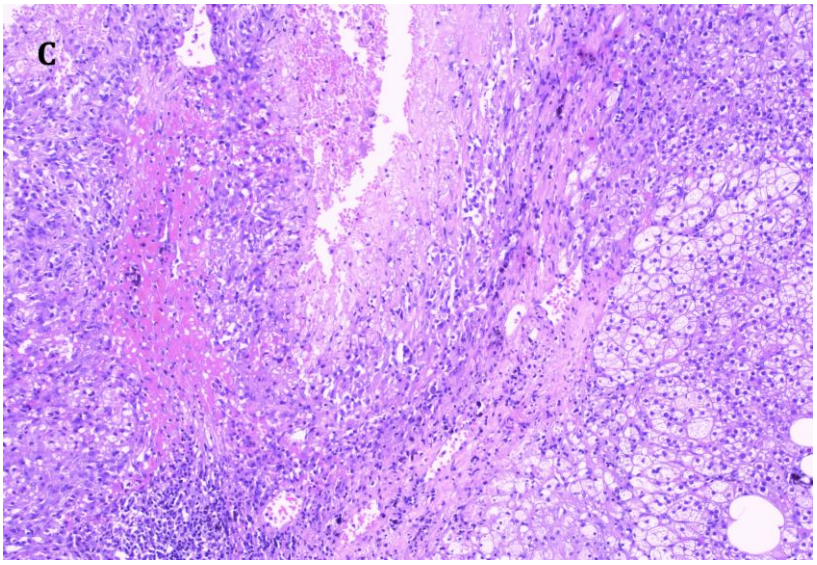

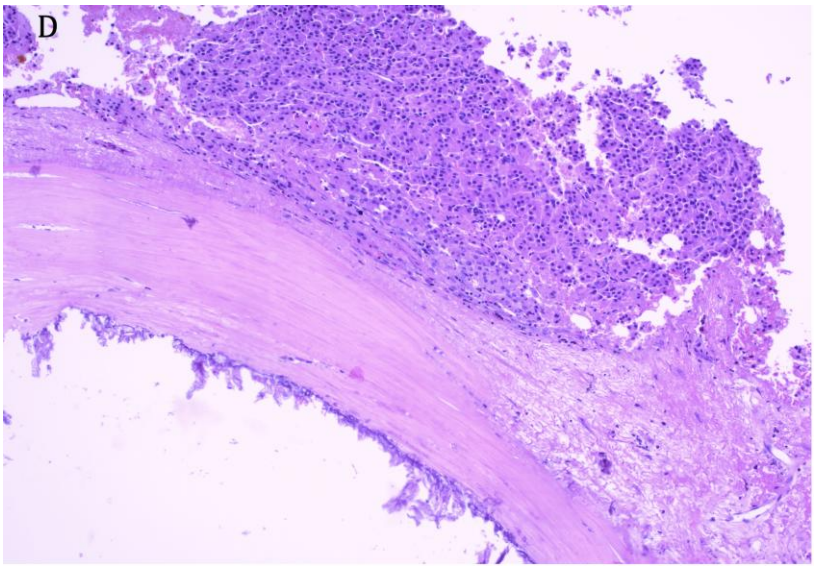

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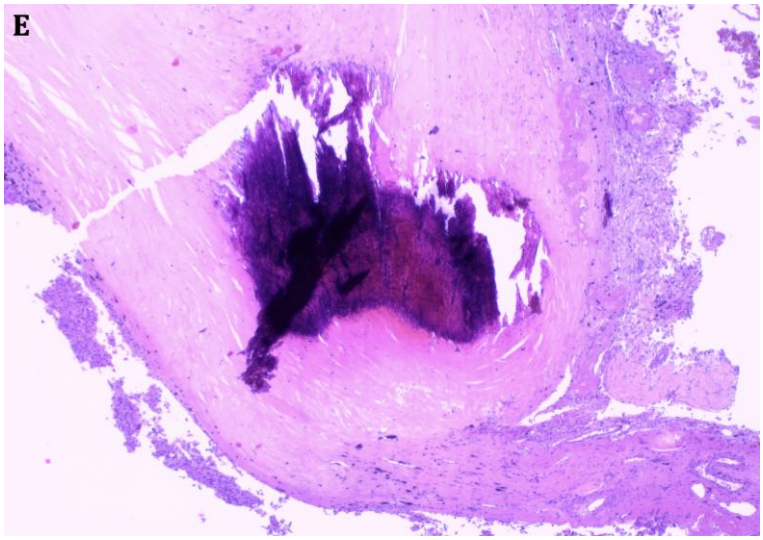

FIGURE 3. Histopathology (A, B, C, D, E)
Histopathology evaluation of the mass showed an adrenal gland with extensive architectural distortion and large central cystic cavity with no epithelial or endothelial lining. (A). Granulation tissue with pigmented histiocytes layered the inner surface of the cystic. Except in the areas of rupture, a thick sclerotic reactive fibrous capsule walled off this cavity contained blood, inflammatory cells, cholesterol cleft (B). The inflammation and hemorrhage extended beyond the adrenal gland into perirenal soft tissue. The adrenal gland showed nodular sclerosis within which entrapped adrenocortical cells were seen. Numerous organizing hematomas were also identified within an ecstatic vascular network. No neoplastic process-bening or malignant, primary or metastatic was seen (C, D, E

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DISCUSSION

As with many other reported cases in the literature, our patient, a middle aged male, presented with hemodynamic instability that required emergency surgical intervention.[1] Hypovolemic shock forms a critical component of the Lenk's triad, a classical presentation of WS which also includes flank pain and a palpable abdominal mass. Our patient did not present with all the features of this triad however this is not unusual and similar cases have been reported by other writers.[10]

Imaging with contrast-enhanced CT scan accurately diagnosed perirenal hemorrhage and the extent of bleeding, although the exact diagnosis of the radiographically confirmed adrenal mass remained a question to be addressed by diagnostic histopathology.

Following initial clinical and imaging assessment, a neoplastic etiology was highly suspected, in keeping with the wider evidence supporting neoplasms as that main cause of peri-renal hemorrhage.[21]Microscopic evaluation however revealed a benign complicated hemorrhagic adrenal mass that had ruptured and induced an extensive tissue response with disruption of the normal architecture of the left adrenal gland and involvement of the perirenal soft tissues.

Considerably fewer cases of adrenal masses have been reported by some as extremely rare causes of perirenal hemorrhage. Among these, myelolipomas and pseudocysts have been the more commonly identified causes of WS, highlighting adrenal lesions as pathologies warranting further investigation and appropriate documentation in the work-up of WS.[3,19,22]

The patient did not develop any immediate or long-term complications following surgery and has had a good prognosis post-operatively which is a commonly reported outcome in patients with Wunderlich syndrome who receive accurate immediate clinical attention.

Over the years since the 1800's, nearly1000 cases of Wunderlich syndrome have been reported to-date.[8]Ourunderstanding of WS has evolved substantially with increasing recognition that causes other than renal masses are of similar clinical significance and multidisciplinary approaches offer superior outcomes in the management of this rare clinical emergency.[23]

Hemodynamic instability requiring urgent intervention has been cited as a common presentation among patients with Wunderlich syndrome and the acute presentation in our patient was no different.[24,25]

While AML is the most common etiology, followed by RCC and renal cysts, cases arising from adrenal masses are of equal clinical significance and remain scant in the literature.[18]This underscores the need for accurate documentation of findings in each case presenting as atraumatic spontaneous subcapsular or perirenal space hemorrhage.

From a clinical diagnostic perspective, CT scan remains an indispensable imaging modality for rapid and accurate evaluation of bleeding, however tissue confirmation ensures accurate

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etiologic classification and prevents misdiagnosis.[12]

Histopathology is central to diagnostic confirmation ofthe presence and nature of neoplastic and non-neoplastic diagnostic entities and distinguishing benign and malignant disease processes, information which is extremely helpful in guiding clinical decision making.[20]

WS exemplifies the importance of clinicopathological correlation in acute adrenal conditions emphasizing the significance of timely and accurate diagnosis which is pivotal to any further treatments following immediate emergency care. Interventional radiology has transformed WS management by reducing nephrectomy rates and improving outcomes with minimally invasive techniques.[1,10]

Areas of future research should include comparative epidemiological data, standardized diagnostic and management algorithms, risk stratification for all causes of WS, histopathological correlates and long-term outcomes following minimally invasive interventions.

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CONCLUSION

Wunderlich syndrome remains a rare and significant entity at the intersection of radiology, urology, and pathology. While renal masses remain the main cause, vasculopathies, coagulopathies and adrenal masses are also important etiologies. CT is still the preferred method for evaluation of perirenal hemorrhage even though its sensitivity for detection of underlying etiology is low. Histopathologic evaluation not only identifies the underlying cause but also directs patient management and prognostication by providing a definite diagnosis. Multidisciplinary collaboration ensures holistic and focused patient management which improves patient outcomes tremendously. Case registries integrating clinical, imaging, and histopathological data should include adrenal etiologies in Wunderlich Syndrome which will be valuable resources that will refine evidence-based clinical practice guidelines.

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