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Wunderlich Syndrome - misdiagnosed mystery: Introduction and case report

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ABSTRACT

Introduction: Wunderlich syndrome is a spontaneous, nontraumatic, and rare subcapsular perinephric hematoma. Since 2013, only about 280 cases have been reported. The main symptoms suggestive of this syndrome are flank or lumbar pain, flank mass, hypovolemic shock. Some patients also experience massive hematuria. Yet, not only the acute symptoms indicate the risks associated with this syndrome. **Methodology:** This case report was conducted by searching for current papers on PubMed and Google Scholar using the search phrases (Wunderlich Syndrome) AND (Angiomyolipoma) AND (Nephrectomy). After eliminating duplicates, we appraised all publications using the titles and abstracts. Following an exact revision of complete manuscripts, 25 articles met the inclusion criteria. The research took place in April 2024. **The Aim:** This work shows how serious complications can occur in people with Wunderlich syndrome and the diagnostic problems. **Case Report:** This work presents a 70-year-old patient with low blood pressure and severe abdominal pain. **Results:** WS is characterized by flank or lumbar pain, flank mass, hypovolemic shock. The diagnosis is based on CT scans and intra-surgical evaluation. **Conclusions:** WS is a rare disease, causes symptoms of severe abdominal pain and internal bleeding. The key to correct diagnosis of the syndrome is imaging tests and surgical intervention. In this case, computed tomography scan and emergency nephrectomy were used to save the patient.

Keywords: Kidney, tumor, urology, wunderlich, emergency medicine, angiomyolipoma, AML.

1. INTRODUCTION

Some patients with long-lasting complaints have been misdiagnosed for other urinary tract conditions, for example kidney stones or urinary tract infections, before admission to the emergency room (Catarino-Santos et al., 2017). Angiomyolipoma is the most common benign tumor responsible for WS (Wunderlich Syndrome), while renal cell carcinoma is the most common malignant tumor. Other causes resulting in spontaneous kidney rupture include vascular causes - polyarteritis nodosa, renal artery aneurysms, arteriovenous malformations and fistulas, venous thrombosis, cystic renal diseases, nephritis, renal infections, calculus disease or coagulation disorders (Aquilina et al., 2023).

Nonmalignant tumors referring to WS are AML, hamartomas or choristomas either being an isolated tumor or a component of the TCS (Tuberous Sclerosis Complex), whereas among malignant kidney tumors connected to WS renal cell carcinoma is indicated as the most common cause (Kapoor et al., 2016). AML as an isolated lesion in 80% of cases is found among women in 4th and 5th decade, yet AML associated with TCS is indicated more often than solitary tumor (Burgueño et al., 2020). In case of AML being a component of TCS, the statistics indicate women as individuals with insignificantly higher chances of disease development. AML is also a part of TCS also referred to as Bourneville-Pringle Syndrome. It is a genetic disorder occurring in 1:10 000 - 1:20 000 individuals, it has relatively poor prognosis as 25% of diagnosed patients have lifespan estimated for less than ten years, whereas 75% of patients die of TCS before reaching the age of 25 (Anthony et al., 2020).

TCS may appear as many symptoms in several body systems including central nervous system (under the form of epilepsy or brain tumors), urinary system complications (kidney insufficiency either as long-term complications or acute hemorrhagic complications) as well as circulatory and respiratory system complications. 50% of pediatric patients suffering from TCS have been diagnosed with *rhabdomyomata*, while complications affecting the respiratory system in a significant number of cases is *lymphangioleiomyomatosis*. Other lesions connected to TCS include vision organ - *phacomata*, *neurocytophacomata*, liver - *AML tumors*, pancreas - *insulinoma*, gastrointestinal tract - *stomach* and *colon polyposis*. Skin lesions like fibrous plaques and pigmentation spots suggest a complex diagnostic approach.

The occurrence of specific complaints coming from different body systems could conceivably persuade one to initiate a diagnosis targeted at possible kidney complications (Lee et al., 2019). AML as a solitary lesion or a component of Tuberous Sclerosis Complex, is associated with cell proliferation, migration and differentiation impairment. Structural changes result in incomplete development of the vessel wall making it more prone to injuries/rupture. Choristoma-type AML is characterized as additional paravascular epithelial cells and is known as a more invasive form (Ding et al., 2024). The percentage of AML occurrence in the general population varies from 0,3% to 3%, and the ratio is estimated to be 4 females to 1 male.

This fact constitutes a reliable argument for the theory of hormone-dependency (Kingswood et al., 2016). With the development of medicine, many diseases considered incurable for decades are no longer a mortal threat to the patient's life. Developments of technology enabled us to see through the human body and make diagnoses that were previously unreachable. Emergency medicine is based on fast imaging diagnosis, which is essential to restrain many unnecessary steps that make the diagnostic process less legible (Trnka and Kennedy, 2021). Specific, hospital-based interventions to prevent a patient's decease, or at least limit the damage that a particular disease causes. It requires decision-making and rapid linking of symptoms into specific disease entities.

But what if the symptoms presented by the patient are present in more than one disease? One of the more insidious diseases is Wunderlich Syndrome - a set of symptoms accompanying spontaneous rupture of the kidney and bleeding into the perinephric capsule (Caliò et al., 2021; Bertolini et al., 2018). Due to its rarity, it is often misdiagnosed as nephrolithiasis and treated as such, which can result in severe complications and even death of the patient. Is there an effective diagnostic method to help distinguish between two diseases with similar symptoms? In this case, we will attempt to provide an insight into the etiology and the optimal diagnosis of Wunderlich syndrome.

2. CASE PRESENTATION

We present the case of a 70-year-old female patient transferred to the emergency department by paramedics with suspected left kidney stones. The paramedics informed the emergency physicians about the patient's reported symptoms of sudden pain in the left kidney area since the morning hours and an episode of renal colic that had occurred a few years earlier. The patient was treated with Tramadol

for several months. She reports a weight loss of approximately 10 kg within the last six months. In a history taken from the patient: Iron deficiency anemia. She denied injury close to the kidney area. Patient's condition was severe.

She was under the influence of analgesedation, blood pressure dropped to 70/40mmHg, disturbance of consciousness, abdominal pain which does not react for high doses of painkillers. In physical examination acute abdomen syndrome. Aggressive fluid therapy was implemented on two intravenous accesses. Patient received 3x500 ml of 0.9% NaCl. CT scans of the abdomen and pelvis without contrast was done. A sample was taken to determine the blood type (Table 1).

Table 1 Blood tests on admission to the ER:

GFR	57ml/min/1.73m ²
Creatinine	0.95mg/dl
CRP	<9.5mg/dl
APTT	23.5sek
INR	8.7sek
Hemoglobin	9.3 g/dL
Hematocrit	28.9%
RBC	3.17x10 ⁶ /uL
MCV	91.2fL
MCH	29.3pg
MCHC	32.2 g/dL
PLT	163x10 ³ /uL
WBC	12.31x10 ³ /uL

Abdomen cavity CT: A large, approximately 11x7x20cm heterogeneous, partially hyperdense fluid structure in the left side of the upper abdominal cavity, closely adhere to the lateral part of the left kidney - the image matches to a hematoma with visible signs of active bleeding (Figure 1-3). The left kidney is barely visible, slightly displaced and compressed, No signs of urine stasis. The left ureter is primarily unnoticeable, merging with areas of fatty tissue density.

Urology department has been informed that life-saving surgery is necessary immediately. Patient was informed about potential side effects of the surgery, including kidney loss or death. Upon intra-surgical evaluation, emergency nephrectomy was performed. A 24 hours post-surgery patient required Levonor infusion. During peri-surgery period five units of whole blood, five units of platelet concentrate and three units of fresh frozen plasma were transfused. Procedure was prosecuted with no complications (Table 2). The patient's stay in hospital ended on the fifth day after admission in good condition and with accurate guidance.

Table 2 Laboratory tests on the day of discharge from the ward:

Creatinine	1.68mg/dl
CRP	4.1 mg/dl
Hemoglobin	9.9 g/dL

Hematocrit	29.7%
RBC	$3.41 \times 10^6/\mu\text{L}$
MCV	87.1 fL
PLT	$135 \times 10^3/\mu\text{L}$
WBC	$6.9 \times 10^3/\mu\text{L}$



Figure 1 Bleeding into the retroperitoneal space



Figure 2 Internal bleeding, visible displaced left kidney



Figure 3 Anterior-posterior projection of the patient during active bleeding

3. DISCUSSION

Diagnosis and preventive factors

The chance of acute renal bleeding is dependent on tumor diameter; thus, check-up systematicity criteria vary. Renal ultrasonography should be used to control tumors with dimensions greater than 4cm every six months, while smaller lesions should be checked once a year (Jinzaki et al., 2017). The risk of acute hemorrhage in the case of more extensive tumors is estimated to be around 51%, and those under four centimeters for around 13% (Kiefer and Stavropoulos, 2017). Due to non-specific symptoms, Wunderlich Syndrome should be differentiated from other abdominal conditions such as acute appendicitis, nephrolithiasis, and peritonitis. Prompt diagnostic imaging is essential. For this reason, ultrasound, CT scans, and magnetic resonance imaging, and the second one is considered the gold standard.

However, physicians should pay attention to the difficulty of detecting tumor lesions during an episode of heavy bleeding (Venyo, 2016). This case demonstrates how essential differential diagnosis of abdominal pain is. If the syndrome is recognized, prompt surgical intervention is fundamental. Due to the presence of a haematoma, the patient may be at risk of hypovolemic shock, so blood pressure should be constantly monitored (Seyam et al., 2016). Blood group determination should be mandatory when WS is suspected. To maximize safety, a cross-matching test should be performed, demonstrating the serological compatibility between the blood of the donor and the recipient. In ultrasonography, AML appears as a lesion of homogenous (mainly in the case of large tumors) echogenicity and is easily mistaken for a malignant tumor, yet no calcification occurs.

The onset of clinical acute symptoms occurs mainly in tumors exceeding eight centimeters in diameter (Chen, 2015). Wunderlich syndrome is characterized by a triad of symptoms: Flank mass, flank pain, and hypovolemic shock, which are called Lenk's triad. While a minority of patients present typical symptoms included in the Lenk Triade, lumbar/flank area pain occurs in 53% of cases (Warncke et al., 2017). Palpable tumors can be recognized in less than half of patients. Massive hematuria is relatively rare, observed in 23% of cases.

Other rare concomitant symptoms can manifest as blood pressure oscillations, fever, and anemia. Most AML tumors do not cause long-term complaints and are diagnosed in imaging examination due to other diseases (Razik et al., 2019). Due to comparatively rare occurrences, non-specific or concealed symptoms, and a high possibility of misguided diagnosis, acute life-threatening hemorrhage is hard to predict. Prevention is possible for patients in a group at risk. It includes systematic blood pressure and heart rate control, prevention from atherogenic lesions, and pharmacotherapy adjusted to maintain a properly diagnosed condition.

Surgical prevention methods

The preferred surgical methods vary depending on the patient's clinical condition and the syndrome's cause. Renal artery embolization can be performed in high-risk groups of patients like individuals with tumors exceeding four centimeters, patients with abdominal compartment syndrome, ones suffering from vascular compliance disorder due to atherosclerosis or autoimmune diseases, acquired kidney failure or renal agenesis as well as women planning pregnancy (Claesen et al., 2023). Renal artery embolization enables the performance of conserving surgical procedures and is more often used as a preparation for the operative treatment rather than a separate treatment method (Feehan et al., 2023).

In the case of AML, the annual increase in tumor size is five percent. Thus, renal artery embolization is crucial, as it is proven to prevent lesion expansion and reduce parenchymal complications (Inoue et al., 2021; Al-Kindi et al., 2023; Makki et al., 2017). Surgical intervention differs when the syndrome is caused by RCC. The standard then is nephrectomy or renal-sparing surgery (NSS) in hemodynamically stable patients and in tumors of approximately up to 4 cm. Also, total nephrectomy or renal-sparing surgery is performed when chronic bleeding or renal artery embolization failure is suspected (Husillos-Alonso et al., 2018). Is there a way to improve the diagnostic process? The truth, as always, lies in the middle, with partial responsibility on the part of the patient and the vast majority on the doctor's part.

The method that can speed up the receipt of necessary medical assistance, particularly in situations requiring immediate surgical intervention or a blood transfusion, is a confirmed blood group test result in the patient's possession, so perhaps it would be good practice to introduce the possibility of carrying out such a test in an outpatient setting before a life-threatening situation ever arises. Asking precise questions about the nature and timing of symptoms is also an essential part of the diagnostic process. It should be a critical element in training and during studies to prepare future doctors to do their job in a way that brings the most significant health benefit to the patient. It also seems reasonable, especially for emergency medicine specialists, to provide specialized training in less common conditions, which could reduce the chance of misdiagnosis (Rabenou and Charles, 2015).

4. CONCLUSION

Due to the rarity of this syndrome, diagnosis and treatment can be challenging. The time from the onset of symptoms suggestive of bleeding to the correct diagnosis is relatively short. Failure to recognize this syndrome in time can result in the death of the patient. Therefore, using abdominal imaging tests, including prehospital ultrasonography and CT scanning in the ER, is essential. The decision on the type of treatment mainly depends on the size of the hemorrhage and the clinical condition of the patient. The diagnosis of the syndrome requires urgent surgical intervention. Angiographic embolization may be used in hemodynamically stable patients. However, this case presents that in hemodynamically unstable patients (fluctuations in blood pressure, disturbance of consciousness, abdominal pain unresponsive to medication), an emergent nephrectomy (total or partial) is required.

Author's Contribution

Kinga Piela: Conceptualization, methodology, investigation

Cezary Bochyński: Methodology, Review and editing

Jolanta Mazurek: Conceptualization, writing- rough preparation

Anna Józefiak: Formal analysis, supervision
 Magdalena Szczepanik: Conceptualization, methodology, investigation
 Gabriela Mazurek: Visualization, data curation
 Maciej Horbaczewski: Review and editing, supervision
 Przemysław Hałasinski: Conceptualization, writing- rough preparation
 Dominika Kropidłowska: Resources, writing- rough preparation
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 Klaudia Włodarczyk: Visualization, data curation
 Project administration: Kinga Piel

Informed consent

Written & Oral informed consent was obtained from individual participants included in the study.

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Ethical approval

Not applicable.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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