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Wunderlich's Syndrome, or Spontaneous Retroperitoneal Hemorrhage, in a Patient with Tuberous Sclerosis and Bilateral Renal Angiomyolipoma

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 33
Final Diagnosis: Renal angiomyolipoma
Symptoms: Abdominal discomfort
Medication: —
Clinical Procedure: —
Specialty: Surgery

Objective: Rare disease

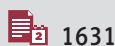
Background: Wunderlich's syndrome, or spontaneous non-traumatic retroperitoneal hemorrhage, can be a life-threatening event. Renal angiomyolipoma is a rare benign tumor that can occur sporadically, or in association with tuberous sclerosis. A case of spontaneous retroperitoneal hemorrhage in a patient with tuberous sclerosis and bilateral renal angiomyolipoma is presented.

Case Report: A 33-year-old female Caucasian patient, with a known medical history of tuberous sclerosis, was admitted to hospital as an emergency, with right-sided abdominal pain. Abdominal computed tomography (CT) imaging showed bilateral renal tumors, consistent with bilateral renal angiomyolipoma. The larger tumor, involving the enlarged right kidney (24.0 cm in length), had a diameter of 21.0 cm and was associated with hemoperitoneum and retroperitoneal hemorrhage, and contrast 'blush' on CT confirmed arterial bleeding. An initial urgent exploratory laparotomy with renal packing was initially performed, but right nephrectomy was required for hemorrhage control. The patient was discharged from hospital on the 23rd postoperative day, without further complications.

Conclusions: This report describes a case of Wunderlich's Syndrome, or spontaneous retroperitoneal hemorrhage, in a patient with tuberous sclerosis and bilateral renal angiomyolipoma, presenting as an emergency. An early diagnosis and timely treatment are important in cases of retroperitoneal hemorrhage to prevent life-threatening complications.

MeSH Keywords: Angiomyolipoma • Hemoperitoneum • Nephrectomy • Tuberous Sclerosis

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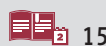
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Background

Renal angiomyolipoma comprises 0.3% of all primary renal neoplasms [1]. Angiomyolipoma is a benign mixed mesenchymal tumor composed of varying proportions of abnormal vessels, immature smooth muscle cells, and adipose tissue [2,3]. There are two types of angiomyolipoma; 80% occur as isolated cases, with the remaining being associated with tuberous sclerosis [1,3]. Solitary angiomyolipoma usually occurs sporadically in the population, mainly in women in the fourth to fifth decade of life [3]. However, angiomyolipoma associated with tuberous sclerosis is typically a larger, multifocal, or bilateral tumor, and occurs in younger patients [3].

Tuberous sclerosis, or Bournville–Pringle disease, is a rare genetic condition that occurs sporadically or as a familial form, and affects cellular differentiation and proliferation, which results in hamartomatous lesions in many organs, most commonly in the brain, heart, eyes, kidneys, skin, and lungs [1,2]. Renal involvement is described in tuberous sclerosis, with renal angiomyolipoma being the most common association [2,4]. The prevalence of renal angiomyolipoma in patients with tuberous sclerosis is reported to be between 50–80%, which means that careful screening for the presence of renal tumors is advised in these patients [3,4]. Renal angiomyolipoma usually has a benign course, but can be a source of bleeding, with Wunderlich's syndrome, spontaneous non-traumatic retroperitoneal hemorrhage, being one of the most serious complications, occurring in 10% of patients with angiomyolipoma [2,4]. An increase in the size of the renal angiomyolipoma (>4.0 cm in diameter), multifocal tumors, and an association with tuberous sclerosis increases the risk of bleeding [2,5].

A case of spontaneous retroperitoneal hemorrhage (Wunderlich's syndrome) in a patient with tuberous sclerosis and bilateral renal angiomyolipoma is described, which presented as an emergency and required nephrectomy. Challenges in the diagnosis and management of these rare associations are discussed.

Case Report

A 33-year-old female Caucasian patient, with a known medical history of tuberous sclerosis, was admitted to hospital as an emergency, with right-sided abdominal pain. She was diagnosed with inherited tuberous sclerosis in 2004, with the involvement of several organ systems, including the brain, kidneys, lungs, skin, bone, and liver. Pulmonary lymphangiomyomatosis (LAM) was previously diagnosed, which was treated by lung resection in 2013. Since 2013, she had suffered from reduced pulmonary function and moderate irreversible obstructive airway disease, with dyspnea on mild exertion.



Figure 1. Abdominal computed tomography (CT) scan. Bilateral renal angiomyolipoma (black arrows) are shown, with retroperitoneal and intraperitoneal hemorrhage. Both kidneys are enlarged, and the masses contain multiple areas of fat density, consistent with a diagnosis of bilateral renal angiomyolipoma. The larger tumor, involving the right kidney, had a diameter of 21.0 cm.

Following emergency admission to hospital, her blood pressure was 135/68 mmHg, with a pulse rate of 110 beats/min, a temperature of 37°C, and oxygenation saturation of 80% on O₂ of 4 L/min. On physical examination, the patient was pale and had right-sided abdominal tenderness. Laboratory investigations showed an hemoglobin (Hb) level of 9.4 mg/dL, mild leukocytosis, a prothrombin time of 14.2 s, C-reactive protein (CRP) of 9.73 mg/dL, and a serum creatinine level of 1.6 mg/dL.

Abdominal ultrasonography showed free fluid in the abdomen, and abdominal computed tomography (CT) imaging (Figures 1–3) showed bilaterally enlarged kidneys, each containing a mass, within which were multiple areas of fat density, consistent with a diagnosis of bilateral renal angiomyolipoma. The larger tumor, involving the right kidney, had a diameter of 21.0 cm and was associated with hemoperitoneum and retroperitoneal hemorrhage, and contrast ‘blush’ on CT confirmed arterial bleeding. There was also evidence of a previous embolization of the left kidney.

Following imaging, on return to the emergency department, the patient became hemodynamically unstable, with a fall in blood pressure to 83/60 mmHg, pulse rate of 131 beats/min and a fall in Hb to 7.1 mg/dL. Because angiography was unavailable, and the patient was in a critically unstable hemodynamic condition, an emergency laparotomy was performed. During surgery, 2 L of blood was drained from the peritoneum, and



Figure 2. Abdominal computed tomography (CT) scan. An arterial 'blush' is shown (black arrow) associated with the right renal angiomyolipoma, which indicates a bleeding vessel.

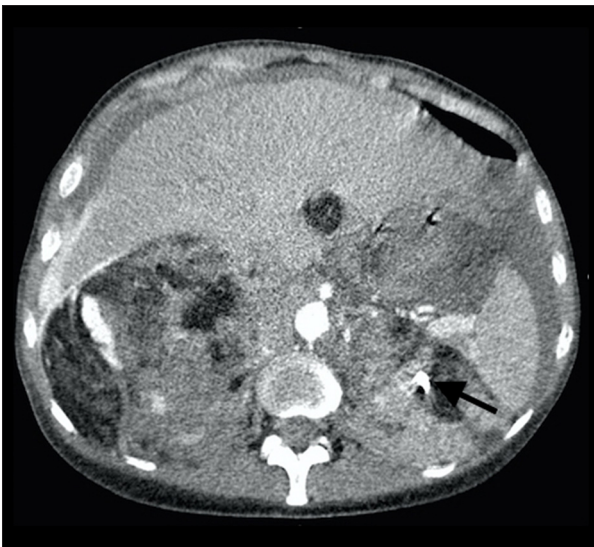


Figure 3. Abdominal computed tomography (CT) scan. The left kidney shows evidence of previous arterial embolization (black arrow).

the source of active bleeding was identified within the large right renal mass. The initial surgical approach was peri-renal packing and temporary abdominal closure (TAC) to preserve renal function (Figures 4, 5). The patient was then admitted to the intensive care unit (ICU). However, as bleeding continued, 18 hours following the initial surgery, an urgent right nephrectomy was performed for definitive control of the retroperitoneal hemorrhage.

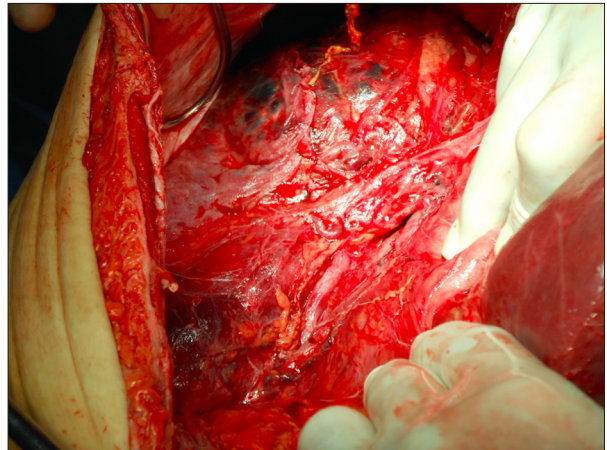


Figure 4. The appearance of a large right renal angiomyolipoma seen at surgery. During exploratory laparotomy, the source of active bleeding was identified within the large right renal mass compatible with renal angiomyolipoma.



Figure 5. The temporary abdominal closure (TAC) procedure. A damage control approach was done with peri-renal right packing and a temporary abdominal closure (TAC) procedure.

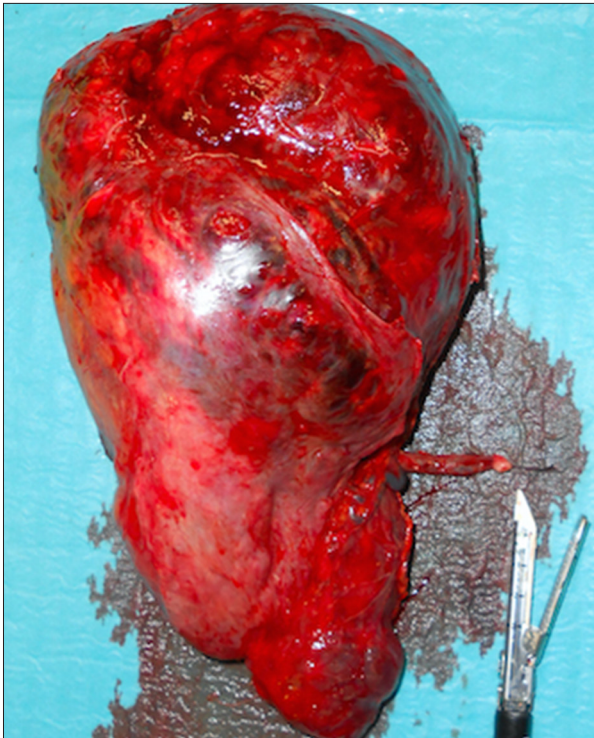


Figure 6. The macroscopic appearance of the right nephrectomy specimen. Macroscopic examination of the right nephrectomy specimen shows that the kidney is enlarged, measuring 24.0×12.0×9.0 cm (weighing 1,236 g).



Figure 7. Right renal angiomyolipoma with no necrosis on its cut surface. Right nephrectomy specimen containing a tumor consistent with renal angiomyolipoma, with no necrosis on its cut surface.

Macroscopic examination of the right nephrectomy specimen showed that the kidney was enlarged, measuring 24.0×12.0×9.0 cm and weighing 1,236 g, and contained a tumor measuring 21.0 cm in diameter, with no necrosis on its cut surface (Figures 6, 7). Histopathology of the excised renal tumor showed a benign neoplasm containing vascular, smooth muscle, and adipose tissue components, confirmed by immunohistochemistry. The histological features were consistent with a diagnosis of a renal angiomyolipoma.

Following right nephrectomy, the patient recovered well, and her serum creatinine returned to normal. She did not require renal dialysis, although her respiratory ventilatory support continued, as before. The patient was discharged from hospital on the 23rd postoperative day.

Discussion

Renal angiomyolipoma is a rare benign tumor with an incidence in the general population of 0.3% [1]. Most small tumors are asymptomatic. However, renal angiomyolipoma can cause abdominal or flank pain, a tender palpable mass, hematuria or other complications, including retroperitoneal hemorrhage [3].

Previously published studies have shown that the frequency of symptoms and risk of bleeding from renal angiomyolipoma are related to the tumor size, occurring more commonly with tumors >4.0 cm in diameter, with multicentric angiomyolipoma, and angiomyolipoma associated with tuberous sclerosis [2,3].

Wunderlich's syndrome, or spontaneous non-traumatic retroperitoneal hemorrhage, is usually confined to the renal subcapsular space or the perinephric space, can present as a medical emergency and is one of the most common causes of mortality in patients with tuberous sclerosis [2,4]. The clinical presentation of Wunderlich's syndrome depends on the degree and the duration of the bleeding [6]. Lenk's triad, which includes flank or abdominal pain, a palpable tender mass, and gross hematuria, is the classic presentation of Wunderlich's syndrome [3,6]. Less common symptoms of Wunderlich's syndrome include nausea or vomiting, fever, anemia, and hypotension [7]. In this case report, the patient presented as an emergency, with life-threatening hemorrhage, hemoperitoneum, and hemorrhagic shock.

In most cases, the diagnosis of renal angiomyolipoma can be made on ultrasonography or computed tomography (CT) scan by the detection of the presence of adipose tissue in a renal mass [5,8]. Although ultrasonography may be sufficient to

detect angiomyolipoma, it may not provide enough information to measure accurately and follow any enlargement of this renal lesion, and can also fail to identify variants of renal angiomyolipoma that contain little or no fat content. Therefore, abdominal CT scan is considered the most sensitive imaging method to identify angiomyolipoma and its location and to identify complications, such as bleeding [10].

Because of the strong association with renal angiomyolipoma, patients with tuberous sclerosis who have no initial evidence of this renal tumor, are advised to have renal imaging at 2–3 yearly intervals, but if renal angiomyolipoma or other renal abnormalities are present, annual follow-up renal imaging is recommended [9]. The size and pattern of growth of renal angiomyolipoma should be followed, as most individuals with renal angiomyolipoma <4.0 cm in diameter have no associated clinical symptoms, but those with renal angiomyolipoma \geq 4 cm in diameter can present with back or abdominal pain, and if tumor growth occurs or symptoms are present, then surgical intervention may be necessary [9]. In the emergency setting, when complications of renal angiomyolipoma are suspected, abdominal CT scan is the most sensitive diagnostic method for tumor and patient evaluation, as shown in this case report, and that early recognition of tumor necrosis, hemorrhage, or active bleeding is essential for early life-saving patient management [10].

Most asymptomatic cases of renal angiomyolipoma that are small (<4.0 cm in diameter) can be managed conservatively [2]. The management of asymptomatic renal angiomyolipoma >4.0 cm is more controversial but includes prophylactic vascular occlusive embolization in selected high-risk patients, who may be difficult to follow-up, or in young women who intend to get pregnant [11,12]. Previous studies have shown that embolization can reduce the size of the tumor and preserves kidney function [13]. However, other studies have recommended that embolization techniques should be reserved for symptomatic patients, due to the potential complications of the procedure and procedural outcome failure, which then require repeat embolization [12,13].

However, when there are complications of renal angiomyolipoma, such as Wunderlich's syndrome, therapeutic options depend on the general medical condition of the patient [6].

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Selective embolization, nephron sparing surgery, or total nephrectomy may be considered as treatment options [3,5], but treatment choice should be made by balancing the need to save life with the preservation of renal function [4]. Selective embolization is considered the treatment of choice in cases of Wunderlich's syndrome, especially in patients with tuberous sclerosis who have bilateral and multiple angiomyolipoma and pre-existing renal impairment [5–7]. Patients with life-threatening bleeding may require urgent surgery, including total nephrectomy [14,15].

In this case report, the CT scan confirmed evidence of previous prophylactic embolization of the contralateral kidney, and so preservation of renal function was an important factor to consider in the management of this patient. Since there was no interventional angiographic radiology readily available at our institution, the initial treatment approach was with perirenal packing and temporary abdominal closure (TAC) to preserve renal function. Because the patient remained unstable and bleeding persisted, a total nephrectomy was required as definitive and life-saving management.

Conclusions

This report has described a case of Wunderlich's syndrome, or spontaneous retroperitoneal hemorrhage, in a patient with tuberous sclerosis and bilateral renal angiomyolipoma, presenting as an emergency. Although renal angiomyolipoma is a rare but benign tumor, large tumor size, and an association with tuberous sclerosis increase the risk of complications that include bleeding. Early diagnosis and treatment are important in cases of retroperitoneal hemorrhage to prevent life-threatening complications. Therefore, clinicians should consider the possibility of spontaneous bleeding from renal angiomyolipoma when a patient with tuberous sclerosis presents as an emergency with abdominal pain and hypovolemic shock, to provide early diagnosis and life-saving treatment.

Conflict of interest

None.

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