Radiology Case Reports 19 (2024) 6286–6291

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Spontaneous angiomyolipoma rupture: A case of hemorrhagic shock and urgent embolization ☆,☆☆

Ameer Awashra[a], *Zaid Sawaftah*[a], *Fathi Milhem*[a], *Dawoud Hamdan*[a,*], *Ali Bani Odah*[a], *Ahmad Sawafta*[a], *Ola Ahmad*[a], *Jehad Khamaysa*[b], *Mohammed Khader*[c], *Omar Naseef*[c]

[a] *Department of Medicine, An Najah National University, Nablus, Palestine*
[b] *Department of Radiology, Tubas Turkish Governmental Hospital, Tubas, Palestine*
[c] *Department of Radiology, An Najah National University Hospital, Nablus, Palestine*

ARTICLE INFO

Article history:
Received 25 August 2024
Accepted 4 September 2024

Keywords:
Tuberous sclerosis
Angiomyolipoma
Angiography

ABSTRACT

This case report discusses a 64-year-old male with tuberous sclerosis complex (TSC), a genetic disorder characterized by benign tumor formation across multiple organ systems. The patient presented with a spontaneous hemorrhage from a right renal angiomyolipoma, a common and potentially life-threatening manifestation of TSC, particularly in patients with TSC2 mutations. The patient's significant comorbidities, including hypertension and dyslipidemia, further complicated his clinical course. Initial management involved aggressive fluid resuscitation and blood product transfusion, followed by urgent embolization to control active bleeding. Despite developing complications such as transfusion-associated circulatory overload (TACO), the patient was successfully stabilized. This case highlights the necessity for careful monitoring and prompt intervention in patients with TSC, given the high risk of hemorrhage from angiomyolipomas, especially those larger than 3 cm. We also emphasize the importance of differentiating TSC-associated angiomyolipomas from other renal masses, considering the variability in clinical presentation and the potential for late-onset symptoms. Additionally, it highlights the critical role of a multidisciplinary approach in managing TSC patients, addressing both acute complications and long-term surveillance to prevent recurrence and other systemic manifestations of the disease.

Introduction

Tuberous Sclerosis Complex (TSC) is an autosomal dominant genetic neurocutaneous disorder that affects multiple organs [1]. Its prevalence is almost 2 million people worldwide [2] with an incidence of 1 in 6000 [2,3]. TSC is characterized by a loss-of-function germline mutation in the TSC protein complex, including TSC1 (known as hamartin) and TSC2 (known as tuberin), identified in 20% and 70% of TSC patients, respectively

☆ Competing Interests: The authors state that they have no conflict of interest to be mentioned.
☆☆ Acknowledgment: We express our deep gratitude to the medical ward staff for their invaluable support in completing this report.

* Corresponding author.
E-mail address: dawoudhamdan@hotmail.com (D. Hamdan).

https://doi.org/10.1016/j.radcr.2024.09.034

[2]. These are tumor suppressor genes that inhibit mTORC1 (mammalian target of rapamycin complex 1) which controls cell growth [4]. The loss of these genes will result in the growth of well-circumscribed benign tumors in the heart, lungs, kidneys, brain, and skin [2,3,5].

In the kidneys, Angiomyolipomas (AML) develop in up to 80% of adult TSC patients [3]. AML components include blood vessels, smooth muscle, and fat, with the ratio of each differing between different lesions within the same kidney [3,6]. Therefore, AML is classified into 3 pathological types: classic, fat-poor, and epithelioid [6]. Although it can occur sporadically or be associated with TSC [7], the latter affects patients at younger ages and at a faster rate [6] especially those with TSC2 mutation which tends to be more severe and prevalent [8]. Multiple modalities have been established for the management of AML; However, mTOR inhibitors are currently considered the first line, whether asymptomatic or measuring more than 3 cm, even if symptomatic [6,9].

In this case, we present a 64-year-old male with a complicated past medical history who presented with acute right upper flank pain and symptoms consistent with hemorrhagic shock. Imaging revealed active bleeding from a right renal angiomyolipoma, necessitating urgent transfer to another hospital for embolization. Despite hemodynamic instability, the patient was stabilized with aggressive fluid resuscitation, blood transfusions, and embolization, which successfully controlled the hemorrhage. Postprocedure, the patient developed transfusion-associated circulatory overload, which was managed effectively with diuretics, and he was monitored in the ICU with a focus on preventing rebleeding, managing his chronic conditions, and planning long-term follow-up.

Case presentation

A 64-year-old male with a known history of tuberous sclerosis, along with significant medical conditions including hypertension, dyslipidemia, and bilateral angiomyolipomas, presented to the emergency department. The patient, who had been in his usual state of health, experienced a gradual onset of moderate to severe right upper flank pain lasting a few hours. The pain was described as sharp and nonradiating, accompanied by nausea, vomiting, sweating, and dizziness. Given the patient's history and clinical presentation, the differential diagnosis included renal artery aneurysm, ruptured renal tumor, or spontaneous hemorrhage from angiomyolipoma. An initial abdominal ultrasound revealed a right perinephric hematoma with free fluid, prompting a subsequent CT scan with IV contrast, which confirmed a large right angiomyolipoma with active extravasation and a smaller left angiomyolipoma with internal sealing extravasation, indicative of ongoing active bleeding (see Fig. 1).

Upon arrival, the patient was hemodynamically stable but had borderline low blood pressure and appeared drowsy. Laboratory tests revealed a significant drop in hemoglobin to 8.3 g/dL from a baseline of 13 g/dL. Other relevant laboratory findings included a slightly elevated INR of 1.7, indicating mild coagulopathy, and a lactate level of 3 mmol/L, suggesting a degree of tissue hypoperfusion (see Table 1). Initial management involved aggressive fluid resuscitation with 1000 cc of Ringer's lactate, transfusion of 2 units of packed red blood cells (PRBCs), and 2 units of fresh frozen plasma (FFP). Given the severity of the hemorrhage, the patient was urgently transferred to another hospital for possible embolization vs right nephrectomy.

At the receiving hospital, the patient's condition deteriorated with a blood pressure of 78/60 mmHg and a heart rate of 115 bpm, consistent with hemorrhagic shock. Despite the critical state, the patient remained conscious and oriented with a Glasgow Coma Scale (GCS) score of 15/15. Immediate interventions included the insertion of a left-sided central line, administration of an additional 1500 cc of Ringer's lactate, and transfusion of more PRBCs and FFP. The patient's oxygen saturation dropped to 88% on room air, necessitating supplemental oxygen via nasal cannula at 4 L/min. Despite significant hemodynamic instability, vasopressors were not required, and the patient was stabilized with fluid resuscitation and blood products.

The patient was swiftly transferred to the catheterization lab for embolization, where angiography confirmed significant bleeding from the lower branch of the right renal artery, controlled with multiple peripheral pushable coils (See Fig. 2). Another bleeder from the superior branch was also coiled. The final angiogram revealed no residual bleeding. Additionally, the postoperative abdominal CT scan without contrast demonstrated multiple angiomyolipomas in a distorted right kidney, along with a large fatty hypodense area consistent with an angiomyolipoma inferior to the left kidney (see Fig. 3).Throughout the procedure, the patient was transfused with 8 units of FFP, 8 units of cryoprecipitate, 8 units of platelets, and 4 units of PRBCs. He developed type 1 respiratory failure, attributed to transfusion-associated circulatory overload (TACO), requiring high-flow oxygen therapy with a nonrebreather mask. This complication was managed effectively with intravenous furosemide, resulting in significant diuresis and a reduction in oxygen requirements. Postprocedure, the patient was transferred to the surgical ICU for close monitoring.

In the ICU, the patient's hemodynamics stabilized, but sinus tachycardia persisted at 110 bpm. Despite aggressive fluid resuscitation, he developed features of congestive heart failure due to TACO, which were managed with furosemide and labetalol infusion for persistent hypertension. The patient's respiratory status gradually improved, allowing a reduction in supplemental oxygen. Repeated blood tests showed no further drop in hemoglobin, and electrolyte imbalances, including hypokalemia and hypomagnesemia, were corrected with intravenous potassium chloride and magnesium sulfate. Monitoring for potential rebleeding was implemented through serial complete blood counts (CBC) and coagulation profiles.

The patient's long-term management plan included careful monitoring for recurrent bleeding and ongoing management of the remaining left angiomyolipoma. Given the patient's history of dyslipidemia and hypertension, a thorough cardiovascular evaluation was recommended to optimize blood pressure control and reduce the risk of further vascular complications. His medication regimen prior to admission was reviewed, and adjustments were made as needed, including the reintroduction of Aspirin and the continuation of antihypertensive therapy with Valsartan/Hydrochlorothiazide

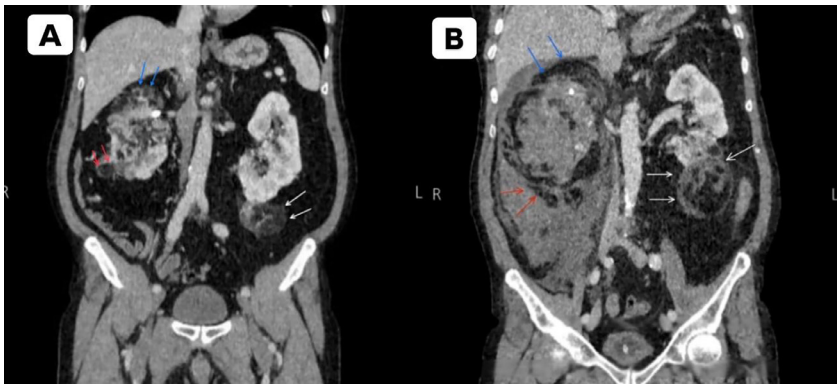

Fig. 1 – Preoperative Abdominal **CT scan: (A) the coronal CT scan shows multiple fatty hypodense areas in both kidneys, consistent with angiomyolipomas that were observed 2 years earlier. The red arrow points to the angiomyolipoma suspected to have ruptured, while the white arrow indicates a large fatty hypodense area below the left kidney. (B) At admission, the CT scan shows hemorrhage caused by the rupture of an angiomyolipoma on the lower right side, indicated by the red arrow.**

Table 1 – Summary of laboratory findings on admission.

Laboratory test	Result	Units	Normal range
White blood cell count	13.5	10^9/L	4.0-11.0 × 10^9/L
Hemoglobin	8.2	g/dL	13.5-17.5 g/dL
Platelets	131	10^9/L	150-450 × 10^9/L
Mean corpuscular volume (MCV)	82	fL	80-100 fL
Fibrinogen	130	mg/dL	200-400 mg/dL
International Normalized ratio (INR)	1.78	-	0.8-1.2
Sodium	138	mmol/L	135-145 mmol/L
Potassium	3.1	mmol/L	3.5-5.0 mmol/L
Chloride	107	mmol/L	98-107 mmol/L
Calcium	7.2	mg/dL	8.5-10.2 mg/dL
Blood urea nitrogen (BUN)	22	mg/dL	7-20 mg/dL
Creatinine	1.3	mg/dL	0.7-1.3 mg/dL
Aspartate Aminotransferase (AST)	36	U/L	10-40 U/L
Alanine Aminotransferase (ALT)	7.2	U/L	7-56 U/L
Total bilirubin	1.39	mg/dL	0.1-1.2 mg/dL
Direct bilirubin	0.6	mg/dL	0.0-0.3 mg/dL
C-reactive protein (CRP)	12	mg/L	< 10 mg/L
pH	7.38	-	7.32-7.43
CO2	36	mmHg	35-45 mmHg
HCO3	22	mmol/L	22-26 mmol/L
Lactate	4.1	mmol/L	0.5-2.2 mmol/L

and Bisoprolol. Nutritional support was provided with a soft diet, and gastrointestinal prophylaxis was maintained with intravenous Esomeprazole. Deep vein thrombosis (DVT) prophylaxis was initiated using a pneumatic compression device, with consideration of pharmacological prophylaxis once the risk of rebleeding was sufficiently low.

The patient's social history, noting his married status and nonsmoking habit, was considered in discharge planning, emphasizing the importance of a supportive home environment for his recovery. Long-term follow-up was arranged to monitor renal function, manage chronic hypertension and dyslipidemia, and assess for any late complications related to the embolization. The patient's expected length of stay was determined by his recovery progress, particularly the stabilization of renal function and resolution of respiratory support needs, ensuring a comprehensive approach to his ongoing care.

Discussion

Tuberous sclerosis complex (TSC) is a rare neurocutaneous autosomal dominant genetic disorder characterized by a group of benign (noncancerous) tumors that affects multiple systems. This disorder is linked to inactivating mutations in the tumor suppressor genes TSC1 (also known as hamartin) and TSC2 (also known as tuberin), which are located on chromosomes 9q34 and 16p13.3, respectively. The clinical manifesta-

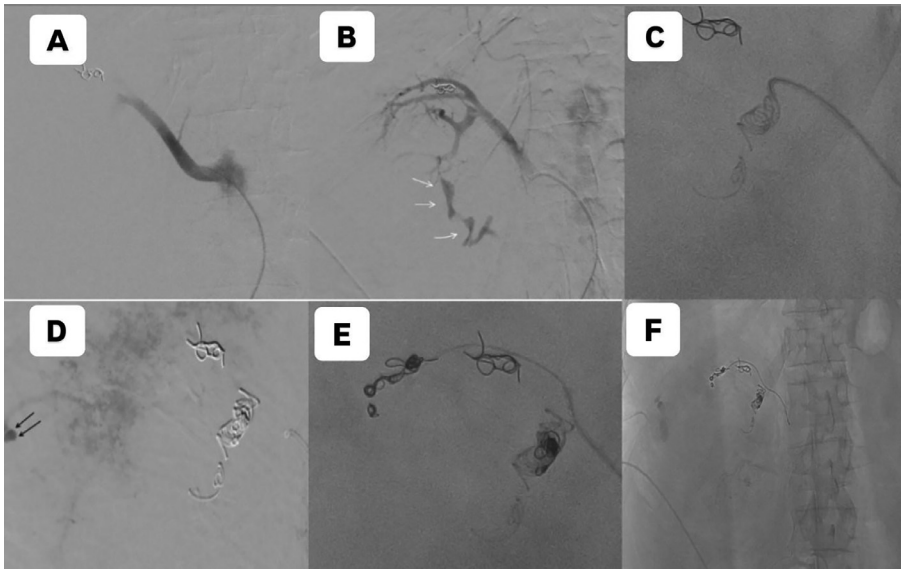

Fig. 2 – Right renal ruptured AML embolization via right femoral artery access: **(A) A Cobra catheter was inserted and advanced to the right renal artery, where the previous coil was observed. (B) Angiography confirmed significant bleeding from the lower branch of the right renal artery indicated by white arrow. (C) Rapid coil embolization was performed using a Progreat microcatheter and a 5F catheter with 8 mm peripheral pushable coils. (D) Another bleeding source was identified from the superior branch of the right renal artery indicated black arrow. (E) Coil embolization was successfully completed, although 1 coil elongated within the right renal artery without causing occlusion. (F) The final angiogram showed no obvious residual bleeding. Blood supply to the kidney was primarily from the upper branch, with some supply from the lower branch.**

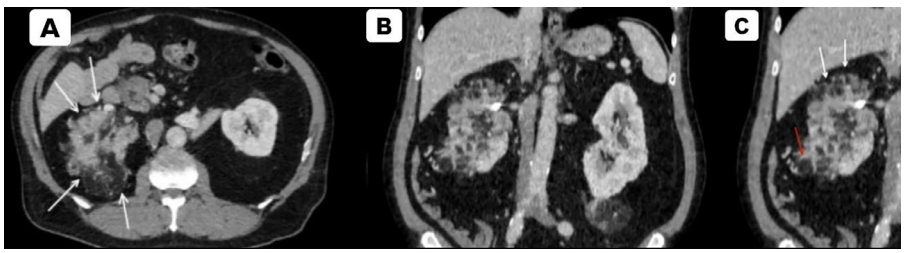

Fig. 3 – Postoperative abdominal CT scan without contrast: **(A) the axial section shows a distorted right kidney with multiple fatty hypodense areas, consistent with multiple angiomyolipomas. (B) The coronal section shows these findings in the right kidney and additionally reveals a large fatty hypodense area inferior to the left kidney, also consistent with an angiomyolipoma. (C) A zoomed-in view of the right kidney reveals a distorted architecture.**

tions of TSC are variable and can range from minimal signs and symptoms with no disabling neurological symptoms, including renal angiomyolipomas, pulmonary lymphangiomyomatosis [LAM], shagreen patches, and facial angiofibromas, to disabling neurological symptoms, including epilepsy, autism, and even mental retardation that involve mainly the central nervous system [10,11].

With an incidence of 1 in 20,000, the tuberous sclerosis complex affects roughly 1 in 6000 to 1 in 10,000 live births. The clinical manifestation varies substantially, typically impacting several organs and affecting all racial groups [12]. Although genetic testing can also be used to diagnose tuberous sclerosis, clinical criteria remain the primary method of diagnosis. If a patient meets the clinical criteria, genetic testing is not necessary, although it can give other family members vital information. 75%-95% of TSC-affected people had positive results for mutations in TSC1 and TSC2, according to genetic testing [13]. The diagnostic criteria for tuberous sclerosis include the following major and minor features: **major features (**Hypomelanotic macules (>2 at least 5 mm in diameter), Angiofibromas (>2) or a fibrous cephalic plaque, Ungual fibromas (>1), Shagreen patch, Multiple retinal hamartomas, Cortical dysplasias, Subependymal nodules, Subependymal giant cell astrocytoma, Cardiac rhabdomyoma, Lymphangioleiomyomatosis, Angiomyolipomas (>1)**, minor features (**Confetti skin lesions, Dental enamel pits (>3), Intraoral fibromas (>1), Retinal achromic patch, Multiple renal cysts, Nonrenal hamartomas**).** Patients with 2 major features or one major feature plus at least 2 minor features are considered to have a definitive diagnosis; patients with one major feature or at least 2

minor features are considered to have a "possible diagnosis" [14].

Variable expression and incomplete penetrance are hallmarks of hereditary tuberous sclerosis complex (TSC), When people with pathogenic mutations in the TSC1 or TSC2 genes do not display the entire spectrum of symptoms commonly linked to the condition, this is referred to incomplete penetrance. Furthermore, this can lead to late onset of symptoms which make identification and treatment more difficult. This delayed presentation emphasises the significance of continuous monitoring and genetic counselling for people with a family history of TSC, even if they don't seem to be affected at first [13,15].

Comprehensive follow-up is necessary for tuberous sclerosis, which frequently manifests as a wide range of multisystemic problems. An extensive dermatologic examination could help detect angiofibromas early on before they develop cosmetic deformities that need to be removed surgically or with laser treatment [11]. Anticonvulsants are frequently necessary for tuberous sclerosis-associated seizures. Surgery might be necessary, though, as roughly one-third of patients experience seizures that are unresponsive to medication. Complications such as hydrocephalus may also necessitate emergency neurosurgery [16].

TSC is known to cause renal lesions which commonly include renal cysts and Angiomyolipoma (AML), in up to 50% and 80% of TSC patients, respectively [17]. Renal AMLs are generally benign tumors composed of varying proportions of blood vessels, smooth muscles, and adipose tissue [3]. AMLs are characterized by continued growth and enlargement, leading to the development of abnormal aneurysms with a significant risk of bleeding, especially AMLs > 3 cm and aneurysms > 5 cm. Therefore, regular monitoring of Blood pressure and renal function and performing abdominal magnetic resonance imaging (MRI) at the time of diagnosis and every 1-3 years thereafter is required [3].

According to genetics, AMLs tend to be more severe and frequent in patients with TSC2 mutations compared with TSC1 mutations [8]. These tumors express HMB-45 and Melan-A, which characterize perivascular epithelioid cell tumors (PEComas), therefore AML is considered a member of the PEComa family, especially when it has a malignant behavior [2,18].

AMLs are classified as classic, fat-poor, and epithelioid. Classic AMLs are hyperechoic, homogenous, and easily detectable by contrast tomography (CT) due to their fat component. Fat-poor has small fat components and is challenging to diagnose, sometimes chemical shift imaging can be useful. Epithelioid AMLs are rare, larger, and more aggressive [2] the smooth muscle component is epithelioid, mimicking renal cell carcinoma [19].

Arterial embolization should be considered for renal angiomyolipomas greater than 3.5 cm to prevent total nephrectomy and lower the risk of renal sequelae. Nevertheless, among tuberous sclerosis patients after partial vs total nephrectomy, the frequency of sequelae, including chronic kidney disease, is comparable. mTOR inhibitor therapy is regarded as a first-line treatment for lesions larger than 3 cm. Renal angiomyolipoma bleeding is a cause of death for patients with tuberous sclerosis, and the recommended course of treatment for patients who come with acute bleeding renal angiomyolipomas is arterial embolization followed by corticosteroids. Recurrence after embolization is common, and if mTOR inhibition is insufficient, surgical excision (including nephron-sparing surgery) and vascular embolization are second-line treatments [20,21].

Conclusion

In conclusion, this case illustrates the complexities of managing renal angiomyolipomas in patients with tuberous sclerosis complex (TSC), especially when accompanied by significant comorbidities like hypertension and dyslipidemia. The successful use of arterial embolization to control life-threatening hemorrhage demonstrates its critical role in treating symptomatic or large angiomyolipomas. The case also highlights the importance of distinguishing TSC-related angiomyolipomas from other renal masses, considering the variability in clinical presentation and the potential for late-onset symptoms. Additionally, it underscores the need for a comprehensive, multidisciplinary approach in managing both the acute and long-term challenges associated with TSC, with continuous follow-up and genetic counseling being vital to improving patient outcomes.

Patient consent

Written informed consent was obtained from the patient's Himself for his anonymized information to be published in this article.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

REFERENCES

[1] Lendvay TS, Marshall FF. The tuberous sclerosis complex and its highly variable manifestations. J Urol 2003;169(5):1635–42.
[2] Henske EP, Jóźwiak S, Kingswood JC, Sampson JR, Thiele EA. Tuberous sclerosis complex. Nat Rev Dis Primer 2016;2(1):16035.
[3] Brakemeier S, Bachmann F, Budde K. Treatment of renal angiomyolipoma in tuberous sclerosis complex (TSC) patients. Pediatr Nephrol Berl Ger 2017;32(7):1137–44.
[4] HUANG J, MANNING BD. The TSC1–TSC2 complex: a molecular switchboard controlling cell growth. Biochem J 2008;412(2):179–90.
[5] Curatolo P, Moavero R, de Vries PJ. Neurological and neuropsychiatric aspects of tuberous sclerosis complex. Lancet Neurol 2015;14(7):733–45.
[6] Hatano T, Egawa S. Renal angiomyolipoma with tuberous sclerosis complex: How it differs from sporadic angiomyolipoma in both management and care. Asian J Surg 2020;43(10):967–72.

[7] Nelson CP, Sanda MG. Contemporary diagnosis and management of renal angiomyolipoma. J Urol [Internet] 2002;168(4):1315–25.
[8] Kingswood JC, Belousova E, Benedik MP, Carter T, Cottin V, Curatolo P, et al. Renal angiomyolipoma in patients with tuberous sclerosis complex: findings from the TuberOus SClerosis registry to increase disease awareness. Nephrol Dial Transplant 2019;34(3):502–8.
[9] Amin S, Kingswood JC, Bolton PF, Elmslie F, Gale DP, Harland C, et al. The UK guidelines for management and surveillance of tuberous sclerosis complex. QJM Int J Med 2019;112(3):171–82.
[10] Henske EP, Jóźwiak S, Kingswood JC, Sampson JR, Thiele EA. Tuberous sclerosis complex. Nat Rev Dis Primer 2016;2(1):1–18.
[11] Crino PB, Nathanson KL, Henske EP. The tuberous sclerosis complex. N Engl J Med 2006;355(13):1345–56.
[12] De Waele L, Lagae L, Mekahli D. Tuberous sclerosis complex: the past and the future. Pediatr Nephrol 2015;30(10):1771–80.
[13] Northrup H, Krueger DA, Northrup H, Krueger DA, Roberds S, Smith K, et al. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 international tuberous sclerosis complex consensus conference. Pediatr Neurol 2013;49(4):243–54.
[14] Krueger DA, Northrup H, Krueger DA, Roberds S, Smith K, Sampson J, et al. Tuberous sclerosis complex surveillance and management: recommendations of the 2012 international tuberous sclerosis complex consensus conference. Pediatr Neurol 2013;49(4):255–65.
[15] Au KS, Williams AT, Roach ES, Batchelor L, Sparagana SP, Delgado MR, et al. Genotype/phenotype correlation in 325 individuals referred for a diagnosis of tuberous sclerosis complex in the United States. Genet Med Off J Am Coll Med Genet 2007;9(2):88–100.
[16] Capal JK, Franz DN. Profile of everolimus in the treatment of tuberous sclerosis complex: an evidence-based review of its place in therapy. Neuropsychiatr Dis Treat 2016;12:2165–72.
[17] Samuels JA. Treatment of renal angiomyolipoma and other hamartomas in patients with tuberous sclerosis complex. Clin J Am Soc Nephrol CJASN 2017;12(7):1196–202.
[18] Bing Z, MacLennan GT. Renal epithelioid angiomyolipoma. J Urol [Internet] 2009;182(5):2468–9.
[19] Eble JN, Amin MB, Young RH. Epithelioid angiomyolipoma of the kidney: a report of five cases with a prominent and diagnostically confusing epithelioid smooth muscle component. Am J Surg Pathol 1997;21(10):1123.
[20] Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. The Lancet 2008;372(9639):657–68.
[21] Sooriakumaran P, Gibbs P, Coughlin G, Attard V, Elmslie F, Kingswood C, et al. Angiomyolipomata: challenges, solutions, and future prospects based on over 100 cases treated. BJU Int 2010;105(1):101–6.