CASE REPORT

DOI: 10.5336/caserep.2022-92982

An Adult Diagnosed as Tuberous Sclerosis After Spontaneous Angiomyolipoma Bleeding

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ABSTRACT Renal angiomyolipomas are the most common benign mesenchymal tumors of kidney and may be associated with tuberous sclerosis complex. The most common cause of non-traumatic retroperitoneal renal bleeding is angiomyolipoma and spontaneous hemorrhage of angiomyolipoma can be life-threatening. Treatment is recommended if angiomyolipoma has bled or it is larger than 4 cm. There are endovascular and surgical treatment options. Endovascular selective embolization is the primary preferred minimally invasive treatment method in angiomyolipoma bleeding. In this case, we aimed to discuss an adult patient, who had seizures which the patient thought to be related to motorcycle accident history, presenting with acute angiomyolipoma bleeding treated with endovascular selective embolization and subsequently diagnosed with tuberous sclerosis.

Keywords: Embolization, therapeutic; tuberous sclerosis; kidney neoplasms; retroperitoneal space; hemorrhage

Renal angiomyolipomas are the most common benign mesenchymal tumors of the kidneys. It can be observed sporadically or may be associated with the tuberous sclerosis complex (TSC).[1] Clinically, the vital concern is life-threatening bleeding.[2] Selective embolization is the primarily preferred minimally invasive method in the treatment of acute hemorrhagic angiomyolipoma.[3]

TSC is a genetic, multisystemic disease that is observed in every 6,000-10,000 live births. The diagnosis is mostly made in childhood.[4] We aimed to present a 30-year-old adult patient with spontaneous angiomyolipoma hemorrhage, who was treated with selective embolization after admission to the emergency department and was subsequently diagnosed with TSC.

CASE REPORT

A 30-year-old male with a known history of seizures and using antiepileptic drugs, but whose seizure etiology is unknown, was admitted to the emergency department of our hospital with abdominal pain in the right lower and upper quadrant for lasting 5 hours. The patient had no history of trauma. At the time of admission, in whole blood count (CBC), hemoglobin was 17 g/dL and within normal limits, leukocyte count was $11x10^3$ µl/mL indicates minimal leukocytosis. Thereupon, the patient was referred to our ultrasonography unit with a preliminary diagnosis of acute appendicitis. In the ultrasonography examination performed on the patient, the appendix was displayed normal, but approximately 165x105 mm in size hematoma was observed in the right retroperitoneal area.

In addition, multiple cysts and several hyperechoic solid lesions thought to be compatible with angiomyolipoma were observed. Abdominal computed tomography (CT) was recommended for the patient with the preliminary diagnosis of spontaneous hemorrhage due to renal angiomyolipoma. In addition, due to the patient's history of seizures, more than 2 renal angiomyolipoma and multiple renal cysts, further

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Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 18 Aug 2022 ***Received in revised form:*** 28 Oct 2022 ***Accepted:*** 28 Oct 2022 ***Available online:*** 08 Nov 2022

evaluation for diagnosis of TSC was recommended to the clinicians following the patient. Meanwhile, in the control CBC taken, it was determined that the patient's hemoglobin value decreased by 3 units.

In the contrast-enhanced abdomen CT of the patient taken on the same day; multiple cysts and few solid lesions with areas of fat density consistent with angiomyolipoma were observed in both kidneys. In addition, a hematoma of approximately 205x135 mm in size, extending inferiorly in the right perirenal and retroperitoneal area, was observed with active contrast extravasation (Figure 1).

The patient was consulted to the interventional radiology department. Informed consent that also clears that patient's images can be used in academic purposes, has been taken from the patient. Selective right renal angiography was performed with the preliminary diagnosis of ruptured angiomyolipoma. In the digital subtraction angiography images taken from the right renal artery, tumoral staining of 75x70 mm in the inferior part of the kidney and 35x30 mm in the upper part were observed. Although active extravasation was not observed during angiography, superselective embolization was decided for the patient who was thought to have bled from an inferior angiomyolipoma (Figure 2). The branches feeding the mass were superselectively catheterized with a microcatheter (Progreat Microcatheter System, 2.7 Fr, Terumo, Japan) and embolization was performed using 300-500 and 500-700 micron sized microparticles (Embosphere Microspheres, Merit Medical, USA). In the control angiography images after the procedure, it was observed that the staining of the mass decreased significantly (Figure 2). After the embolization, the patient was followed up for 1 day in the intensive care unit of our hospital, and no decrease was observed in the hemoglobin value. Multiple subependymal nodules located in both hemispheres were observed in the brain CT. The patient, whose condition was stable one day after the procedure left the hospital voluntarily, so long-term follow-up of the patient could not be performed (Figure 3).

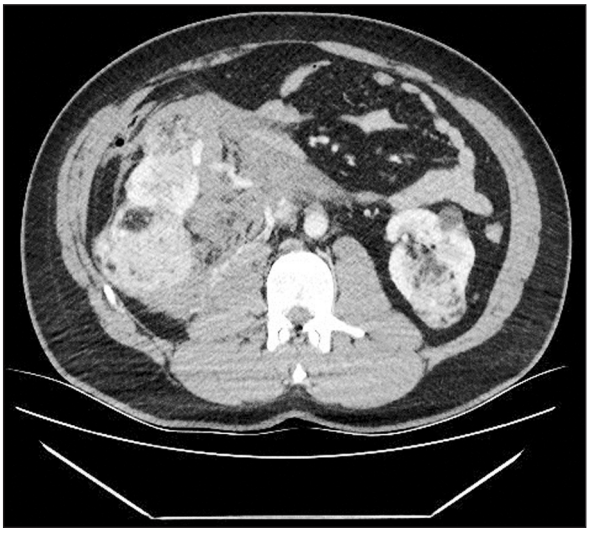

FIGURE 1: A hematoma of approximately 205x135 mm in size, extending inferiorly in the right perirenal and retroperitoneal area.

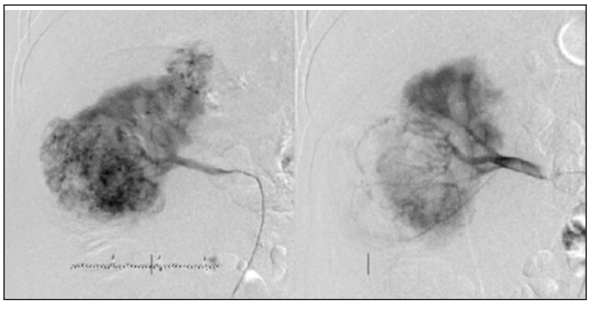

FIGURE 2: In the digital subtraction angiography images from the renal artery, tumoral staining of 75x70 mm in the inferior part of the kidney and 35x30 mm in the upper part of the kidney observed. In the control angiography images after the superselective embolization it was observed that the staining of the mass decreased significantly.

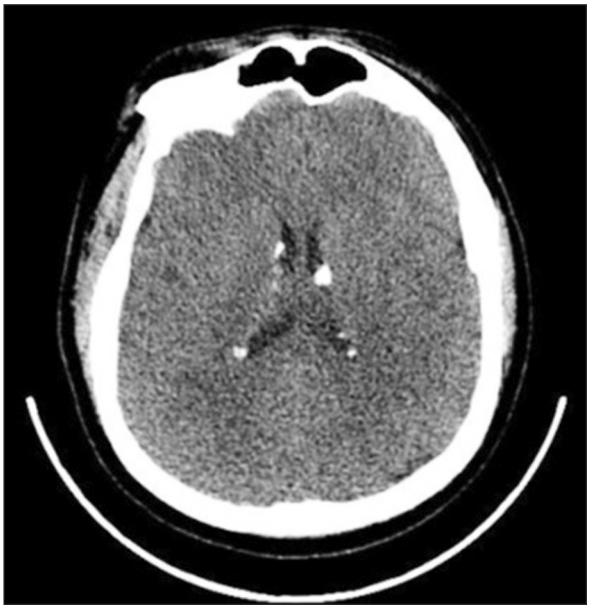

FIGURE 3: Multiple subependymal nodules in both hemispheres in brain CT.

DISCUSSION

TSC complex is a genetic, multisystemic disease that affects many systems such as brain, retina, kidneys, heart, skin and lungs. It is seen in one in 6,000-10,000 live births.[4] The diagnostic criteria defined in 1998 were updated in 2012 at the TSC consensus conference. Genetic test results have been added to the diagnostic criteria, and diagnostic classes have been updated as definitive and probable (Table 1).[5] The diagnosis is mostly made in childhood while investigating the etiology of seizures.[4] The age at diagnosis of TSC ranges from birth to 73 years in a retrospective study conducted by Staley in 2011. In 81% of the patients, the age at diagnosis is under 10. However, it has been reported that patients diagnosed in adolescence and adulthood are not rare.[6] In a retrospective study conducted by Kocak et al., attention was drawn to the fact that the average age of diagnosis was 13 despite the easy accessibility of imaging methods.[4]

Renal angiomyolipoma is the most common benign mesenchymal tumors of the kidneys.[1] They consist of fat, smooth muscle, and abnormal vascular structures. They may be sporadic or associated with TSC.[2] Multiple angiomyolipoma in both kidneys are more likely to be associated with TSC than solitary angiomyolipoma.[7]

Detection of fat content by CT and magnetic resonance imaging is an important finding for the diagnosis of angiomyolipoma. Although clinically they are mostly asymptomatic, they can be life-threatening.[3] Spontaneous renal angiomyolipoma hemorrhages may present with acute flank pain, palpable mass, and hypovolemic shock.[7] The lack of internal elastic lamina of the vascular structures in angiomyolipoma creates a predisposition to bleeding.[8] Many studies have shown that the risk of bleeding is directly proportional to their size. In addition, it has been reported that the size of angiomyolipoma and the risk of bleeding increase during pregnancy.[1]

Treatment of angiomyolipomas that are symptomatic or larger than 4 cm is recommended. The chosen treatment method may be partial nephrectomy or selective embolization.[2] Selective embolization is the first preferred method in the treatment of acute hemorrhagic angiomyolipoma.[3] Discussions on the choice between embolization and surgery mainly focus on safety, efficacy, preservation of kidney tissue, and pregnancy. Although both surgery and embolization are beneficial in patients with angiomyolipoma <4 cm in diameter, renal artery

TABLE 1: Diagnostic criteria for tuberous sclerosis complex 2012.

A. Genetic diagnostic criteria	
The identification of either a TSC1 or TSC2 pathogenic mutation in DNA from normal tissue is sufficient to make a definite diagnosis of tuberous sclerosis complex (TSC).	
B. Clinical diagnostic criteria	
Major features	Minor features
Hypomelanotic macules (≥3, at least 5-mm diameter)	"Confetti" skin lesions
Angiofibromas (≥3) or fibrous cephalic plaque	Dental enamel pits (>3)
Ungual fibromas (≥2)	Intraoral fibromas (≥2)
Shagreen patch	Retinal achromic patch
Multiple retinal hamartomas	Multiple renal cysts
Cortical dysplasias*	Nonrenal hamartomas
Subependymal nodules	
Subependymal giant cell astrocytoma	
Cardiac rhabdomyoma	
Lymphangioleiomyomatosis	
Angiomyolipomas (≥2)	

Definite diagnosis: Two major features or one major feature with ≥2 minor features.
Possible diagnosis: Either one major feature or ≥2 minor features.

embolization is currently recommended as first-line therapy for bleeding angiomyolipoma and is increasingly used as preventative therapy for angiomyolipoma at risk of bleeding. Moreover, compared to surgical alternatives, embolization has many advantages such as low complication rate, less trauma, preservation of renal function, and satisfactory short-term (<5 years) outcome.[1] Although embolization is currently the preferred treatment for symptomatic or ruptured renal angiomyolipoma, embolization has its limitations. Embolization causes tumor shrinkage in most patients, it is stated that tumor shrinkage alone is not a reliable exclusion criterion for recurrent bleeding.[1] As seen in TSC and lymphangioleiomyomatosis, angiomyolipoma with multiple or giant aneurysms may respond poorly to embolization, embolization efficiency is low in angiomyolipoma with high fat/vascularity ratio and may require repeated embolization; and finally, the procedure can not be applied to pregnant women due to radiation.[1] As a conclusion, renal-originated retroperitoneal hemorrhages should also be considered in young patients presenting with non-traumatic acute abdomen, and the possibility of tuberous sclerosis should be kept in mind in the presence of angiomyolipoma in such patients, even if the patient is not diagnosed. Although there is no consensus on the treatment of asymptomatic angiomyolipoma smaller than 4 cm, endovascular super selective embolization is the first treatment option that should be considered as a minimally invasive method with proven efficacy and very low complications in patients presenting with acute angiomyolipoma bleeding.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Elif Çiğdem Karataylı;* ***Design:*** *Elif Çiğdem Karataylı;* ***Control/Supervision:*** *Onur Ergun;* ***Data Collection and/or Processing:*** *Elif Çiğdem Karataylı;* ***Analysis and/or Interpretation:*** *Elif Çiğdem Karataylı;* ***Literature Review:*** *Elif Çiğdem Karataylı;* ***Writing the Article:*** *Elif Çiğdem Karataylı;* ***Critical Review:*** *Onur Ergun;* ***References and Fundings:*** *Elif Çiğdem Karataylı;* ***Materials:*** *Elif Çiğdem Karataylı;* ***Other:*** *Azad Hekimoğlu, Erdem Birgi, Behlül Atalay.*

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