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CASE REPORT

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Renal manifestation of tuberous sclerosis (Bourneville's disease) – case presentation

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Summary

Background: Tuberous sclerosis is a phacomatosis-type disease that causes the growt of non-malignant tumors in the brain as well as in other vital organs such as kidneys, heart, eyes, lungs, liver and skin. Abdominal symptoms usually include kidney disorders that can precede the appearance of symptoms from other organs. Kidney failure is also the main cause of deaths in adults over the age of 30. One of the most characteristic findings in diagnostic imaging of patients with tuberous sclerosis are multiple angiomyolipoma tumors and cysts of the kidneys. Patients with TSC are also more likely to develop clear cell renal cell carcinoma.

Case Report: Presentation of a clinical case of a patient with tuberous sclerosis complicated by bleeding from the right kidney tumor treated by embolization.

Conclusions: Diagnostic imaging (including ultrasonography, CT scans and MRI) plays a crucial role in diagnosis and management of visceral lesions in patients with TSC.

Regular check-ups to manage the development of the disease are necessary, because tumors can be multiple and bilaterally located; they also tend to grow very rapidly and reach very large sizes.

Retroperitoneal hemorrhage caused by tumor's rupture, also known as the Wunderlich syndrome, is a life-threatening complication of TSC.

MeSH Keywords: Diagnostic Imaging • Tuberous Sclerosis • Uterine Artery Embolization

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Background

Tuberous sclerosis (TSC, Bourneville's disease) is one of the group of diseases referred to as neuroectomesodermal dysplasias of phacomatoses, characterized by the presence of dermal lesions and hypertrophic lesions within the nervous system, organ of vision and internal organs such as kidneys, liver, heart, or lungs [1]. The disease is chronic and progressive.

The incidence is estimated at 1:10,000, and 1:6,800 in the pediatric population [2].

Tuberous sclerosis is inherited by the autosomal dominance pattern Familial morbidity accounts for about one third of cases; remaining cases are occasional or due to gonadal mosaicism of one of the parents [3,4].

Tuberous sclerosis may also cause significant diagnostic problems due to a wide range of clinical forms, from very severe to hardly detectable, oligosymptomatic forms.

For many years, TSC was diagnosed on the basis of Vogt's triad including mental impairment, epilepsy and facial lesions known as adenoma sebaceum of Pringle.

However, it has been determined that all three symptoms coexist in as little as 29% of patients, while 6% of patients present with none of these symptoms being detected (Tables 1 and 2).

Table 1. Diagnostic criteria for tuberous sclerosis by Roach et al.

Major symptoms	Minor symptoms
Multiple pits in dental enamel	Multiple renal cysts
Rectal polyps	Facial angiofibroma or forehead plaques
Bone cysts	Non-traumatic periungual fibromas
White matter migration foci	Leukodermal lesions (>3)
Gingival fibromas	Shagreen patches
Extrarenal hamartoma	Multiple retinal hamartomas
Retinal changes	Cortical brain nodular lesions
Confetti-type skin lesions	Periventrical, subependymal nodular brain lesions
	Giant cell astrocytoma
	Cardiac rhabdomyoma
	Pulmonary lymphangioleiomyomatosis
	Renal angiolipoma

Table 2. Diagnosis of tuberous sclerosis.

Certain diagnosis	Two major symptoms or one major and two minor symptoms
Probable diagnosis	One major and one minor symptom
Possible diagnosis	One major symptom or two or more minor symptoms

Case Report

A 16-year-old male patient with drug-resistant epilepsy, intellectual disability and diagnosed with tuberous sclerosis was admitted to the Pediatrics Department due to abdominal pains. Previous imaging studies revealed, among others, the following organ lesions: numerous subependymal nodular lesions and hamartomata-type focal lesions within the central nervous system (partly due to surgical treatment), myoma within cardiac intraventricular septum, diffuse angiomyolipoma lesions in liver and kidneys with elevated echogenicity of the cortical layer of both kidneys and an additional isolated, large angiomyolipoma-type tumor within the right kidney.

Abdominal CT scan upon admission revealed bleeding from the aforementioned large tumor in the right kidney with penetration into the pyelocalyceal system (Figures 1 and 2).

Patient was qualified for embolization of right kidney.

Femoral arterial puncture was used to perform plain aortonephrography followed by selective angiography of the right renal artery that pathological vascularization of renal tumor part from renal artery branches in the upper part of the tumor and arteriovenous fistula in the lower part of the tumor (Figure 3).

Next, PVA embolization was performed to close the vascular bed of the upper part of the tumor and spiral MDS embolization was carried out to close the trunk of the artery supplying blood to the arteriovenous fistula in the lower part of the tumor.

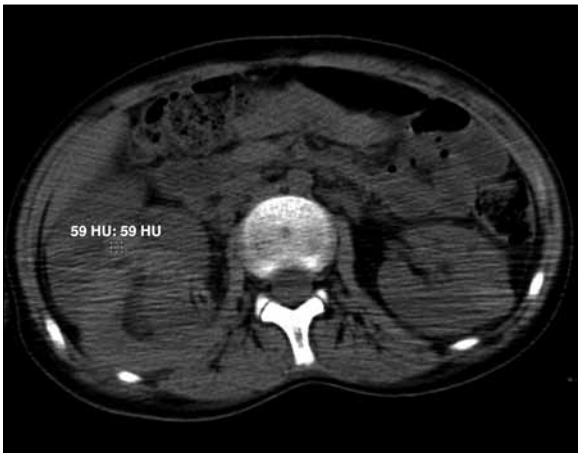

Figure 1. Abdominal CT, native phase. Right kidney tumor with foci of fatty – AML – bleeding into pyelocalyceal system.

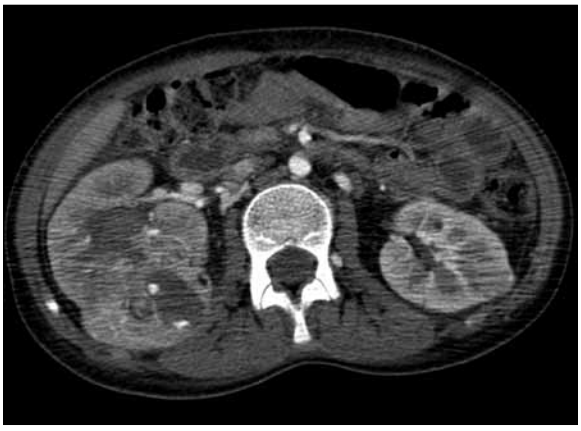

Figure 2. Abdominal CT after administration of the contrast agent. Right kidney tumor with foci of fatty – AML – bleeding into pyelocalyceal system.

Follow-up angiography revealed no contrast enhancement in tumor vessels and maintenance of normal renal vascularization (Figure 4).

Subsequent imaging examinations revealed reduction in the size of the aforementioned tumor lesion within the right kidney.

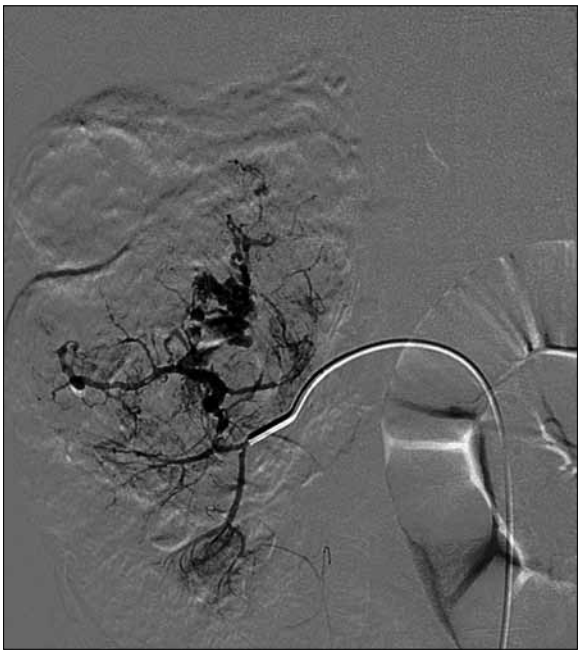

Figure 3. Selective angiography of the right renal artery – pathological vessels in the tumor.

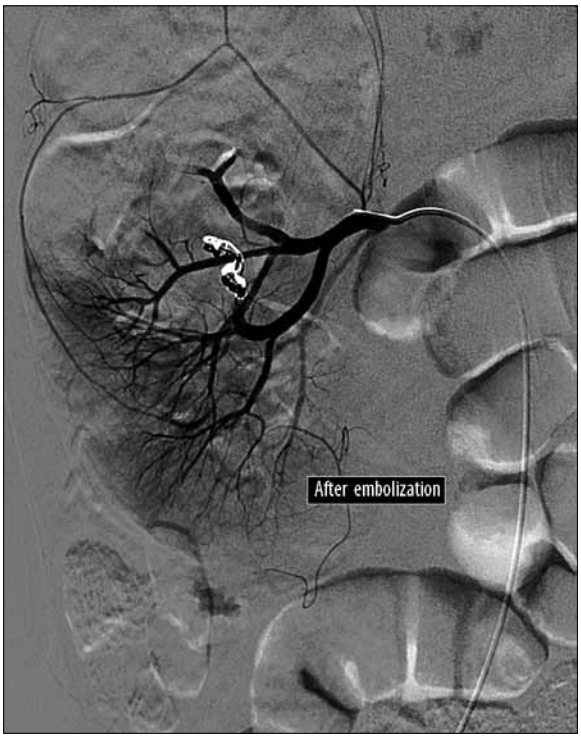

Figure 4. Control angiography after embolization.

Discussion

Abdominal symptoms of TSC usually include kidney disorders that can precede the appearance of symptoms from other organs. At the same time, kidney failure is the main cause of deaths in adults over the age of 30.

In more than one half of patients, first lesions are detected in periodic follow-up of patients and include reduced endogenous creatinin clearance and changes in renal structure (echogenicity) in ultrasound examinations. One half of cases involves multicystic kidneys (with small or large cysts) or complete renal involvement with angiomyolipoma. End-stage renal disease is observed mainly in adult patients, and much less commonly in pediatric patients.

Renal lesions characteristic for TSC and detected in imaging studies include multiple angiomyolipoma (AML)-type tumors and renal cysts. Patients with TSC are also more likely to develop clear cell renal cell carcinoma as compared to the overall population.

Angiomyolipoma (AML) is a benign tumor consisting of various proportions of smooth muscle tissue, adipose tissue and vascular tissue, with vascular structure changes leading to the thickening of vessel walls and incomplete growth of internal elastic lamina, predisposing patients to hemorrhagic complications [5,6].

AML is the most common renal complication of tuberous sclerosis. Multiple, bilateral renal AMLs are observed in 70–90% of patients with TSC, more frequently in women [7,8]; at the same time, ca. 20% of all AML cases are associated with TSC.

AML may have the form of bilateral and/or multiple renal tumors causing pain within the lumbar region, hematuria, arterial hypertension and symptoms of renal insufficiency, although no significant clinical symptoms are usually observed in relation to renal lesions.

Angiomyolipoma may be diagnosed from a characteristic ultrasound image featuring a hyperechogenic focal lesions with echogenicity often higher than that of the adipose tissue within the renal hila.

Computed tomography (CT) is the recommended method for detection of adipose tissue in diagnostically difficult cases, since demonstration of even the tiniest amounts of adipose tissue is considered to be pathognomic for AML.

T1-weighted magnetic resonance (MRI) scans feature high intensity signals of the adipose tissue; these should be confirmed by fat-saturation sequences [9].

The management of AML-type lesions depends on their size and clinical symptoms – small, asymptomatic AMLS require only close monitoring, particularly in the pediatric population where a trend for their rapid growth is observed. Large lesions (larger than 4 cm) often require treatment by partial or total nephrectomy. If bleeding symptoms are observed, the first line treatment consists of angiographic embolization [10].

Renal cysts are the second most common renal complication of TSC.

Most commonly, the cysts are multiple and bilateral, with onset times being shorter for multiple renal cysts as compared to AMLs. Very intense lesions may lead to complete destruction of renal parenchyma and end-stage renal disease.

Tuberous sclerosis is also associated with higher incidence of clear cell renal cell carcinoma than that observed in the overall population – in the group of TSC patients, the morbidity is at the level of 2–3% [11].

In addition, the disease is diagnosed more often in younger patients (usually in the third decade of life) compared to overall population, as well as in women and in bilateral localization – bilateral tumors are detected in nearly one half of the TSC cases.

Considering the above, detailed differential diagnostics is required in TSC patients, for example allowing to differentiate atypical AML lesions from renal cell carcinoma. The assessment of calcifications within the tumor may be helpful, as they are more common in carcinomas or oncocytomas than in AMLs.

Of key importance is the identification of adipose foci that are characteristic for AML; however, it should be kept in mind that ca. 5% of all AMLs are lesions with minimum quantities of adipose tissue that is difficult to detect in CT scans (MRI scans provide easier identification of these lesions).

One should also remember about potential complications posing direct threat to the lives of patients. In tuberous sclerosis, such complication associated with the presence of AML lesions is massive bleeding into the retroperitoneal space due to spontaneous tumor rupture; this complication is known as Wunderlich syndrome [12–14].

An important feature of the etiology of this syndrome is the lack of evident trauma in patient's history; the spontaneous rupture of tumor structures is due to the weak and elastic fibers-deficient vascular components of AML. This complications is usually observed in case of tumors larger than 4 cm, and the treatment of choice is embolization or partial resection [15–17].

Conclusions

Abdominal symptoms of TSC usually include kidney disorders, and renal complications are the main cause of deaths in adults over the age of 30.

Multifocality of lesions, significant dynamics of growth, common bilateral location of lesions and, mostly, their proneness to reach large sizes requires early and regular monitoring by means of imaging techniques.

Spontaneous tumor rupture with bleeding into the retroperitoneal space, also known as the Wunderlich syndrome, is a relatively common complication posing threat to patients' lives.

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