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CASE REPORT

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# Imaging studies in a 17-year-old boy with tuberous sclerosis complex – a case report

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## Summary

**Background:** Tuberous sclerosis complex is e genetic disorder characterized by lesions affecting the brain, skin, eyes and internal organs – kidneys, heart, liver and lungs.

**Case Report:** The case of a 17-year-old boy with delayed proper diagnosis of tuberous sclerosis complex and multiple lesions in brain, lungs, heart and kidneys has been described.

**Conclusions:** The authors would like to underline the very rare incidence of sclerosis tuberous complex and the need for periodic follow-up imaging of central nervous system, chest (with thorough evaluation of heart and lungs), and abdominal cavity. Moreover, the authors would like to underline a significantl delay in a process of reaching a final diagnosis of the disease.

**Key words:** children • tuberous sclerosis complex • imaging studies

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## Background

Tuberous sclerosis complex (TSC) is a genetically determined disorder, inherited as a dominant autosomal trait with differentiated gene penetration [1–6]. Mutations within the following genes: *TSC1* encoding tuberine and *TSC2* encoding hamartine (located respectively on chromosomes 9q34 and 16q13) play the key role in pathogenesis [1–4]. The disease is manifested by anomalies located within the brain, lungs, heart and kidneys, as well as bones and eyes [1–6]. The diagnosis is based on *Desch* criteria (it can be established with certainty if 2 major and 2 minor criteria are met) [1–4]. The clinical symptoms include epileptic seizures, mental retardation, skin lesions of albinotic and shagreen patch type, perionychial fibromas and fibroangiomas of the face. Additionally, there are numerous anomalies of the internal organs: angiomyolipomas and cysts in the kidneys, hamartomas in the cerebral cortex, rhabdomyomas in the heart, or lymphangioleiomyomatosis in the lungs [1–6]. No causal treatment is available. The prognosis is poor – ca. 25% of patients die before reaching 10 years of age, and another 50% – before reaching 25 years of age [2].

## Case Report

A 12-year-old boy was referred to our Department in 2003 with suspected hypertension and renal lesions (cysts and suspicion of an angiomyolipoma), history of a few clonaltonal seizures in infancy and mild mental retardation (the child attended a special school). The physical development was normal

The boy's parents were young, healthy and unrelated to each other. The familial history for genetic anomalies was non-contributory.

On the day of admission the child did not report any symptoms. Physical examination revealed numerous (round or ellipsoid) skin discolorations located primarily on the lower extremities and the trunk, as well as two longitudinal discolorations resembling an ash leaf in shape. On facial skin – two small sebaceous adenomas. Additionally, single paronychial fibromas were found on both hands.

The laboratory findings included: ESR, BCC, hepatic and renal function parameters and serum ionogram within

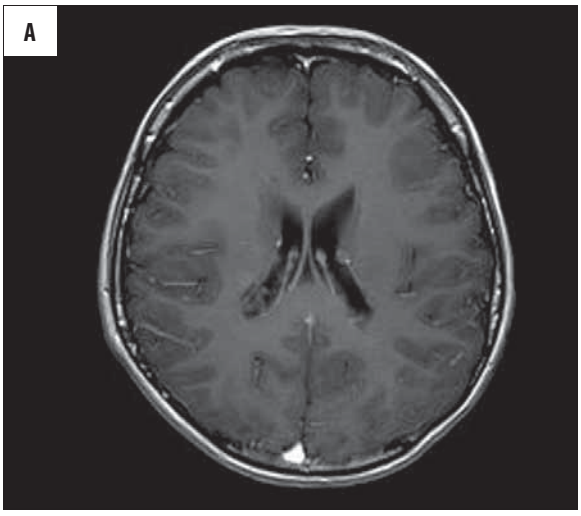


**Figure 1A.** MR tomography of the head; T1-weighted, contrast-enhanced images – a few contrast-enhanced tumors up to 9 mm in diameter (hamartoma) visualized in the walls of both lateral ventricles.

normal limits, no significant abnormalities in urinalysis. Magnetic resonance tomography of the head revealed a few contrast-enhanced nodules up to 9 mm in diameter in the walls of both lateral ventricles, two cortico-subcortical irregular foci up to ca, 20 mm, non-contrast-enhanced, surrounded by cortex with signs of pachygyria, in the parietal lobes (Figure 1). Chest CT did not reveal any abnormalities. No abnormalities were found in EEG, USG of the heart and ECG, either.

Abdominal USG: normal position and shape of both kidneys, ca. 9 cm in the longitudinal dimension. Bilateral single hyperechoic solid lesions 3–10 mm in diameter in the right kidney, the largest lesion ca. 20 mm in diameter (a suspected angiomyolipoma) located in the left one, and small cysts (Figure 2). Abdominal CT confirmed the presence of angiomyolipomas and cysts in both kidneys (Figure 3). On dynamic scintiscan with $Tc^{99m}$-labeled DTPA, radiopharmaceutical uptake and elimination was normal in both kidneys.

On the basis of anamnesis, physical examination and imaging results, the diagnosis of tuberous sclerosis complex was established. The treatment of hypertension with an ACE inhibitor was instituted with a good result. For the subsequent 5 years, the patient was remained under close observation in nephrological, cardiological, genetic and neurological outpatient departments.

In control examinations performed in 2008 (after 5-year follow-up), MR tomography of the head revealed no differences in comparison with the results of 2003. Chest CT detected 2 nodules 10 mm in diameter, which had not been visible in the earlier scans (Figure 4).

On abdominal USG, increased sizes of angiomyolipomas was found – in the right kidney, the largest lesion reached a diameter of 16mm (Figure 5), a solid lesion of angiomyolipoma type 20 mm in diameter was visualized in the inferior pole cortex of the left kidney, as well as a tumor 56 mm in diameter extending beyond the outline of the kidney with normal renal function and normal scintigraphy results of the former lesions. Abdominal CT confirmed the results obtained on USG (Figure 6). Static scintiscan with $Tc^{99m}$-labeled DTPA, visualized a focal decrease of radioligand uptake, corresponding to the location of an extrarenal tumor, in the lower pole of the left lung.

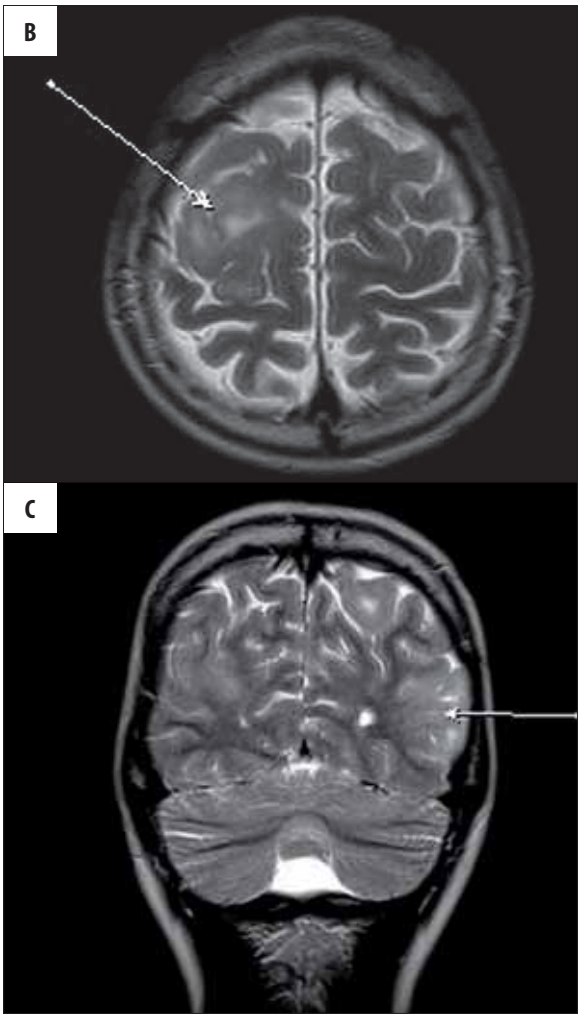


**Figure 1B,C.** Additionally, in both parietal lobes, two cortico-subcortical irregular foci up to ca. 20 mm in diameter, surrounded by the cortex with signs of pachygyria, showing no contrast enhancement, were visualized

Ultrasound scan of the heart revealed the presence of a hyperechoic tumor of ca. 10×14 mm in the IVS on the LV side (at $^1/_3$ of its length). The tumor had been described for the first time in 2007. It caused no hemodynamic abnormalities.

## Discussion

The incidence of tuberous sclerosis complex in children is estimated at 1:6800, or even 1:23000 on the general population [1–3,5,7–10]. These data are inconsistent with our observations. In 1990–2008, 3 children with TSC were diagnosed in the Department of Radiology.

The typical symptoms of TSC include: seizure, delayed psychomotor development, sebaceous adenomas of the facial

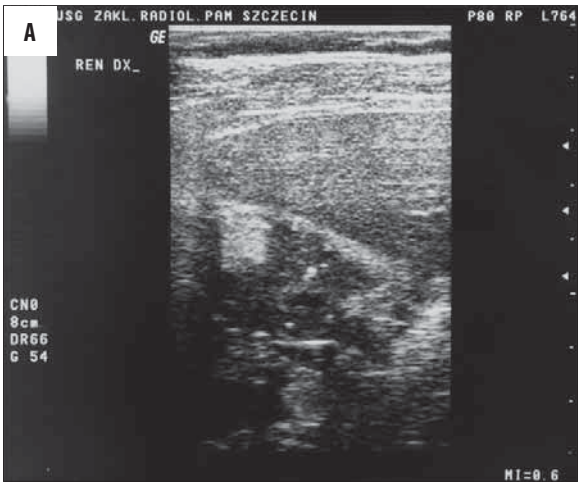


**Figure 2A.** US scan of the right kidney – a solid lesion of angiomyolipoma type 8 mm in diameter visible in the renal cortex.

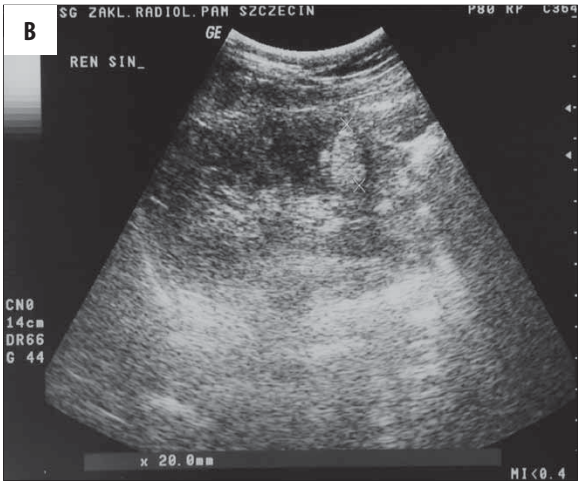


**Figure 2B.** US scan of the left kidney (2003) – in the cortex of the inferior pole, a 2 cm hyperechoic tumor of angiomyolipoma type.

skin, paronychial fibromas, discolorations of the skin, renal angiomyolipomas and cysts, hamartomas of the brain and lymphangioleiomyomatosis of the lungs [1,3,5,7,8,10].

The boy described by us had presented most of these symptoms (seizures, mental retardation, typical skin lesions, paronychial lesions) since early childhood. Despite frequent contacts with physicians of various specialities (GPs, neurologists, pediatricians), the correct diagnosis was established as late as at the age of 12 years. The diagnostic errors seem to be due to low level of knowledge concerning TSC, which is associated primarily with its very low incidence.

Cerebral lesions are observed in ca. 90–95% of patients with TSC [1,3]. They include primarily small cortical tumors and subependymal tumors localized along the lateral ventricular walls, as well as in the cerebellum and the spinal cord [1–4].

Because of characteristic calcifications of subependymal tumors, CT is considered to be the best modality for their identification [1–4]. In contrast, cortical tumors are best visualized by MR tomography [1,4]. In the reported case,

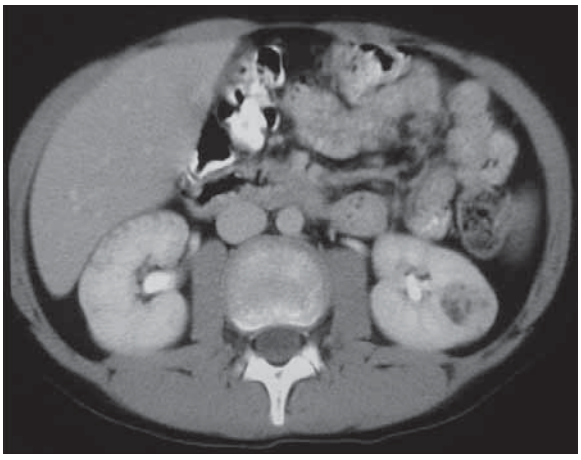

**Figure 3.** Abdominal CT with contrast enhancement (2003) in the same patient – a 2 cm tumor (angiomyolipoma) in the inferior pole of the left kidney.

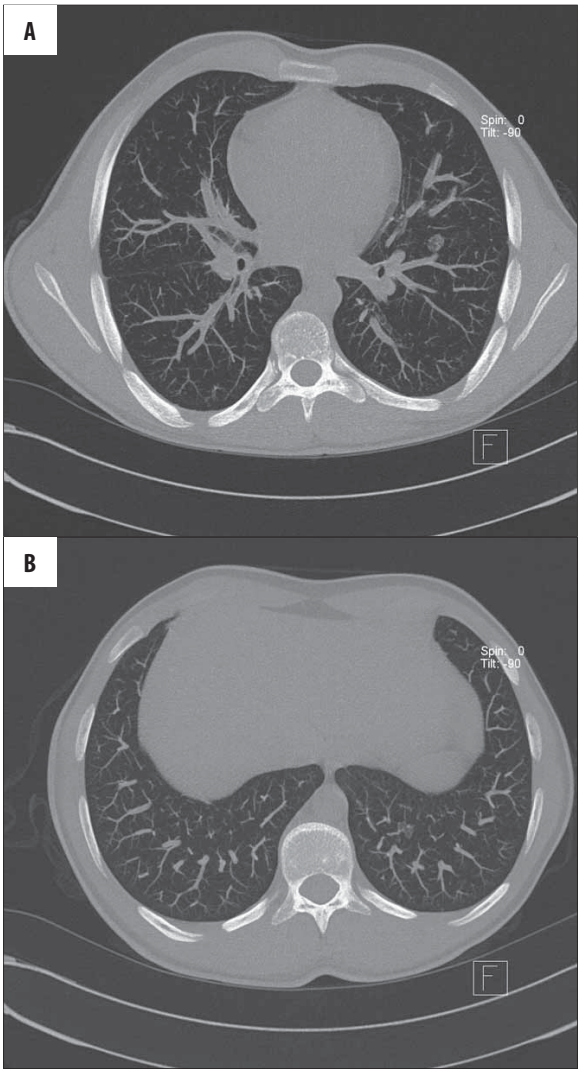


**Figure 4AB.** Chest CT – two solid lesions visible.

MR tomography visualized single tumors up to 9 mm diameter in the walls of both lateral ventricles and two corticosubcortical irregular foci ca. 20 mm in diameter located in

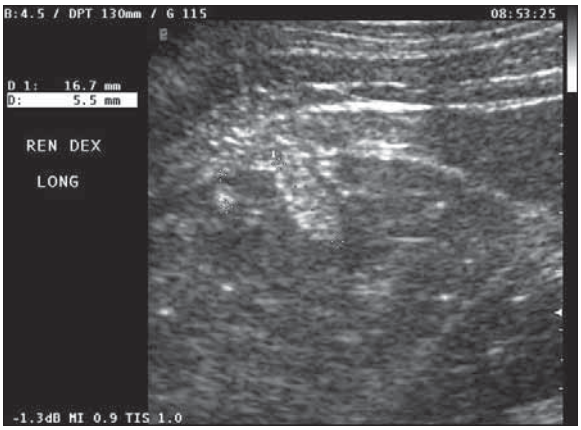


**Figure 5.** Control US scan performed after 5 years – a solid lesion of angiolipoma type ca. 16 mm in diameter visible in the cortex of the right kidney.

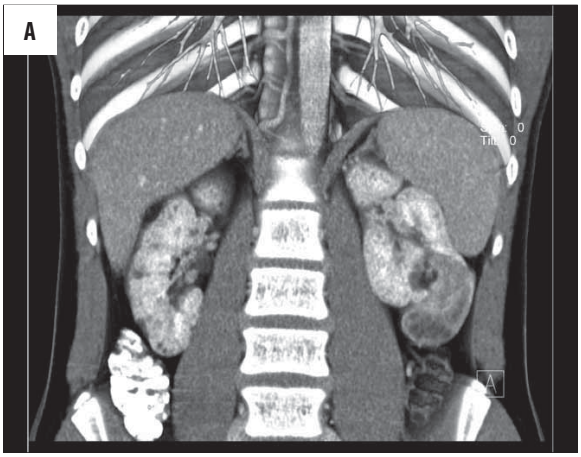


**Figure 6A.** Control TK with contrast enhancement of the kidneys performed after 5 years – a large tumor extending beyond the kidney outline in the inferior pole.

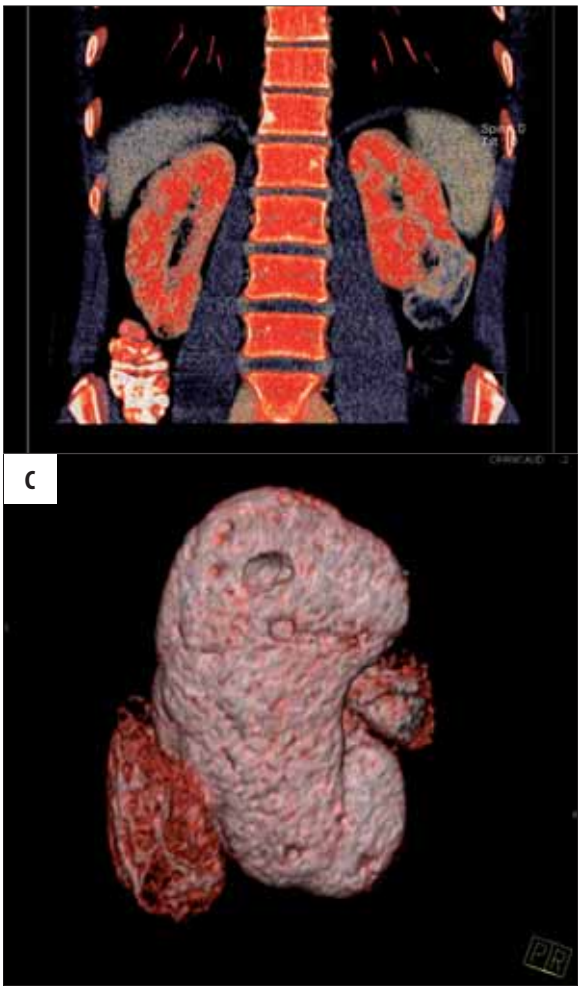


**Figure 6B,C.** TK VRT in the same patient – large vascular component visible within the tumor.

the parietal lobes with thickened layer of the gray matter – pachygyria.

Angiomyolipomas – benign tumors with varied histological structure (containing vascular, adipose tissue and smooth muscle components) are the most common kidney lesions developed in the course of TSC [1–6]. They are observed in 75–80% of patients [2–6]. According to the reports by Yates et al. and Roach et al., the tumors of this type can appear even in early childhood [1,4]. In our case, the moment when such lesions appeared is difficult to determine because the patient had undergone no imaging diagnostics before 12 years of age.

As recommended by the National Institutes of Health, single or multiple angiomyolipomas up to 40 mm diameter require observation only (periodic abdominal US scans), whereas lesions 40–60 mm in diameter (and larger), or vith vascular abnormalities, are additionally examined with angio-NMR [5]. Thus, abdominal USG is a first-line examination used in the diagnostics of such lesions in the course of TSC.

According to Arslan et al., CT or MR tomography of the abdominal cavity seems to be necessary as well to assess precisely the number, size and location of the tumors and to differentiate them from renal cell carcinoma [6].

In the reported case, the first abdominal USG already revealed angiomyolipomas of 3–10 mm diameter in the right kidney and ca. 20 mm in the left one. The diagnosis was confirmed by CT. No anomalies of the renal blood vessels were demonstrated on angio-NMR.

Angiomyolipomas tend to increase in size. This is consistent with our observations. Abdominal USG and CT scans revealed marked enlargement of the tumors in both kidneys up to ca. 20 mm, with one lesion in the left kidney reaching 56 mm in diameter. For this reason, the patient was qualified for enucleation of the tumor (histopathological diagnosis – renal cell carcinoma).

Another renal complication observed in the course of TSC are multiple bilateral cortical cysts present in ca. 91% of cases [2,4], This is also consistent with our observations. The presence of the cysts was confirmed by abdominal USG and CT both during the diagnostics of TSC and after 5-year follow-up. No significant changes in their number and size were observed, in contrast to the findings concerning angiomyolipomas.

The heart is also affected by organic abnormalities developed in TSC, predominantly by tumors of rhabdomyoma type, occurring in 50–80% of patients [Arslan, Franz, Baskin]. According to Baskin, Franz, Roach et al., the lesions can be visualized by echocardiography as early as in weeks 22–28 of gestation [1,3–5]. The imaging modalities routinely used in the diagnostics of tumors developing in this location include USG of the heart and chest CT.

Heart USG performed in our patient in 2003 demonstrated no abnormalities. The subsequent, routine scans detected the presence of a hyperechoic tumor (10×14 mm) in the left ventricle of the heart only after 4 years (the lesion caused no clinical symptoms).

Pulmonary lesions of lymphangioleiomyomatosis type developed in the course of TSC are found most frequently in young women [1,3–6]. On histopathological analysis they present as aggregates of smooth muscle tissue and thin-walled cysts. According to Arslan, Roach et al., they are present in 0.1–1% of the patients [4,6]. The tumors of this type are generally asymptomatic – clinical symptoms (dyspnea, cough, hemoptysis) are usually observed between 30 and 40 years of age [4].

A routine technique used in the diagnostics of such abnormalities is conventional radiography, although it seems to be insufficient. According to Yates et al., chest CT is necessary.[1]. In the reported case, control CT allowed to detect the presence of two tumors 10 mm in diameter in the left lung as alte as after 5 years of observation.

Detection of malignant cells in the resected tumor of the left kidney provides additional evidence for the necessity of control imaging studies in children with tuberous sclerosis complex.

To date, the patient has not reported any symptoms and all the abnormalities visualized during the examinations have been asymptomatic.

## Conclusions

The authors would like to emphasize the very low incidence of tuberous sclerosis complex and the need for periodic follow-up imaging of the CNS, chest (with thorough evaluation of heart and lungs), and abdominal cavity.

Additionally, the authors would like to emphasize significantly delayed final diagnosis.

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