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A rare presentation of tuberous sclerosis complex: Complicated renal cyst leads to sepsis

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ABSTRACT

Introduction: Tuberous sclerosis complex is a rare autosomal dominant genetic disease, having multi systemic involvement. Kidneys are affected up to 80% of patients, in the form of renal angiomyolipomas, renal cysts or renal cell carcinoma. Renal cysts are presented as single or multiple lesions that are infrequently symptomatic. Rarely, tuberous sclerosis co-exists with polycystic kidney disease with poor prognosis through renal failure or hematuria. The complication of the renal cysts with the form of abscess is extremely rare. Here we present a case of tuberous sclerosis in which complicated renal cyst led to sepsis.

Case Report: A 30-year-old female, with a history of tuberous sclerosis, presented with a week-long fever and a left pleuritic chest pain. Chest radiograph disclosed a left costophrenic angle blunting. Thoracic ultrasound followed, surprisingly revealed a big subdiaphragmatic renal cystic formation pressing against left hemidiaphragm, not previously known. While the patient was septic with no reply to the empirical antibiotic therapy and with a gradually worsening dyspnea, the cystic drainage was decided, resulted in a fast clinical improvement. Proteus mirabilis was cultured from cystic content.

Conclusion: Renal disease is the most common cause of death in population affected by tuberous sclerosis. Thus, monitoring and serial radiologic examination are necessary to improve the prognosis of kidney damage. Abscess following simple renal cyst infection constitute another rare but potentially life-threatening renal complication should be taken under consideration.

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Keywords: Abscess, Complicated renal cyst, Sepsis, Tuberous sclerosis complex (TSC)

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INTRODUCTION

Tuberous sclerosis complex is a rare autosomal dominant genetic disease with incomplete penetrance. Two major loci have been identified: one in 9q34 (TSC1), the other in 16p13 (TSC2) which encode hamartin and tuberin, respectively. They are believed to function as tumor suppressors by forming a complex that regulates cellular proliferation [1]. Thus loss of heterozygosity seems to drive to tumor development causing benign tumors in vital organs such as the brain, kidneys, heart, eyes, lungs and skin [2]. Tuberous sclerosis is classically characterized by mental retardation, epilepsy and skin

lesions and the multi systemic involvement varies among affected population. Its incidence estimates in approximately 1 in 5000 to 10,000 live births [3–5]. The kidneys are affected up to 80% of patients in the form of renal angiomyolipomas, renal cysts or renal cell carcinoma [6]. Renal angiomyolipomas are the most common renal manifestations whereas renal cell carcinomas are the least. Renal cysts on the other hand, are observed with a frequency of 14–32% in the affected population with tuberous sclerosis [7]. In the more common presentation, cysts are single or multiple small lesions that are uniform in histology and rarely symptomatic [7, 8]. In less than 2% of cases, tuberous sclerosis complex co-exists with polycystic kidney disease, which carries a poor prognosis for renal survival through distortion of the renal architecture, hematuria and renal failure [7]. The complication of the renal cysts with the form of abscess is extremely rare. Here we present a rare case of tuberous sclerosis with cystic kidneys in which complicated renal cyst led to sepsis. The aim of this report is to emphasize the crucial role of monitoring in order to diagnose and improve the prognosis of renal damage.

CASE REPORT

A 30-year-old female with a history of tuberous sclerosis, presented with a week-long fever up to 40°C and a left pleuritic chest pain. Medical history included mental retardation and spontaneous pneumothorax twice before five and two years respectively, treated with a chest drain insertion. The existence of any mutation was not known by the patient and her family. She had no smoking history and did not take any medication. She did not mention alcohol use. On admission the patient was alert. She had high grade fever up to 40°C, hypoxemia with arterial blood gases showing PaO_2 66 mmHg, PCO_2 29 mmHg, pH 7.48, HCO_3 21.6 mmol/L, breathing room air (FiO_2 = 0.21). She had sinus tachycardia with 130 pulses per minute, tachypnea with 16 breaths per minute and low blood pressure of 100/60 mmHg. Clinical examination revealed hypomelanotic macules on the trunk and limbs, facial angiofibromas and shagreen patch (Figure 1A) in addition to subungual fibromas (Figure 1B). The lung auscultation revealed reduced lung sounds in the left lower lung field. She had absence of pain in abdominal examination with no hepatosplenomegaly.

The initial laboratory work-up showed elevated inflammatory markers. C-reactive protein leveled up to 30 mg/dL and ESR up to 65 mm. She had leukocytosis with neutrophilia. The white blood cell counted 15,000 per microliter and had also elevated serum d-dimer level of 600 ng/mL (normal values ≤ 250 ng/mL). Tests of liver and renal function were normal, as were levels of plasma electrolytes, glucose, calcium, total protein, albumin and urinalysis. The urinary to creatinine ratio was normal as well. Chest radiograph disclosed a blunting of the left costophrenic angle (Figure 2). The patient was treated like suffering from left lower lobe pneumonia with an ipsilateral small parapneumonic effusion. Thoracic ultrasound followed demonstrated a subtle pleural effusion, while, it was surprisingly detected a big sub diaphragmatic cystic formation pressing against hemidiaphragm, not previously known (Figure 3). According to the ultrasound images this was a cyst with mixed content, both a cystic area and a solid component. Computed tomography pulmonary angiography was conducted because of the elevated levels of d-dimers in addition to suspicious clinical features which was negative for pulmonary embolism. It disclosed a severe lung cystic disease, an atelectasis-related consolidation in left lower lung lobe and a subtle pleural effusion. (Figure 4A–C) From the lower slices of the imaging the subdiaphragmatic cystic formation was detected (Figure 4D). Computed tomography scan of abdomen showed swelling of kidneys (longitudinal axis of right kidney ~18 cm and left kidney ~20 cm), multiple cysts and angiomyolipomas bilaterally. Furthermore, it revealed a sizeable cyst (14x9x8 cm) with thin wall, increased fluid density and septations, dashing out from upper lobe of the left kidney, pressing against the adjacent structures and left hemidiaphragm (Figure 5A–B). The patient medicated with piperacillin/tazobactam and moxifloxacin intravenously with no clinical response. While she was septic with fever waves coming back every four to six hours with no reply in the antibiotics and a gradually worsening respiratory deficiency, the cystic drainage was decided. It was made through a nephrostomy catheter and it resulted in an immediate remission of fever. *Proteus mirabilis* was cultured from cystic content and targeted antibiotic treatment with ciprofloxacin resulted in fast clinical improvement. She hospitalized for still four days and totally medicated for twenty days. Two years later in follow-up examinations appeared to be in good physical condition without any symptoms or renal insufficiency.

DISCUSSION

In this patient, we faced a previously unknown kidney involvement of the tuberous sclerosis complex, with numerous renal cystic formations and renal angiomyolipomas bilaterally. According to literature, the majority of individuals with tuberous sclerosis complex will develop some form of kidney disease including, especially angiomyolipomas and/or renal cysts during their lifetime with various complications [3]. Different stages of renal insufficiency, hypertension or lethal hematuria, caused by mass effects, through compressing urine outflow and/or distorting normal renal parenchyma will be manifested. Especially, angiomyolipomas cumulate risk factors for bleeding and should be preventively treated, if possible by embolization. Renal cystic disease is the second most common renal manifestation after angiomyolipomas. Three different types of renal cystic disease have been associated with tuberous sclerosis complex and these

Figure 1: The clinical examination of TSC patient revealed: (A) Facial hypomelanic macules and angiofibromas, (B) Subungual fibromas (arrow).
Abbreviations: TSC: Tuberous Sclerosis Complex.

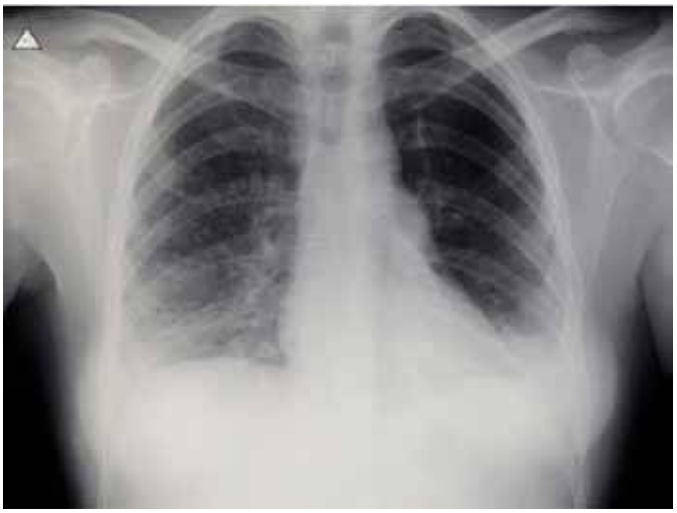

Figure 2: Chest radiograph showing a hyperlucent left upper and mid zone, a blunting of the left costophrenic angle and a normal cardiothoracic ratio.

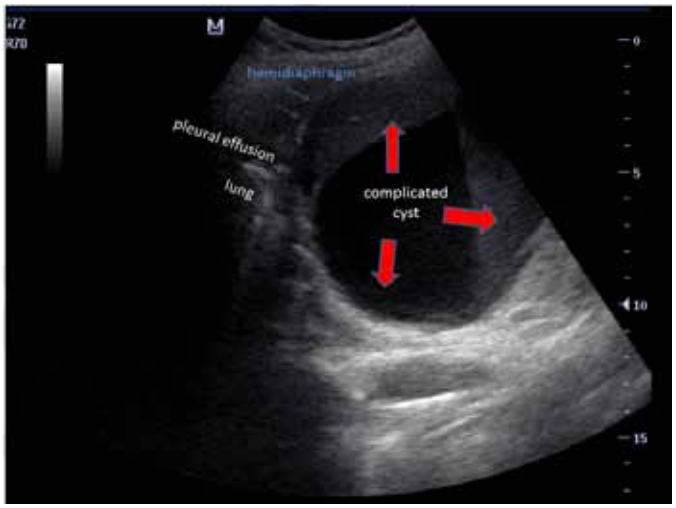

Figure 3: Thoracic ultrasound showing a big sub diaphragmatic cystic formation pressing against hemidiaphragm with mixed content, both a cystic area and a solid component (arrows). The splenic border was displaced by cystic formation effect. It showed also a small pleural effusion in left costophrenic angle.

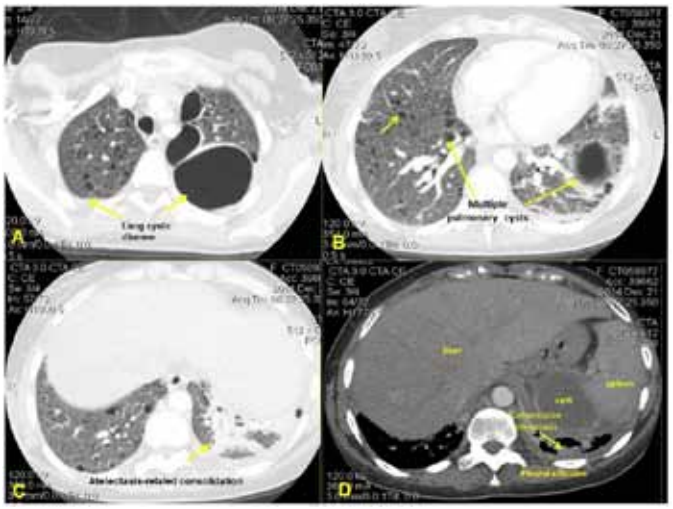

Figure 4: Computed tomography pulmonary angiography showing: (A) A severe lung cystic disease with three big lung cysts (arrows) in left upper lobe which destroyed lung *parenchyma,* (B) Multiple intrapulmonary smaller lung cysts bilaterally (arrows), (C) A compressive *atelectasis*-related *consolidation in left lower lung lobe (arrow) and a subtle pleural effusion because* of the displacement of the left-sided *diaphragm, and (D) Lower slices of the imaging demonstrated a big* subdiaphragmatic cystic formation pressing against left hemidiaphragm.

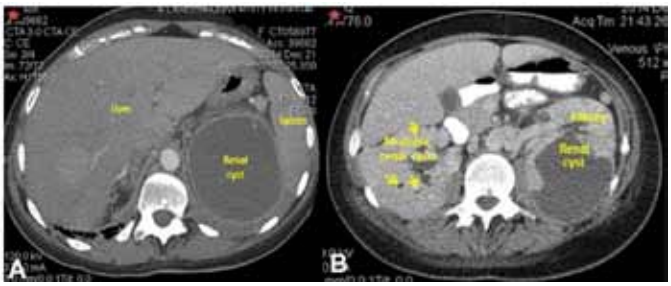

Figure 5: Contrast-enhanced arterial-phase computed tomography scan of the abdomen showed: (A) A sizeable cyst (14x9x8 cm) with thin wall, pressing against spleen and adjacent structures, (B) Enormous renal cyst dashed out from upper lobe of the left kidney, while multiple smaller simple *cysts* revealed in the right kidney.

are: (a) single or multiple renal cysts, (b) TSC2/PKD1 contiguous gene syndrome, and (c) glomerulocystic kidney disease [7].

Cysts, although frequently occurring in TSC, are usually few in number, their size is small, and they cause no symptoms. They are more common related to TSC2 mutations. When these mutations exist tend to result in a more severe clinical profile, including more acute renal involvement in younger individuals [7, 9]. The prevalence of renal cysts increases with age and is more common in males than females [7].

Concerning to TSC2/PKD1 contiguous gene, it is characterized by deletions which inactivate major genes for tuberous sclerosis and autosomal dominant polycystic kidney disease, TSC2 and PKD1, respectively, lying adjacent to each other at chromosome 16p13.3. When the

tumor suppressor genes are inactivated by mutations, cell growth is unchecked, leading to tumors. Cysts may, therefore, be the result of excess growth of kidney epithelial cells, which surround a fluid-filled cavity. Affected patients are usually diagnosed during the first year of life or early childhood, but rarely patients are not diagnosed until adulthood, with hypertension and renal insufficiency being the major manifestations [7].

Finally, glomerulocystic kidney disease is a rare finding that is usually diagnosed during the neonatal period. Affected kidneys were typically enlarged and had renal cysts on imaging studies and glomerular cysts on histologic examination.

In our case study, no any known mutations of TSC2 or PKD1 were mentioned, the renal cystic disease was unknown for years, the patient had no systemic follow up and was asymptomatic. To the best of our knowledge this is the first case report in which severe sepsis caused by a complex renal cyst, was the first manifestation of a previously unrecognized renal involvement of tuberous sclerosis complex. It is of high importance the monitoring and regular screening of affected population in order to diagnose and prevent renal complications as well as malignant transformation. This case study also emphasizes the significant value of the thoracic ultrasound as a handy bedside diagnostic tool in the management of disease of pleura and neighboring structures.

CONCLUSION

Renal complications are the most common cause of death in adult patients with tuberous sclerosis complex, thus renal involvement has a crucial importance on the course of this disease. Monitoring and serial radiologic examination are necessary to improve the prognosis of renal damage. Abscess following simple renal cyst infection constitutes a rare but lethal complication due to renal involvement, must always kept in mind in affected individuals.

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Author Contributions

Kotsiou Ourania – Substantial contributions to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Gourgoulianis Konstantinos – Substantial contributions to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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