ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2021 August 26; 9(24): 6964-7291

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

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RESPONSIBLE EDITORS FOR THIS ISSUE

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NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

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PUBLICATION DATE
August 26, 2021

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World J Clin Cases 2021 August 26; 9(24): 7085-7091

DOI: 10.12998/wjcc.v9.i24.7085

ISSN 2307-8960 (online)

CASE REPORT

Tuberous sclerosis complex-lymphangioleiomyomatosis involving several visceral organs: A case report

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Author contributions: Chen HB and Xu XH designed the report; Chen JL collected the patient's clinical data; Yu CG, Wan MT, Feng CL, Zhao ZY, and Mei DE analyzed the data and wrote the paper; all authors have read and approved the final manuscript.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest to report.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and

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Abstract

BACKGROUND

Lymphangioleiomyomatosis (LAM) is a rare cystic lung disease characterized by the proliferation, metastasis, and infiltration of smooth muscle cells in the lung and other tissues, which can be associated with tuberous sclerosis complex (TSC). The disorder of TSC has a variable expression, and there is great phenotypic variability.

CASE SUMMARY

A 32-year-old Chinese woman with a history of multiple renal angioleiomyolipoma presented with a productive cough persisting for over 2 wk. High-resolution chest computed tomography revealed interstitial changes, multiple pulmonary bullae, bilateral pulmonary nodules, and multiple fat density areas of the inferior mediastinum. Conventional and contrast ultrasonography revealed multiple high echogenic masses of the liver, kidneys, retroperitoneum, and inferior mediastinum. These masses were diagnosed as angiomyolipomas. Pathology through thoracoscopic lung biopsy confirmed LAM. Furthermore, high-throughput genome sequencing of peripheral blood DNA confirmed the presence of a heterozygous mutation, c.1831C>T (p.Arg611Trp), of the *TSC2* gene. The patient was diagnosed with TSC-LAM.

CONCLUSION

We highlight a rare case of TSC-LAM and the first report of a mediastinum lymphangioleiomyoma associated with TSC-LAM.

Manuscript source: Unsolicited manuscript

Specialty type: Medicine, research and experimental

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: April 29, 2021
Peer-review started: April 29, 2021
First decision: May 23, 2021
Revised: May 30, 2021
Accepted: July 2, 2021
Article in press: July 2, 2021
Published online: August 26, 2021

P-Reviewer: Oley MH
S-Editor: Gao CC
L-Editor: Wang TQ
P-Editor: Li JH

Key Words: Tuberous sclerosis complex; Lymphangioleiomyomatosis; Angioleiomyolipoma; High-resolution chest computed tomography; Contrast ultrasonography; Case report

Core Tip: Lymphangioleiomyomatosis is a rare cystic lung disease that can be associated with tuberous sclerosis complex (TSC). The disorder of TSC has a variable expression and there is great phenotypic variability. A 32-year-old Chinese woman with a history of multiple renal angioleiomyolipoma since the age of 14 was diagnosed with TSC-lymphangioleiomyomatosis by high-resolution computed tomography, conventional and contrast ultrasonography, pathology through thoracoscopic lung biopsy, and high-throughput genome sequencing of peripheral blood DNA.

Citation: Chen HB, Xu XH, Yu CG, Wan MT, Feng CL, Zhao ZY, Mei DE, Chen JL. Tuberous sclerosis complex-lymphangioleiomyomatosis involving several visceral organs: A case report. *World J Clin Cases* 2021; 9(24): 7085-7091
URL: https://www.wjgnet.com/2307-8960/full/v9/i24/7085.htm
DOI: https://dx.doi.org/10.12998/wjcc.v9.i24.7085

INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a rare, cystic lung disease. It belongs to a family of neoplasms with perivascular epithelioid differentiation that causes a multisystemic disorder characterized by the proliferation, metastasis, and infiltration of smooth muscle cells in the lungs and other tissues. The disorder is thought to be caused by the loss of the tuberous sclerosis complex-2 (*TSC2*) gene heterozygosity in the 16p13 chromosome[1]. LAM can occur either sporadically or in association with TSC disease (TSC-LAM) (13%-40% of cases)[1,2]. TSC-LAM is characterized by the presence of pulmonary cysts and other lesion sites, including the brain, heart, kidneys, and skin[1,3]. Symptoms and severity of TSC differ widely between individuals and there is great phenotypic variability because, despite the nearly complete penetrance, this disorder has a variable expression[3]. We hereby present a rare case of TSC-LAM with skin, kidney, liver, retroperitoneum, inferior mediastinum, and lung involvement.

CASE PRESENTATION

Chief complaints

A 32-year-old woman was admitted to hospital with a 2 wk history of a productive cough.

History of present illness

The patient produced white foamy sputum that began 2 wk ago.

History of past illness

The patient was diagnosed with multiple renal angioleiomyolipomas in 2002 when she was 14 years old. In 2002 and 2008, she had multiple renal angioleiomyolipomas excised (Figure 1). After she was pregnant and had a cesarean section in 2013, cutaneous facial angiofibroma developed (Figure 2). In 2016, she was hospitalized for chylothorax. Bilateral pulmonary nodules were found, and thoracic surgery was performed (Table 1).

Personal and family history

The patient had no family history of similar illnesses.

Table 1 Timeline of the case

Year	Summary from initial and follow-up visits	Diagnostic testing	Intervention
2002	Multiple renal angioleiomyolipomas	Ultrasonography	Angioleiomyolipoma resection
2008	Multiple renal angioleiomyolipoma	Ultrasonography	Angioleiomyolipoma resection
2013	Facial angiofibroma after pregnancy and cesarean section	None	None
2016	Chylothorax	HRCT: Bilateral pulmonary nodules	Thoracic operation
2019	TSC-LAM and pulmonary infection	HRCT; Thoracoscopic lung biopsy; High-throughput genome sequencing of peripheral blood DNA; Conventional and contrast-enhanced ultrasonography	Anti-infective symptomatic supportive treatment

HRCT: High-resolution computed tomography; LAM: Lymphangioleiomyomatosis; TSC: Tuberous sclerosis complex.

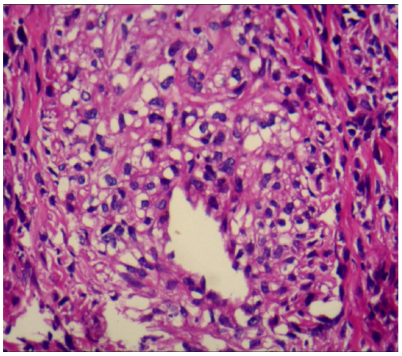

Figure 1 Pathology of the renal angioleiomyolipoma (hematoxylin-eosin staining). The patient had multiple renal angioleiomyolipomas excised in 2002 and 2008. Magnification: × 800.

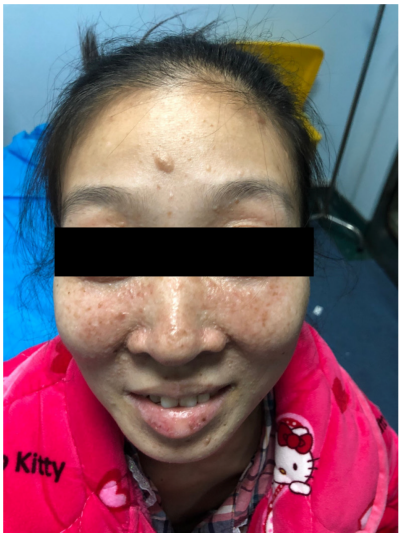

Figure 2 Facial angiofibroma developed after the patient was pregnant in 2013.

Physical examination

Tachycardia, hypertension, and low breath sounds throughout the bilateral chest field were observed. There were no other significant findings.

Laboratory examinations

Thoracoscopic lung biopsy was performed. Pathology confirmed LAM, and immuno-

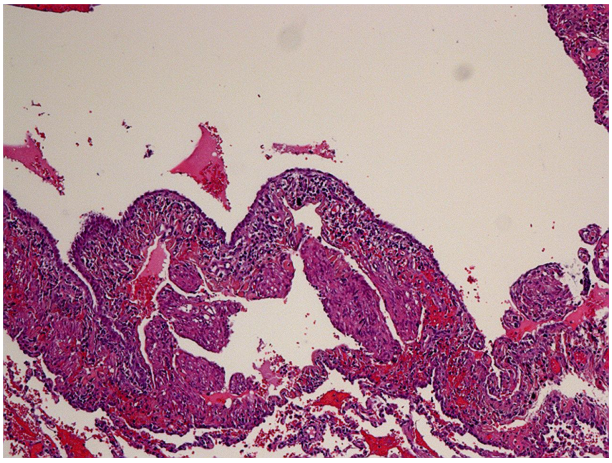

Figure 3 Pathology of lung lymphangioleiomyomatosis (hematoxylin-eosin staining). Magnification: × 200.

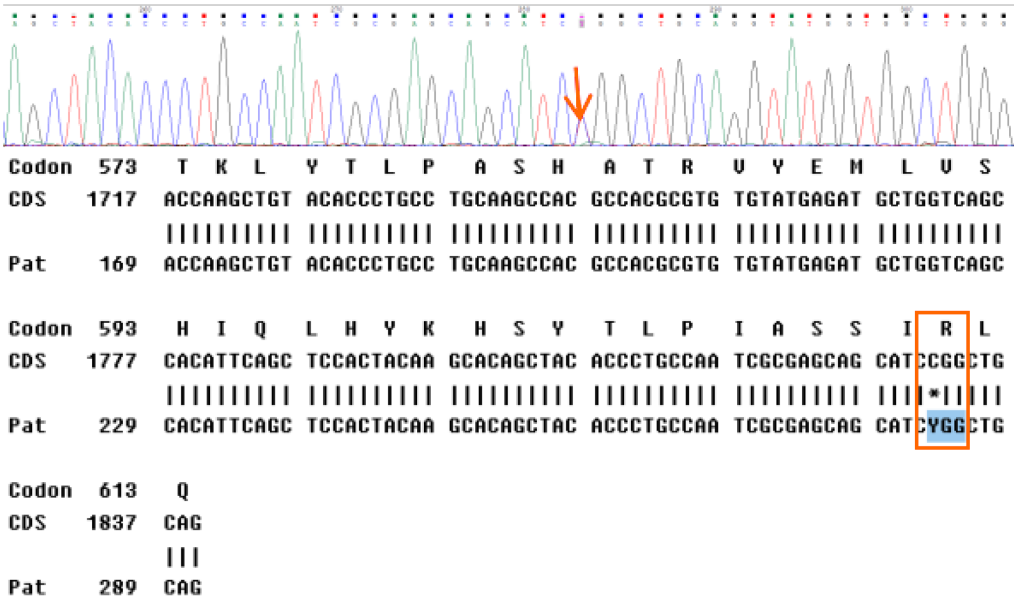

Figure 4 High-throughput sequencing of peripheral blood DNA. The heterozygous mutation c.1831C>T (p.Arg611Trp) in the *TSC2* gene was confirmed.

histochemistry showed human melanoma black-45 (+, sporadic), smooth muscle actin (+), Ki67 (+, 3%), and melan-A (+) (Figure 3). Furthermore, high-throughput genome sequencing of peripheral blood DNA confirmed the presence of the c.1831C>T (p.Arg611Trp) heterozygous mutation in the *TSC2* gene (Figure 4).

Imaging examinations

High-resolution chest computed tomography revealed interstitial changes, multiple pulmonary bullae, bilateral pulmonary nodules, and multiple fat density areas in the inferior mediastinum (Figure 5). Pulmonary function tests showed that the diffusing capacity of the lung for carbon monoxide decreased mildly (67%), forced expiratory volume in 1 s was reduced, and ratio of forced expiratory volume to forced vital capacity decreased, which contributed to severe obstructive ventilatory syndrome.

Conventional (Figure 6) and contrast ultrasonography (Figure 7) revealed multiple high echogenic masses in the liver, kidney (bilateral), retroperitoneum, and right thorax (inferior mediastinum). The masses were diagnosed as angiomyolipomas.

FINAL DIAGNOSIS

TSC-LAM.

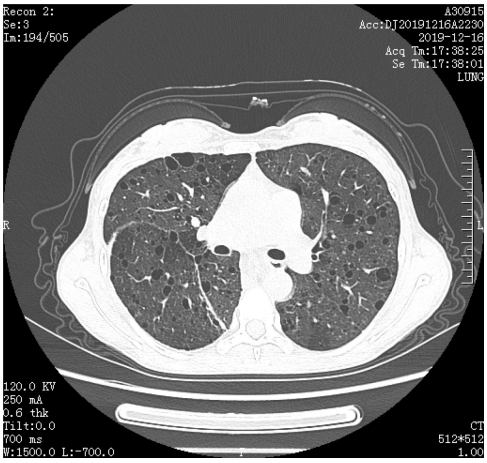

Figure 5 High-resolution chest computed tomography. Computed tomography revealed interstitial changes, multiple lytic and lucent lesions of varying sizes, bilateral pulmonary nodules, and multiple fat density areas in the inferior mediastinum.

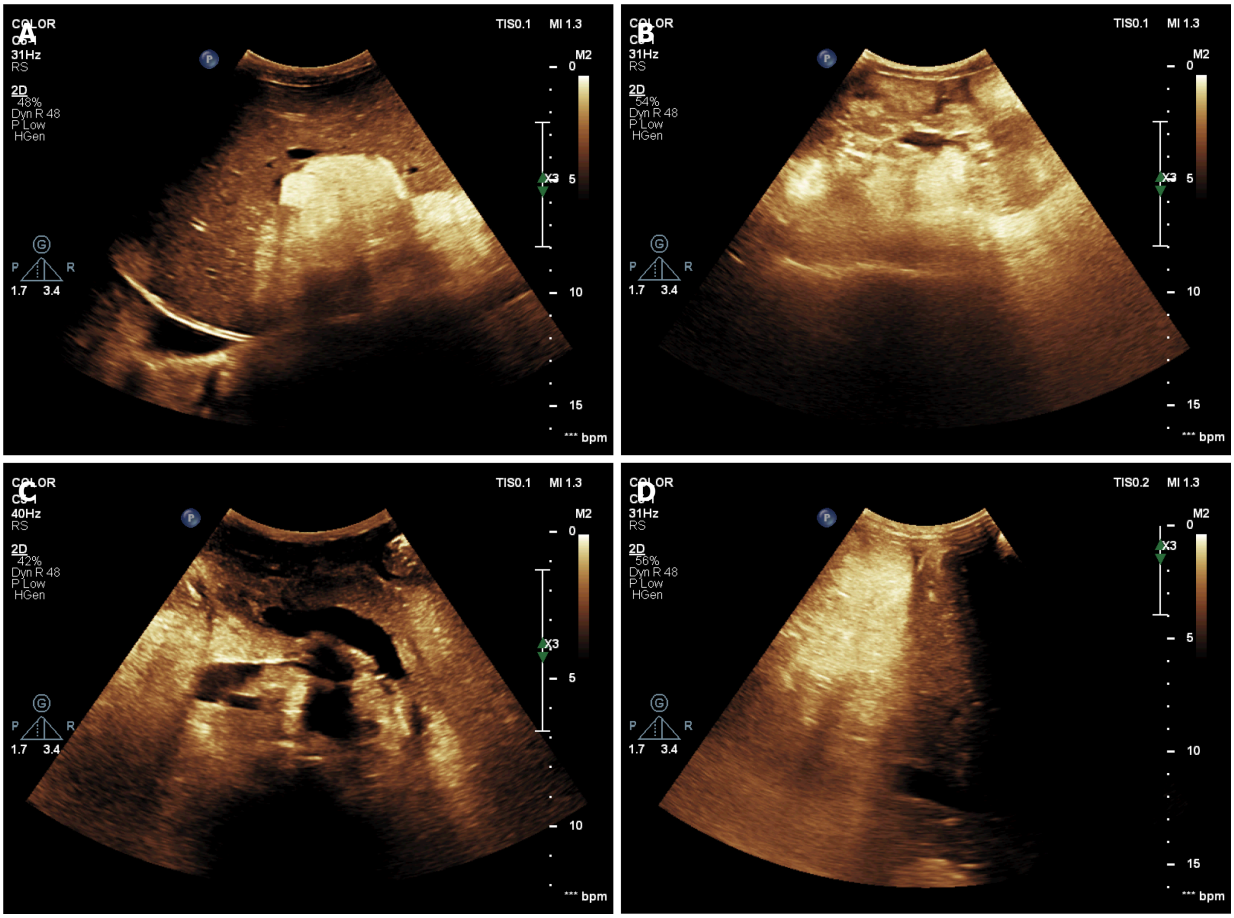

Figure 6 Ultrasonography revealed multiple high echogenic masses. A: Liver; B: Right kidney; C: Retroperitoneum; D: Inferior mediastinum.

TREATMENT

The patient was referred for specific consultation and treatment with sirolimus after recovery of the pulmonary infection.

OUTCOME AND FOLLOW-UP

The patient's symptoms decreased after drug treatment but did not resolve

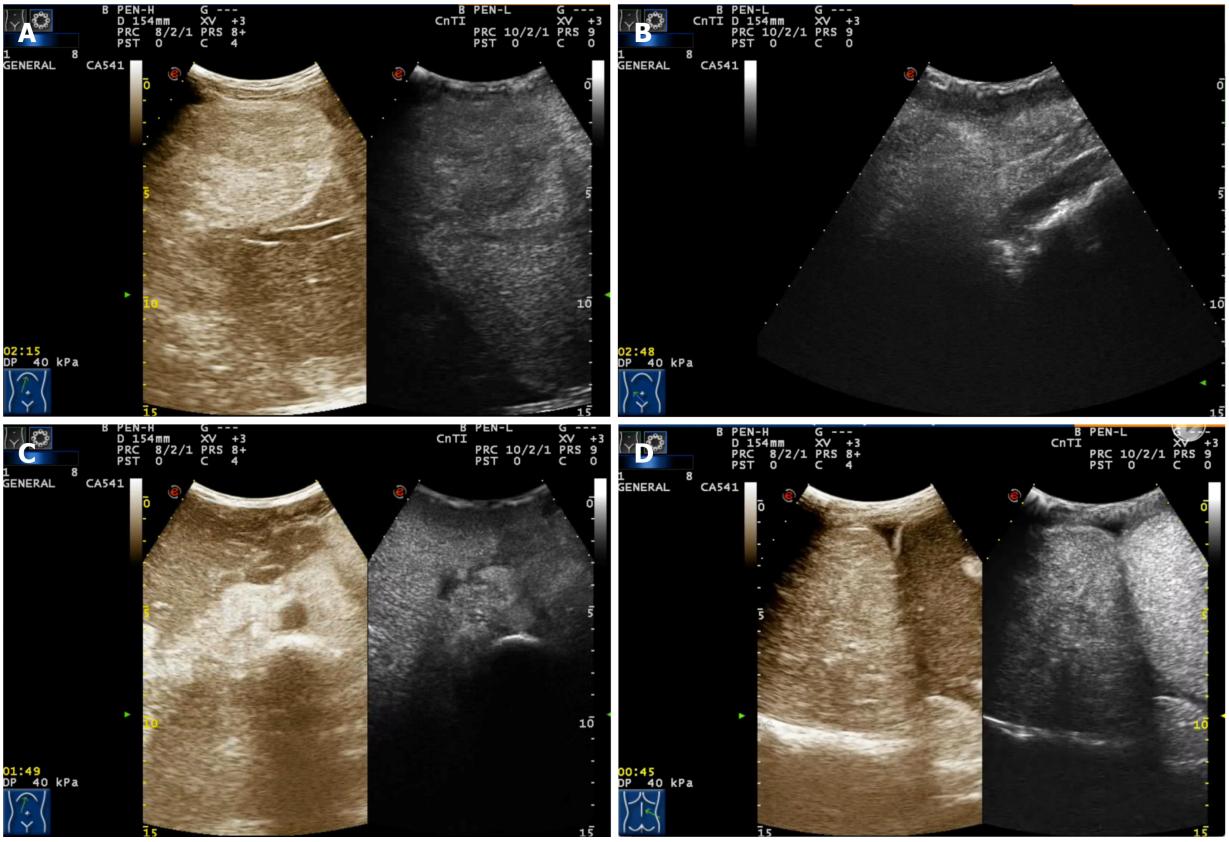

Figure 7 Contrast-enhanced ultrasonography revealed high enhancement of the masses. A: Liver; B: Right kidney; C: Retroperitoneum; D: Inferior mediastinum.

completely. We followed the patient regularly during sirolimus treatment, including ultrasound and lung function evaluation every 3 mo and computed tomography every 6 mo. At the 1-year follow-up, the effects of TSC-LAM on the skin, kidneys, liver, retroperitoneum, inferior mediastinum, and lungs were still observable by imaging analyses, and nothing had changed.

DISCUSSION

LAM is a rare interstitial lung disease[4]. It has an unknown etiology and is characterized by cystic destruction of the lung caused by infiltration of smooth muscle cells. It predominantly affects women in their reproductive years. The average age at diagnosis is 41 years old[2]. The patient in this case was 32 years old, which is much younger than the average age. Although LAM is predominantly a lung disorder, extrapulmonary involvement, such as renal angiomyolipomas and retroperitoneal masses, can occur in up to 75% of cases. A rare finding of abdominal aneurysm was reported before[5].

This patient was previously diagnosed with renal angiomyolipomas but no pulmonary involvement was documented until 2016. Angiomyolipomas or lymphangioleiomyomas of the inferior mediastinum, liver, and retroperitoneum were observed during the patient's most recent hospitalization. To our knowledge, this is the first report of a patient with mediastinum lymphangioleiomyomas associated with TSC-LAM or sporadic LAM. The conventional and contrast ultrasonography imaging of the inferior mediastinum masses were similar to the renal angiomyolipoma imaging. The pathogenesis of mediastinum lymphangioleiomyomas in LAM may be similar to the mechanism of retroperitoneal lymphangioleiomyoma pathogenesis, but further research is needed to confirm this hypothesis.

The prognosis of patients with TSC-LAM is poor. Respiratory insufficiency and death often occurs within 5 years from onset of symptoms, while positive management of the disease and its complications would improve the long-term survival of these patients. The patient in this case accepted a complete evaluation first, and then received a specific consultation and treatment with sirolimus after recovery of her

pulmonary infection.

CONCLUSION

The diagnosis of TSC-LAM in this patient was multisystemic. Affected organs included the skin, kidneys, liver, retroperitoneum, mediastinum, and lungs. This is the first reported case of a patient with a mediastinum lymphangioleiomyoma associated with TSC-LAM. High-resolution chest computed tomography and ultrasonography are critical to detect abnormalities, which may require specific treatment to prevent disease progression and poor outcomes.

REFERENCES

1 **Harari S**, Torre O, Moss J. Lymphangioleiomyomatosis: what do we know and what are we looking for? *Eur Respir Rev* 2011; **20**: 34-44 [PMID: 21357890 DOI: 10.1183/09059180.00011010]

2 **Johnson SR**, Cordier JF, Lazor R, Cottin V, Costabel U, Harari S, Reynaud-Gaubert M, Boehler A, Brauner M, Popper H, Bonetti F, Kingswood C; Review Panel of the ERS LAM Task Force. European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis. *Eur Respir J* 2010; **35**: 14-26 [PMID: 20044458 DOI: 10.1183/09031936.00076209]

3 **Caban C**, Khan N, Hasbani DM, Crino PB. Genetics of tuberous sclerosis complex: implications for clinical practice. *Appl Clin Genet* 2017; **10**: 1-8 [PMID: 28053551 DOI: 10.2147/TACG.S90262]

4 **De Pauw RA**, Boelaert JR, Haenebalcke CW, Matthys EG, Schurgers MS, De Vriese AS. Renal angiomyolipoma in association with pulmonary lymphangioleiomyomatosis. *Am J Kidney Dis* 2003; **41**: 877-883 [PMID: 12666075 DOI: 10.1016/s0272-6386(03)00006-4]

5 **Chérrez-Ojeda I**, Espinoza-Plaza J, Cottin V, Chérrez S. A Rare Case of an Abdominal Aneurysm in a Patient with Lymphangioleiomyomatosis: A Case Report. *Perm J* 2019; **23** [PMID: 30939284 DOI: 10.7812/TPP/18-170]

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