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Pulmonary Lymphangioleiomyomatosis: A Rare Diffuse Cystic Lung Disease

Pulmoner Lenfanjiyoleyomiyomatozis: Nadir ve Diffüz Kistik Akciğer Hastalığı

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Abstract

Pulmonary lymphangioleiomyomatosis is a rare disease that affects women of reproductive age, and causes progressive dyspnea on exertion. Patients may present with a clinical picture of recurrent pneumothorax, hemothorax, chylothorax and hemoptysis. We present here the case of a 42-year-old female patient who presented with dyspnea on exertion and non-productive cough. High-resolution computed tomography scans revealed multiple air cysts in all zones, affecting the central and peripheral parts of both lungs. The patient underwent VATS wedge resection, and a diagnosis of lymphangioleiomyomatosis was established based on a histopathological examination. We present this case to literature as a rare disease, the preliminary diagnosis of which was confirmed histopathologically.

Keywords: *Lung cystic disease, dyspnea, cough.*

Öz

Pulmoner lenfanjiyoleiyomyomatozis (LAM), reprodüktif dönem kadınlarda görülen nadir bir hastalıktır. Eforla artan ilerleyici nefes darlığına yol açar. Klinik olarak hastalar, tekrarlayıcı pnömotoraks, hematoraks, şilotoraks ve hemoptizi ile başvurabilirler. Bu olgu sunumunda efor dispnesi ve non-prodüktif öksürük şikayetiyle başvuran 42 yaşındaki kadın hastayı sunuyoruz. Hastanın yüksek rezolüsyonlu bilgisayarlı tomografisinde her iki akciğerde tüm zonlarda, santrali ve periferi etkileyen çok sayıda hava kistleri saptandı. Hastaya VATS wedge rezeksiyon yapıldı ve histopatolojik olarak lenfanjioleiomyomatozis tanısı konuldu. Olgumuzu nadir görülen bir hastalık olması ve ön tanımızı histopatolojik olarak kesinleştirdiğimiz için sunmak istedik.

Anahtar Kelimeler: *Akciğer kistik hastalığı, dispne, öksürük.*

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Lymphangioleiomyomatosis (LAM) is a disease with an unknown etiology that often affects women of reproductive age, and is characterized by cystic destruction of the lungs and infiltration by smooth muscle-like cells (1,2). The condition manifests with cystic lung lesions and results in respiratory failure (3), with the potential to cause pneumothorax, chylothorax, hemoptysis and hemosiderosis. The condition has a progressive course and may result in death from respiratory failure years after the initial diagnosis (4,5). Our aim intention from this case report is to emphasize that the condition should be kept in mind in the differential diagnosis of female patients of reproductive age who present with shortness of breath upon exertion.

CASE

A 42-year-old female patient presented with an approximately one-year history of progressive dyspnea and non-productive cough that had worsened over the last three months. The patient's symptoms were not aggravated by an allergen, and her past medical history was unremarkable for chronic conditions other than cervical cancer, for which she had undergone an operation four years earlier. She had a 25-pack/year smoking history and was a current smoker. Her family history was unremarkable. Her breathing sounds were bilaterally normal and equal. Chest X-ray and pulmonary function tests were planned, and a high-resolution thoracic computed tomography was scheduled upon the observation of bilateral, multiple air cysts on chest X-ray (Figure 1).

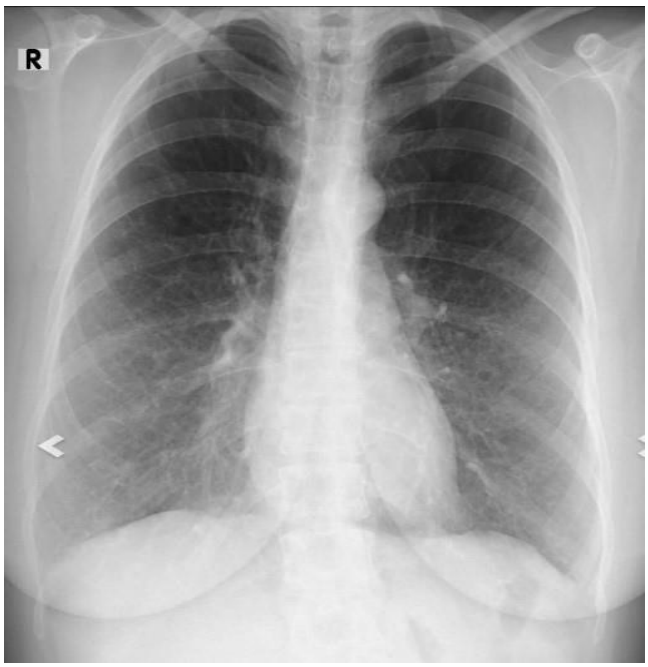

Figure 1: Bilateral, multiple air cysts on chest X-ray

The pulmonary function tests revealed a forced vital capacity (FVC) of 95% (3,000 ml), forced expiratory volume in the first second (FEV1) of 57% (1,560 ml) and FEV1/FVC of 52%, while the results of an arterial blood gases analysis were pH 7.39, pO_2 75.6 mmHg, pCO_2 35.6 mmHg, HCO_3 22.4 and oxygen saturation 94.3%. All other laboratory tests revealed normal findings.

Thoracic computed tomography scans revealed multiple, thin-walled cysts scattered throughout both lungs (Figure 2). The patient was re-examined, and the system data were reviewed considering the patient's clinical status, history and radiological imaging findings.

A pre-diagnosis of lymphangioleiomyomatosis was made based on the fact that the patient had presented with similar symptoms in the past, and thoracic computed tomography scans six months earlier had revealed similar thin-walled diffuse air cysts. A genetic analysis was conducted considering the clinical and radiological findings of the patient with unremarkable results, and transthoracic echocardiography revealed normal findings.

The patient underwent left video-assisted thoracic surgery for a wedge resection and apical pleurectomy, performed in the Thoracic Surgery Department.

A histopathological examination suggested a diagnosis of lymphangioleiomyomatosis based on focal HMB-45 and diffuse smooth muscle actin positivity (Figure 3 and 4).

The patient was encouraged to quit smoking and placed on close follow-up, and had subsequent repeat admissions due to exacerbations of the symptoms. No decline in oxygen saturation in room air was observed. The patient was placed on therapy with sirolimus 1 mg twice daily and continued to attend follow-up visits.

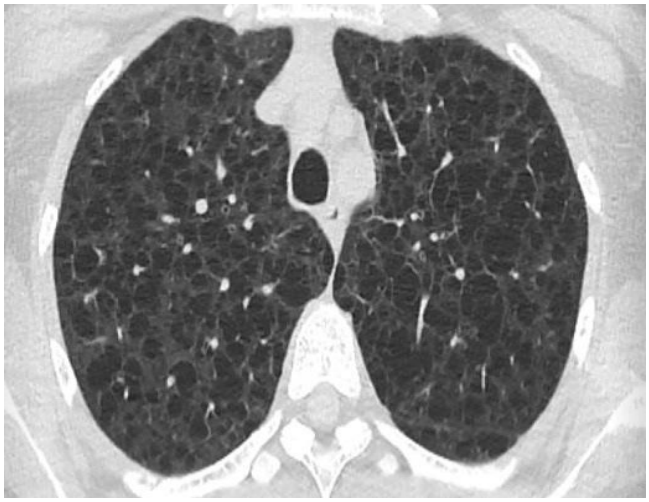

Figure 2: Thoracic computed tomography scans revealing multiple, thin-walled cysts scattered throughout both lungs

DISCUSSION

LAM generally affects young women of reproductive age, with symptoms and signs that can vary depending on the affected organs. The most common symptoms and signs are associated with lung disease, although patients may also present with extrapulmonary manifestations, particularly those with renal angiomyolipoma and those with diseases involving the lymphatic system. LAM can be associated with typical neurocutaneous manifestations of the tuberous sclerosis complex (TSC) (i.e., angiofibroma, shagreen patches, seizures, intellectual disability) occurring sporadically. Our patient had dyspnea on exertion and dry cough, but no other complaints. Genetic analysis results were unremarkable, she had no neurocutaneous symptoms, and an abdominal ultrasound revealed normal findings.

The characteristic presenting symptoms of patients with LAM have been well-established in a registry study of 230 patients conducted in the United States, and the most common symptoms noted in the above-mentioned study have been further supported by smaller-scale studies conducted before and after the registry study (6). The most common symptoms are as follows:

- Fatigue (in approximately two-thirds of cases),
- Progressive dyspnea (in approximately two-thirds of cases),
- Spontaneous pneumothorax (in approximately one-third of cases), and
- Pleural effusion (in approximately one-quarter of cases).

Less common symptoms include:

- Chest pain (<15%),
- Cough and phlegm (<%15),
- Pulmonary hypertension (<7%),
- Chyloptysis (<10%),
- Chyle in urine, feces, vaginal discharge (<10%), and
- Hemoptysis (<5%).

Dyspnea on exertion is the most common symptom of LAM, but as dyspnea is a non-specific symptom and LAM is a rare disorder, women with LAM may be started on therapy with a diagnosis of asthma, emphysema or chronic obstructive pulmonary disease (COPD) before the suspicion of LAM is raised. The results of observational studies have suggested the following findings (6-12):

- Normal spirometry (30 – 60%),
- Obstructive pattern on spirometry (25 – 60%),
- Restrictive or mixed obstructive and restrictive pattern spirometry (<25%), and
- Low lung diffusing capacity for carbon monoxide (DLCO) (60 – 90%).

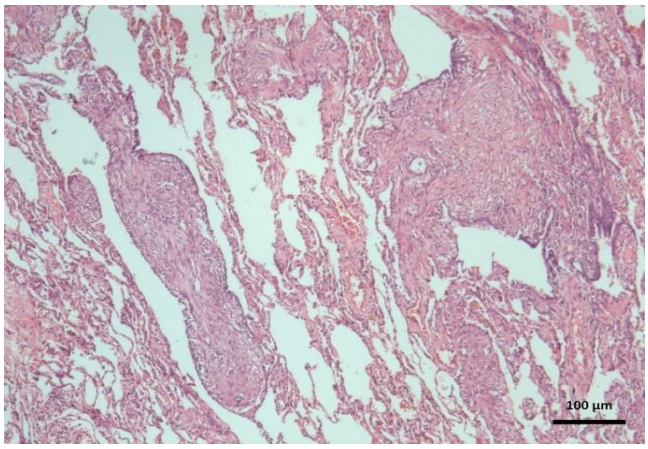

Figure 3: Ecstatic lymphatics and muscle tissue proliferation in the alveolar wall (H&E, x10)

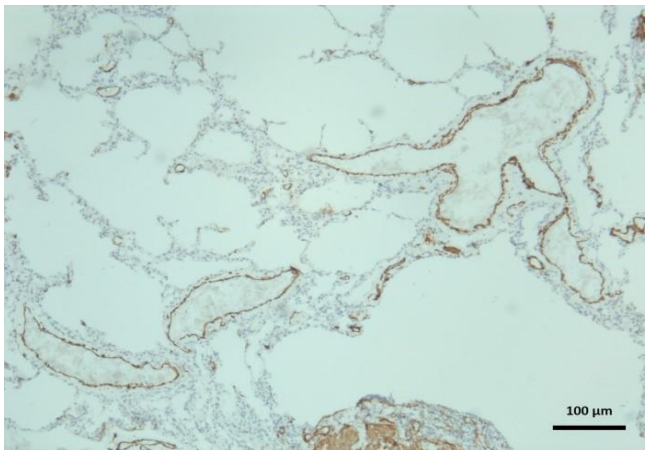

Figure 4: Diffuse Smooth Muscle Actin positivity (SMA, x10)

Spirometry revealed an obstructive pattern in our patient with a value of 25–60%. Although a diagnosis of LAM can be established based on clinical and radiological findings, surgical lung biopsy (lung biopsy through video-assisted thoracoscopy or invasive thoracotomy) has a high diagnostic yield approximating 100 percent, and is considered the optimum approach to the diagnosis of LAM (13). In our patient, the diagnosis of LAM was confirmed from a pathological examination of a surgical specimen obtained by VATS.

The treatment options for LAM include:

Progesterone: Although some case series and case reports have reported favorable effects of progesterone therapy, no placebo-controlled randomized study has been conducted in this regard to date. The routine use of progesterone preparations is not recommended, although intramuscular administration can be attempted in cases experiencing a rapid decline in pulmonary function (14).

Sirolimus: The mTOR pathway is genetically active in patients with LAM. Although prospective studies have demonstrated that sirolimus reduces AML volume, it is not recommended as a first-line therapy for the treatment of angiomyolipoma. The effect of sirolimus on pulmonary function remains unclear, and there is a risk of side ef-

fects associated with the use of sirolimus. Although sirolimus is not routinely recommended, it can be used in experienced centers after weighing the risk of side effects against the potential benefits with close monitoring of patients who experience a rapid decline in pulmonary function (1).
The lung transplantation option can be considered in patients with end-stage disease.

CONCLUSION

Through this case report the authors seek to improve the understanding of this rare condition, which should be kept in mind in the differential diagnosis of female patients of reproductive age presenting with dyspnea on exertion.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - P.M., A.M, T.Ç., H.O.K.; Planning and Design - P.M., A.M, T.Ç., H.O.K.; Supervision - P.M., T.Ç., H.O.K., A.M.; Funding - P.M., A.M, T.Ç., H.O.K.; Materials - P.M., A.M, T.Ç., H.O.K.; Data Collection and/or Processing - T.Ç., A.M., P.M.; Analysis and/or Interpretation - T.Ç., P.M., A.M.; Literature Review - P.M., A.M, T.Ç.; Writing - T.Ç., P.M.; Critical Review - T.Ç., P.M.

REFERENCES

1. Sullivan EJ. Lymphangioleiomyomatosis: a review. Chest 1998; 114:1689-703. [CrossRef]
2. McCormack FX. Lymphangioleiomyomatosis. A clinical update. Chest 2008; 133:507-16. [CrossRef]
3. Taveira-DaSilva AM, Stylianou MP, Hedin CJ, Hathaway O, Moss J. Decline in lung function in patients with lymphangioleiomyomatosis treated with or without progesterone. Chest 2004; 126:1867-74. [CrossRef]
4. Oh YM, Mo EK, Jang SH, Yoo CG, Kim YW, Seo JW, et al. Pulmonary lymphangioleiomyomatosis in Korea. Thorax 1999; 54:618-21. [CrossRef]
5. Eliasson AH, Phillips YY, Tenholder MF. Treatment of lymphangioleiomyomatosis. A meta-analysis. Chest 1989; 196:1352-55. [CrossRef]
6. Ryu JH, Moss J, Beck GJ, Lee JC, Brown KK, Chapman JT, et al. The NHLBI lymphangioleiomyomatosis registry: characteristics of 230 patients at enrollment. Am J Respir Crit Care Med 2006; 173:105-11. [CrossRef]
7. Baldi BG, Freitas CS, Araujo MS, Dias OM, Pereira DA, Pimenta SP et al. Clinical course and characterisation of lymphangioleiomyomatosis in a Brazilian reference centre. Sarcoidosis Vasc Diffuse Lung Dis 2014; 31:129-35.
8. Taylor JR, Ryu J, Colby TV, Raffin TA. Lymphangioleiomyomatosis. Clinical course in 32 patients. N Engl J Med 1990; 323:1254-60. [CrossRef]
9. Park HY, Nam HS, Chung MP,Jeong SH, Kim YJ, Cha SI, et al. A nationwide survey of lymphangioleiomyomatosis in Korea: recent increase in newly diagnosed patients. J Korean Med Sci 2010; 25:1182-6. [CrossRef]
10. Hayashida M, Seyama K, Inoue Y, Fujimoto K, Kubo K. The epidemiology of lymphangioleiomyomatosis in Japan: a nationwide cross-sectional study of presenting features and prognostic factors. Respirology 2007; 12:523-30. [CrossRef]
11. Urban T, Lazor R, Lacronique J, Murris M, Labrune S, Valeyre D, Cordier JF. Pulmonary lymphangioleiomyomatosis. A study of 69 patients. Groupe d'Etudes et de Recherche sur les Maladies "Orphelines" Pulmonaires (GERM"O"P). Medicine (Baltimore) 1999; 78:321-37. [CrossRef]
12. Kitaichi M, Nishimura K, Itoh H, Izumi T. Pulmonary lymphangioleiomyomatosis: a report of 46 patients including a clinicopathologic study of prognostic factors. Am J Respir Crit Care Med 1995; 151:527-33. [CrossRef]
13. Yılmaz E, Özdemir K, Başaran C, Keskin Ş, Erturgut P, Serdaroğlu E. Tuberosklerosis Kompleksinde Renal Tutulum. Dicle Med J 2015; 42:66-71. [CrossRef]
14. Johnson SR, Cordier JF, Lazor R, Cottin V, Costabel U, Harari S, et al. European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis. Eur Respir J 2010; 35:14 - 26. [CrossRef]