International Journal of Research in Medical Sciences
Sen D et al. Int J Res Med Sci. 2025 Nov;13(11):4973-4975
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20253632

Case Report

Pulmonary lymphangioleiomyomatosis: a rare and challenging case report with unusual presentation of human melanoma black-45

Debadrita Sen[1], Mili Das[1], Suddha S. Bandopadhyay[1]*, Prithwiraj Sengupta[2]

[1]Department of Pathology, ABV Regional Cancer Center, Agartala, Tripura, India
[2]Department of Radiodiagnosis, ABV Regional Cancer Center, Agartala, Tripura, India

Received: 30 August 2025
Accepted: 09 October 2025

***Correspondence:**
Dr. Suddha S. Bandopadhyay,
E-mail: drsuddha@gmail.com

ABSTRACT

Lymphangioleiomyomatosis (LAM) is a very rare disease that generally affects young women of reproductive health group. It is characterized by abnormal proliferation of smooth muscle like cells (LAM cells) in the lungs (pulmonary LAM) and extrapulmonary sites (extrapulmonary LAM). Patients usually present with spontaneous pneumothorax, hemoptysis and progressive dyspnea. There is a poor awareness, knowledge and records about this disease making it a difficult diagnosis. Herein this report presents a case of pulmonary LAM in a 63 years old female with h/o dyspnea and chest pain. Her imaging studies showed fibrosis and nodular lesions in both lungs suggesting metastatic lesions. Later on, after a lung biopsy the diagnosis of lymphangioleiomyomatosis was given and immunohistochemical staining was positive for spinal muscular atrophy (SMA), CD34 and negative for human melanoma black-45 (HMB45). HMB45 negative PLAM is very rare with only few instances in the literature making it a difficult diagnosis. Our patient was given mTOR inhibitors along with supportive and conservative management and she responded well to the treatment. This rare cystic lung disease can be devastating as it causes progressive lung damage. Limited options in the management of PLAM makes early diagnosis as key and there is also a need for high index suspicion with cystic lung disease in women.

Keywords: HMB45, Lymphangioleiomyomatosis, Lung cystic disease, mTOR

INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a very rare diffuse progressive lung disease primarily affecting women of reproductive age group. It primarily affects lung parenchyma but can affect other organs like kidney, brain, liver. LAM is characterized by cystic lung lesions and extra pulmonary features consisting of renal angiomyolipomas and lymphatic involvement such as chylous effusion and lymphangioleimyomas. In pulmonary LAM there is peribronchial, perivascular and perilymphatic proliferation of smooth muscle resulting in airway obstruction and decline in lung function. The estimated prevalence of LAM is 3-7 cases per million women with 15% cases associated with tuberous sclerosis complex.[1] Tuberous sclerosis complex can be diagnosed with the identification of either TSC1 or TSC2 mutation. The most common presenting symptom is dyspnoea, hemoptysis and chest pain including pneumothorax and pleural effusion.[2] Symptoms can be easily mistaken for common diseases like asthma or chronic obstructive lung disease in primary care setting.

Interdisciplinary management and prompt diagnosis of such rare disease like LAM is required to assist primary care physicians in treatment of such illness.

CASE REPORT

A 63 years old female with h/o hypertension presented to the emergency with progressive dyspnea, chest pain and vomiting. Her vitals were significant for tachycardia, tachypnoea and low oxygen saturation. Her physical examination was notable for diminished breath sounds

bilaterally. Chest X-ray revealed bilateral diffuse opacities. High-resolution computed tomography (HRCT) thorax showed multiple enhancing nodular lesions in bilateral lungs with evidence of fibrosis suggestive of metastatic lesions (Figures 1a and b).

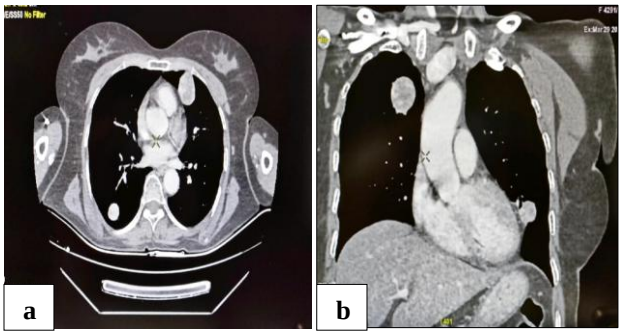

Figure 1 (a and b): HRCT thorax showing enhancing nodular lesions involving both lungs largest measuring 2.35 cm along with fibrosis.

All other investigations were normal. Computed tomography (CT) guided fine needle aspiration cytology (FNAC) was performed from the lung nodule which showed features of poorly differentiated non-small cell carcinoma (Figure 2).

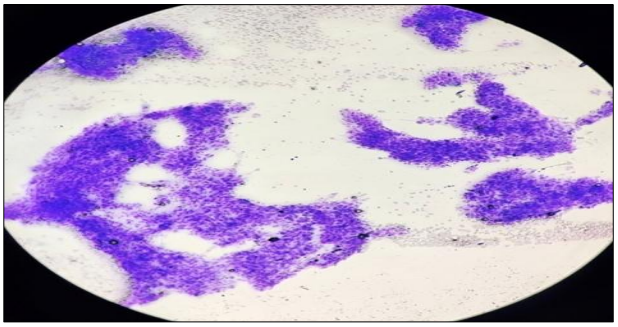

Figure 2: FNAC smears showing oval to spindle shaped cells in clusters with mild pleomorphism and moderate nuclear to cytoplasmic ratio, Leishman stain 10x.

There was no improvement in her symptoms despite various treatments. However, then a lung biopsy was performed and a possibility of PLAM was done morphologically and immunostaining was positive for SMA (smooth muscle actin) and CD34, negative for HMB45 (Figures 3 and 4).

While HMB45 is typically positive in PLAM there are rare instances where cells do not express the protein. This Patient had history of multiple tumors throughout the body for which she underwent bilateral nephrectomy, hysterectomy and cholecystectomy almost 12 years ago outside the state. Pulmonary LAM is often found associated with Tuberous Sclerosis a multisystem genetic disorder that causes multiple tumors throughout the body.

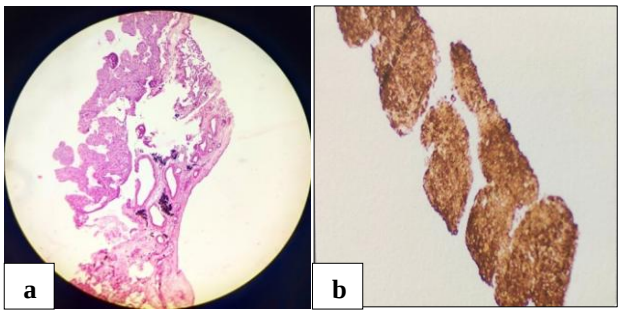

Figure 3: (a) Lung parenchyma shows cystic spaces surrounded by spindled smooth muscle like cells having clear to eosinophilic cytoplasm, intermixed with hemosiderin laden macrophages, H and E 10X, and (b) strong diffuse positivity for SMA.

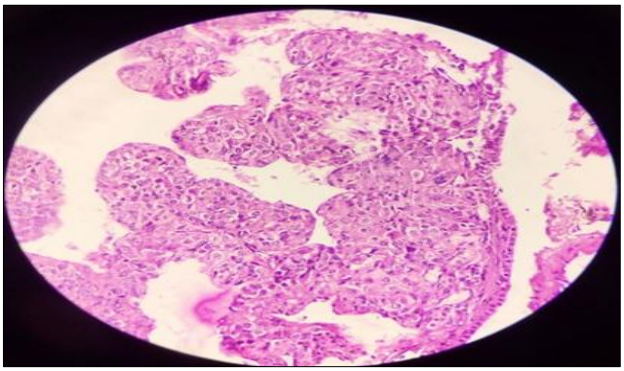

Figure 4: Cells are spindled-epithelioid in shape with bright eosinophilic cytoplasm and mildly pleomorphic nuclei.

DISCUSSION

PLAM is an uncommon progressive disorder predominantly affecting women of child bearing age. This tumor is characterized by presence of multifocal smooth muscle cells surrounding lymphatic vessels and their walls. The mean age of onset in eight series of over 300 patients is 35 years.[3] Clinical manifestation of LAM are dyspnea, cough, chest pain, spontaneous pneumothorax, chylothorax. Common extrapulmonary features are retroperitoneal adenopathy, renal angiomyolipomas which can cause abdominal pain. LAM has two specific types sporadic and congenital. Sporadic cases comprise 60% occurring later in life and congenital cases are 40% occurring in younger age group in which patients have alterations in tuberous sclerosis complex genes (TSC1 and TSC2.).[4] These genes regulate mammalian target of rapamycin (mTOR) signaling pathway.[5] The primary genetic mutations involve TSC1/TSC2 with TSC2 mutations predominating. The pathophysiology of LAM includes the rapid expansion of smooth muscle cells in the lung parenchyma and airway walls, as well as lymphatic system.[6]

The European respiratory society guidelines state that we need to have CT scan lung cysts as well as evidence of

tuberous sclerosis, kidney tumors or chylous effusions. It is helpful to obtain blood level of VEGF-D protein. In presence of radiologic findings and serum levels of vascular endothelial growth factor (VEGF) D equal or greater than 800 pg/ml are now accepted as diagnostic of LAM.[7]

Diagnosis can also be made by lung biopsy and immunohistochemical staining. The gold standard IHC diagnostic for LAM is immunopositive reaction with HMB45 antibody but specificity and sensitivity have not been defined. LAM cells are positive for HMB45 only in 17-67% and represent the more epitheloid fraction of immature smooth muscle cells.[8] Besides HMB-45 the most commonly used markers are alpha-smooth muscle actin (SMA), estrogen receptor (ER) and progesterone receptor (PR).

CONCLUSION

This case illustrates that immunohistochemistry for HMB45 can be negative, although LAM is present. If clinical suspicion for LAM is high, repeated HMB-45 can be done in additional histological sections. The establishment of definite diagnosis has relevant therapeutic implications, especially regarding mTor-inhibitor therapy.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Partha Sarathi Sutradhar, Radiation Oncologist, ABV Regional Cancer Center, Agartala for his support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Harknett EC, Chang WY, Byrnes S, Johnson J, Lazor R, Cohen MM, et al. Use of variability in national and regional data to estimate the prevalence of lymphangioleiomyomatosis. QJM. 2011;104(11):971-9.
2. Hohman DW, Noghrehkar D, Ratnayake S. Lymphangioleiomyomatosis: A review. Eur J Intern Med. 2008;19(5):319-24.
3. Verma SK, Verma SK. Pulmonary lymphangioleiomyomatosis (PLAM). Lung India. 2007;24(4):150-2.
4. Moss J, Avila NA, Barnes PM, Litzenberger RA, Bechtle J, Brooks PG, et al. Prevalence and clinical characteristics of lymphangioleiomyomatosis (LAM) in patients with tuberous sclerosis complex. Am J Respir Crit Care Med. 2001;164(4):669-71.
5. Krymskaya VP. Smooth muscle like cells in pulmonary lymphangioleiomyomatosis. Proc Am Thorac Soc. 2008;5:119-26.
6. Taveira-DaSilva AM, Moss J. Epidemiology, pathogenesis and diagnosis of lymphangioleiomyomatosis. Expert Opin Orphan Drugs. 2016;4:369-78.
7. Glasgow CG, Avila NA, Lin JP, Stylianou MP, Moss J. Serum vascular endothelial growth factor-D levels in patients with lymphangioleiomyomatosis reflect lymphatic involvement. Chest. 2009;135(5):1293-300.
8. 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(1):14-26.

Cite this article as: Sen D, Das M, Bandopadhyay SS, Sengupta P. Pulmonary lymphangioleio-myomatosis: a rare and challenging case report with unusual presentation of human melanoma black-45. Int J Res Med Sci 2025;13:4973-5.