SUNTEXT REVIEWS

SunText Review of Case Reports & Images
ISSN: 2766-4589

Open Access
Case Report
Volume 6:1

Incidentally Detected Diffuse Cystic Lung Disease: A Possible Case of Lymphangioleiomyomatosis in a 60-Year-Old Female

Zachary Hunt[1] and Kumar P[2,*]

[1]6th year medical student to "Intern Mackay base hospital", Australia
[2]FRACP, Respiratory Physician, Mackay Base Hospital, Queensland Health, Australia

***Corresponding author:** Kumar P, Mackay Base Hospital, 475, Bridge Road, Mackay, Queensland, Australia

Received date: 03 February 2025; **Accepted date:** 10 February 2025; **Published date:** 19 February 2025

Citation: Hunt Z, Kumar P (2025) Incidentally Detected Diffuse Cystic Lung Disease: A Possible Case of Lymphangioleiomyomatosis in a 60-Year-Old Female. SunText Rev Case Rep Image 6(1): 149.

DOI: https://doi.org/10.51737/2766-4589.2025.149

Abstract

Lymphangioleimyomatosis (LAM) is a rare cause of diffuse cystic lung disease which is caused by a slowly progressive, metastasising neoplasm. LAM is often associated with Tuberous sclerosis however can occur due to somatic mutations without tuberous sclerosis which is confined to a female population. This case report looks at a possible case of LAM in a 60 year old asymptomatic female who on incidental chest CT was found to have diffuse cystic lung disease.

Keywords: Lymphangioleiomyomatosis; Cysts and cavities; Cystic lung disease

Introduction

Cysts and cavities are often discovered on chest imaging and it is vital to be able to distinguish these and differentiate different causes [1]. Further to this to help differentiate different disease processes distribution of these lesions becomes important. Both cysts and cavities are areas of decreased lung density with discernible walls that can be found on chest imaging [1]. Cysts and cavities are differentiated by their wall with cysts having thin walls (≤2 mm) with often uniform thickness whereas cavities often have thick walls (>4mm) [1]. The distribution of cysts can be focal, multifocal or diffuse with the presence of diffuse cysts leading to a limited number of differential diagnoses [1,2]. This case report will focus on Lymphangioleiomyomatosis an uncommon cause of cystic lung disease. Lymphangioleimyomatosis (LAM) is a rare, slowly progressive, low-grade, metastasising neoplasm found predominantly in women [1-5]. This disease is a systemic metastatic disease often associated with cystic lung disease, abdominal tumours and chylous fluid accumulation [3]. The cells that invade the lung parenchyma are abnormal smooth muscle-like cells of unknown source that lead to progressive cystic destruction of the lungs [3,4]. LAM is often associated with tuberous sclerosis complex genes, TSC1 or TSC2 [2,3,4]. LAM associated with TSC is termed as TSC-LAM, however, Sporadic LAM can also occur with somatic mutations in TSC2 gene and is only found in women [1,3,5]. LAM cells have oestrogen and progesterone receptors leading to its strong link with rapid changes in premenopausal women [3,5]. Estimates of prevalence of LAM fall at approximately 3.4/7.8/1,000,000 women worldwide with approximately 80,000–160,000 patients with Tuberous sclerosis associated LAM and 8000-21000 patients with sporadic LAM [3,5].

LAM can present in a variety of ways including recurrent pneumothorax, progressive dyspnoea, history of chylothorax or incidental finding of diffuse cystic lung disease on HRCT [1,3]. Abdominal tumours are another common finding in LAM [1]. The most common of which are Angiomyolipomas which are benign mesenchymal tumours often found on the kidneys and are found in 30-40% of women with sporadic LAM and almost 90% of women with TSC-LAM [1,3]. These tumours can also occur anywhere in the chest or abdomen [1,3]. This case report will focus on a 60-year-old asymptomatic female with a possible

diagnosis of LAM of chest CT to differentiate radiological features between different diffuse cystic lung diseases.

Case Report

A 60-year-old female presented to the outpatient respiratory clinic after experiencing chest pain post-COVID vaccination. On further investigation, this chest pain was attributed to an infection of the axilla. Further to this she received a cholecystectomy in 2022 due to ongoing pain in the arm. In the processes of investigation for this chest pain, a CT chest was completed in October 2022 which revealed multiple pulmonary thin-walled cysts. There were bilateral variable sized sub centimetre pulmonary cysts involving the whole lung, lung bases and costophrenic angles, the largest measuring 8mm. A 3mm nodule is shown within the apical segment of the Right Lower Lobe. No pulmonary consolidation or masses were visualised. There was no mediastinal, axillary or supraclavicular lymphadenopathy. She has had no features of tuberous sclerosis including no past history of seizures, cognitive impairment, characteristic cutaneous lesions or other lesions found on scans. She had no history of dyspnoea, recurrent pneumothorax, chylothorax or abdominal haemorrhage. She is a non-smoker and has no significant exposure to asbestos, silica or coal dust. Serum-level VEGFD or MMP tests were unavailable in the regional area of this case. Autoimmune and vasculitis screens were negative. Lung function was unremarkable showing normal lung volumes and DLCO. Ultrasound of the kidney was undertaken in December 2022 to rule out angiomyolipoma. This scan revealed normal appearance of both kidneys, with appropriate size for the patient's age. There was no evidence of hydronephrosis, nephrocalcinosis or cortical scarring (Figure 1-7).

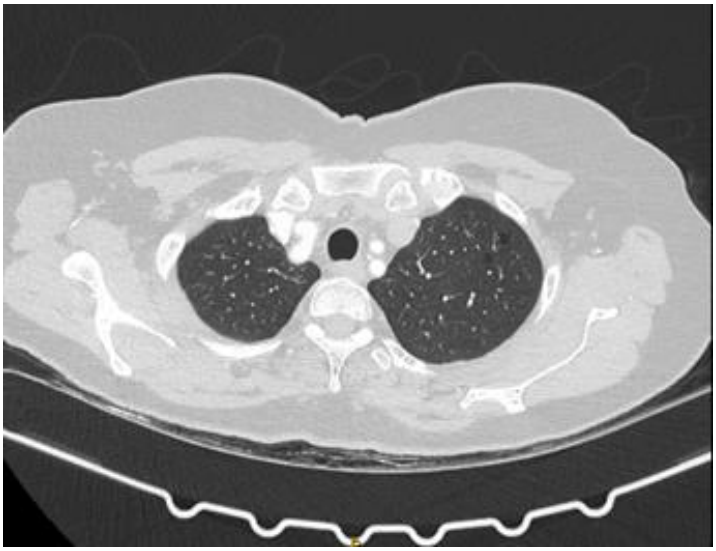


Figure 1: *Shows cysts in the upper zone of the lungs.*

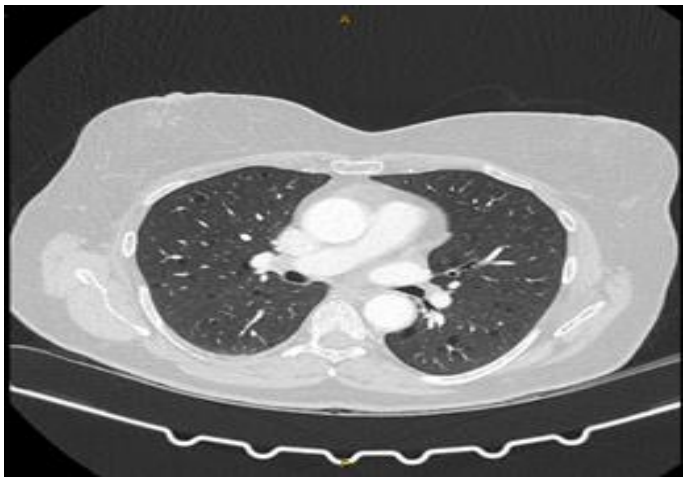


Figure 2: *Shows >10 cysts in the middle zone of bilateral lung fields with no parenchymal changes.*

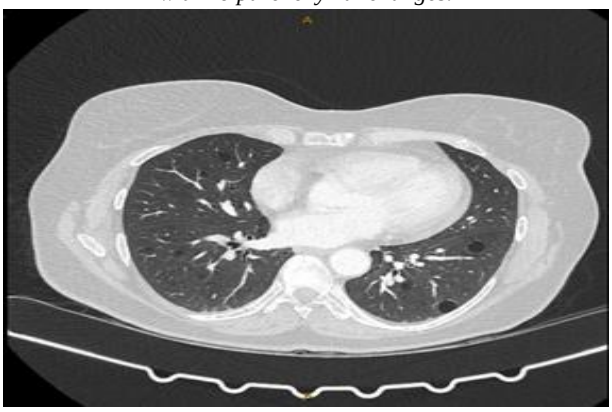
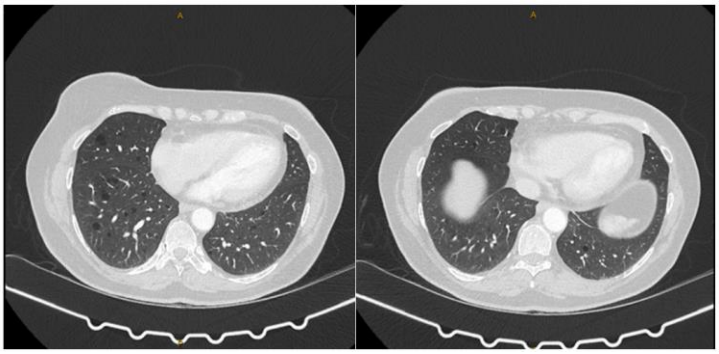


Figure 3: *Shows some larger thin walled cysts with 1 cyst on the border of the lung.*



Figures 4 and 5: *Shows >10 cysts in the lower zones of the lung.*

Discussion

Lymphangioleiomyomatosis is the most likely diagnosis in this case due to the characteristic cysts found on the CT chest. However, this patient has an absence of symptoms in keeping with LAM with no history of any pneumothorax, no progressive dyspnoea and no history of chylothorax [1,3]. However, it has been found that LAM is a slowly progressive disease with half the

patients developing exertional dyspnoea within 10 years, 20% requiring oxygen, and 10% have died [2]. Incidental discovery of cysts on chest imaging is a common presentation of LAM [1]. LAM can be diagnosed utilising the European Respiratory Society guideline which allocates LAM diagnoses into definite, probable or possible cases [6]. A definite diagnosis of LAM requires Lung HRCT features and lung biopsy in-keeping with LAM or any of angiomyolipoma, thoracic or abdominal chylous fusion, lymphagioleimyoma or lymph node involvement.6 Probable LAM cases are determined by characteristic HRCT and compatible clinical history or compatible HRCT and any of angiomyolipoma, thoracic or abdominal chylous fusion, lymphagioleimyoma or lymph node involvement [6].

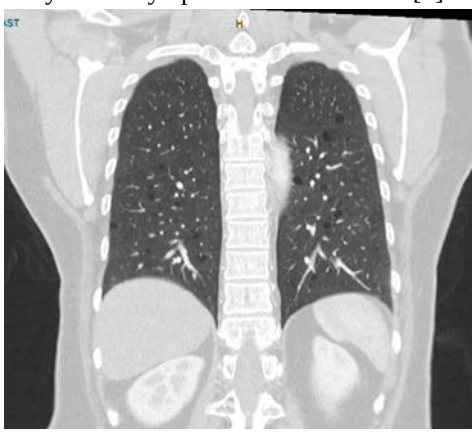


Figure 6: *Shows multiple thin walled cysts distributed bilaterally in all zones of the lungs.*

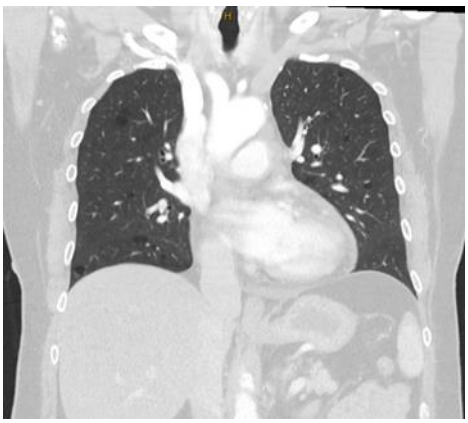


Figure 7: *Shows 1 cysts on the right costophrenic sulci.*

Possible LAM cases either have characteristic or compatible features on HRCT [6]. The characteristic CT of LAM is classificed by the European Respiratory Society as multiple (>10) thin-walled round well-defined air-filled cysts with no other significant pulmonary involvement including no parenchymal changes [6]. LAM can have features of multifocal micronodular pneumocyte hyperplasia in the TSC type of the disease [6]. The guidelines also state that HRCT is compatible with pulmonary LAM when only 2-10 cysts are present [6]. The CT scan in this case is highly suggestive of LAM. The distribution of the cysts randomly dispersed throughout the whole lung with no lobe predominance is highly suggestive of LAM [2-4]. These cysts should be thin-walled, and range from a few mm to several cm which is what is present in this case [1-4]. Additionally, there is also a lack of any lung parenchyma changes which also supports a diagnosis of LAM [1,3,4].

Gold standard diagnosis of LAM is made through tissue biopsy showing infiltration of abnormal smooth muscle cells or LAM cells [4]. However not all patients require a tissue biopsy as LAM has characteristic features on CT scans as mentioned above [4]. A clinical diagnosis can be made with a CT scan and at least one of: high VEGF-D greater than or equal to 800pg/mL, renal angiomyolipoma, lymphagioleimyoma, tuberous sclerosis complex, or chylous effusions [3]. This patient did not have features of tuberous sclerosis complex and there was a lack of any renal angiomyolipoma on renal ultrasound. Unfortunately, due to the regional location of the patient a VEGF-D was not a feasible investigation and therefore could not confirm the diagnosis. Although for definitive diagnosis of LAM in this case this patient would require a surgical or transbronchial biopsy looking for LAM cells [3]. The objective of the diagnosis of LAM is to make the diagnosis with the least invasive technique available [3]. Due to the mild nature of the disease in this case the benefit of diagnosis did not outweigh the risks associated with biopsy, therefore, this case was diagnosed as a possible case of LAM with characteristic CT features of the disease. LAM has many diseases which can mimic its radiological appearance including emphysema, Birt Hogg Dube Syndrome, Lymphoid interstitial pneumonia, Amyloidosis, Light chain deposition disease and pulmonary cell histiocytosis [3]. When considering LAM via CT scan it is vital to rule out these other causes for cystic lung changes to increase the likelihood of a diagnosis of LAM. Lymphocytic interstitial pneumonia (LIP) is a benign lymphoproliferative disorder that can cause bilateral lower lobe predominant cysts in the periobronchovascular area [1,2,7,8]. Usually LIP is associated with parenchymal changes including ground-glass opacities, poorly defined centrilobular and subpleural nodules, reticulonodular shadowing and alveolar consolidation [1,7,8]. Further to this, this disease is almost always associated with an underlying autoimmune disorder or immunodeficiency most commonly Sjogren syndrome [2,7,8]. Idiopathic LIP is exceedingly rare and therefore this disease is highly unlikely as the cause of cysts in this case [2,7]. Overall LIP is unlikely in this case due to the normal appearance of the parenchyma with no Sjorgren Syndrome.

Langerhans Cell Histiocytosis is a differential for LAM which often occurs in smokers and occurs typically in younger adults in their 20-40s [1,2]. Langerhans Cell Histocytosis typically has

upper lobe predominant cysts with variable wall thickness with lower lobe sparing there is also often associated nodules/lung parenchyma changes [1,2,4]. Presence of cysts in the costophrenic sulci can provide a more likely diagnosis of LAM over Langerhans cell histiocytosis [1]. Due to this case having cysts in the costophrenic sulci, lack of nodules, no smoking history and older age this makes Langerhans cell histiocytosis unlikely. Centrilobular emphysema is unlikely in this case due to the well-defined nature of the cystic lesions in the lung with no change in the distribution of vessels both of which being more typical features of emphysema.4 Emphysematous changes are more defined by an absence of this well-defined cysts [4]. Birt Hogg Dube syndrome should be considered as a rare multisystemic disease involving skin, pulmonary and renal findings that can cause cysts within the lungs [1,2]. Its prevalence is estimated at 1 in 200,000 and can affect patients at any age [2]. Birt Hogg Dube Syndrome can manifest with skin lesions, renal tumours and/or multiple lung cysts with pulmonary cysts being the most common systemic manifestation [1,2]. The lung cysts in Birt Hogg Dube syndrome are usually lower lobe predominant and in the subpleural areas including the paramediastinal and perifissural locations within the lungs [1,2]. The presence of elliptical and paramediastinal cysts are especially indicative of Birt Hogg Dube syndrome [2].

Amyloidosis and Light chain deposits should also be considered as differentials in this case. Amyloidosis often presents with systemic involvement in 80-90% of cases however can present localised [2]. Pulmonary involvement with pulmonary cysts, nodular parenchymal, diffuse interstitial disease occurs in around 50% of patients with Amyloidosis [1,2]. Amyloidosis is also often associated with Sjorgren Syndrome [1,2]. However to differentiate from LAM, Amyloidosis usually presents with calcification within nodules [2]. Light chain deposition another cause of cystic lung changes however is almost always associated with Multiple myeloma or Waldenstrom disease. Therefore evaluation for Multiple myeloma is essential in differentiating from other cystic lung diseases [2]. The management of LAM is often with inhibition of mTORC1 signalling. Inhibition of mTOR by drugs such as Sirolimus is currently the best management for LAM according to the MILES trial showing that this therapy almost holts its progression [1,3,5]. In Sirolimus and Everolimus appears to have similar efficacy for the treatment of LAM however Everolimus has less research [3]. Studies have found that by utilising sirolimus for 12 months there was a 50% reduction in angiomyolipioma size and improvement of lung function including reduction in residual volume, improvement of FEV1 and forced vital capacity [3]. Further to this Sirolimus has a better side effect profile and is generally well tolerated [3]. This therapy is indicated for those with compromised lung function, progressive ling disease or clinical features of chylous effusion [1]. Currently there are trials examining the use of low dose mTOR inhibition for the preservation of lung function in early disease changes [1]. Other pharmacological management can include bronchodilators for those with airway obstruction [3]. Other pharmacological management has been found less effective in LAM with trials investigating usefulness of hormonal therapy with links of LAM to oestrogen with inconsistent and inconclusive results [3]. Further research is warranted in this area especially in the use of a combination of mTOR inhibitors and anti-oestrogen therapies [3].

Conclusion

In conclusion, LAM is an uncommon disease which can present with recurrent pneumothorax, progressive dyspnoea, chylothorax or on incidental imaging. The disease is diagnosed from a mixture of clinical history, HRCT, tissue biopsy, VEGFD levels and presence of typical lesions such as renal angiolipoma or tuberous sclerosis. The typical features on a CT which lead to a possible diagnosis of LAM is diffuse thin walled cysts throughout both lungs which include cysts in the costophrenic sulci. LAM typically does not have lung parenchyma changes which differentiates the disease from some of the differential diagnoses for cystic lung disease.

References

1. Koslow M, Lynch DA, Cool CD, Groshong SD, Downey GP. Lymphangioleiomyomatosis and other cystic lung diseases. Immunol Allergy Clin North Am. 2023; 43: 359-377.
2. Martinez BC, Pallerio AF, Florindez SPM. Cystic lung disease. Radiol. 2022; 64: 265-276.
3. McCarthy C, Gupta N, Johnson SR, Yu JJ. Lymphagioleiomyomatosis: pathogenesis, clinical features, diagnosis, and management. Lancet Respir Med. 2021; 9: 1313-1327.
4. Shahani L. Lymphangioleimyomatosis: a radiological diagnosis. BMJ Case Reports.
5. Kundu N, Holz MK. Lymphangioleiomyomatosis: a metastatic lung disease. Am J Physiol. 2023; 324: C320-C326.
6. Johnson SR, Cordier FJ, Lazor R, Cottin V, Costabel U, Harari S. et al. European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis. Eur J Respir Med. 2010; 25: 14-26.
7. Panchabhai TS, Farver C, Highland KB. Lymphocytic interstitial pneumonia. Clin Chest Med. 2016; 37: 463-74.
8. Liu Q, Chen Z, Deng P, Jing W, Shengchu Z, Lihua T, et al. Lymphocytic interstial pneumonia presenting with a ground glass nodule: A case report and literature review. Med. 2023; 102: 33613.