Diagnosis of lymphangioleiomyomatosis in a 75-year-old woman

Introduction

Lymphangioleiomyomatosis should be considered in the setting of previous pneumothoraces, angiomyolipoma and respiratory symptoms when young, even in elderly female patients with supposed chronic obstructive pulmonary disease. Computed tomography scanning of the chest should be undertaken.

Discussion

Lymphangioleiomyomatosis is a rare, progressive, multisystem disease primarily affecting women. It occurs either sporadically or in association with tuberous sclerosis complex (TSC). Mutations of tumour suppressor genes (TSC1 or TSC2) are thought to be causative in both instances. The average age of diagnosis is 41 years; the oldest presentation being 76 years, with an average time between symptom onset and diagnosis of 3–6 years (Ryu et al, 2006).

Lymphangioleiomyomatosis is characterized by immature smooth muscle cell hyperplasia and metastasis (Carrington et al, 1977) leading to cystic destruction of the lungs, obstruction of peripheral lymphatics by lymphangioleiomyomas and angiomyolipoma formation, typically in the kidneys. Patients commonly present with pneumothorax, chylothorax and occasionally haemoptysis.

Prognosis is variable: sporadic lymphangioleiomyomatosis tends to be more severe but lung function testing is the best indicator of survival (Johnson et al, 2010). At 10 years mortality is 9% with 23% of surviving patients requiring oxygen therapy (Johnson et al, 2004). At present there is no cure for lymphangioleiomyomatosis. Bronchodilators provide some clinical benefit in 25% of patients (Johnson et al, 2010). Sirolimus has been shown to shrink angiomyolipomas (Bissler et al, 2008), stabilize lung function and improve quality of life but its use can lead to increased numbers of infections. Progesterone has been shown to slow disease progression but there is little evidence to support its use, although in cases of rapid decline a 12-month trial may be considered (Johnson et al, 2010). Transplantation is offered to those with severe disease and has comparatively good post-transplant survival: 86% at 1 year, 65% at 5 years (Kpodonu et al, 2005).

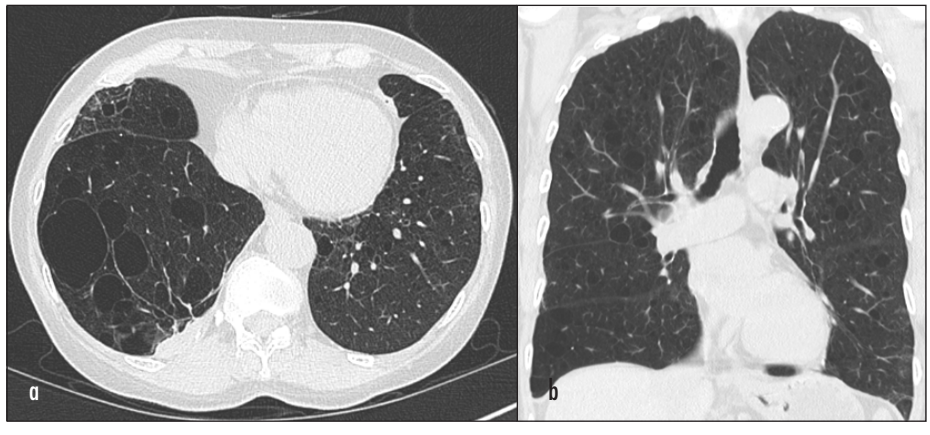
Conclusions

Lymphangioleiomyomatosis is rarely encountered outside specialist centres so diagnosis may be delayed or missed. This

Dr LH Rich *is Locum Specialist Registrar in Endocrinology in the Department of Endocrinology and* **Dr AR Medford** *is Consultant and Honorary Senior Lecturer in Thoracic Medicine, North Bristol Lung Centre and University of Bristol, Southmead Hospital, Bristol BS10 6TD*

Correspondence to: Dr AR Medford (andrewmedford@hotmail.com)

Figure 1. a. High resolution computed tomography of the chest (axial view) showing widespread cysts in both lungs especially in the right base. b. High resolution computed tomography of the chest (coronal view) showing upper zone emphysema and widespread cyst formation.



Case Report

A 75-year-old woman with chronic obstructive pulmonary disease presented to outpatients with increasing exertional dyspnoea. She had had three previous spontaneous right-sided pneumothoraces aged 30 years requiring pleurodesis, and a right nephrectomy for an angiomyolipoma, and had a 50 pack year smoking history.

Her chronic obstructive pulmonary disease had been diagnosed 17 years previously in primary care. Medication comprised inhaled ipratropium, salbutamol and combination salmeterol/fluticasone. On examination she had signs of hyperinflation with prolonged expiration and oxygen saturations 93% on air. Her chest radiograph showed hyperinflation and chronic right-sided changes related to her pleurodesis. Lung function showed airways obstruction with reduced gas transfer: forced expiratory volume in 1 second 0.85 (60% predicted), forced vital capacity 1.35 (77% predicted), ratio 63%, transfer factor for the lung for carbon monoxide 4.18 (72% predicted).

Given the previous history of pneumothoraces, angiomyolipoma, her gender and respiratory problems in her youth, an alternative diagnosis of lymphangioleiomyomatosis was considered. A high resolution computed tomography scan of the chest showed widespread well-defined cysts in both lungs in addition to upper zone centrilobular emphysema (*Figures 1a* and *b*) consistent with lymphangioleiomyomatosis given the history.

Because of her limited pulmonary reserve, she was unsuitable for a surgical lung biopsy. Sirolimus was not started because of her increased respiratory infections. She remains stable.

case highlights the importance of maintaining a high index of suspicion. The major clues in this case were the recurrent pneumothoraces, renal angiomyolipoma, and chronicity of respiratory symptoms in a woman. Further investigation was undertaken because even a late diagnosis of lymphangioleiomyomatosis is helpful to anticipate complications, guide prognosis and assess for anti-lymphangioleiomyomatosis therapy. BJHM

Bissler JJ, McCormack FX, Young LR et al (2008) Sirolimus for angiomyolipoma in tuberous sclerosis complex or lymphangioleiomyomatosis. *N Engl J Med* **358**: 140–51 (doi: 10.1056/NEJMoa063564)
Carrington CB, Cugell DW, Gaensler EA et al (1977) Lymphangioleiomyomatosis. Physiologic-pathologic-radiologic correlations. *Am Rev Respir Dis* **116**: 977–95
Johnson SR, Whale CI, Hubbard RB, Lewis SA, Tattersfield AE (2004) Orphan lung disease. Survival and disease progression in UK patients with lymphangioleiomyomatosis. *Thorax* **59**: 800–3
Johnson SR, Cordier JF, Lazor R et al (2010) European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis. *Eur Respir J* **35**: 14–26 (doi: 10.1183/09031936.00076209)
Kpodonu J, Massad MG, Chaer RA et al (2005) The US experience with lung transplantation for pulmonary lymphangioleiomyomatosis. *J Heart Lung Transplant* **24**: 1247–53
Ryu JH, Moss J, Beck GJ et al (2006) The NHLBI lymphangioleiomyomatosis registry: characteristics of 230 patients at enrolment. *Am J Respir Crit Care Med* **173**(1): 105–11

LEARNING POINTS

- Consider lymphangioleiomyomatosis in female patients respiratory symptoms at a young age, especially with previous pneumothoraces, renal angiomyolipoma.
- It is possible to diagnose lymphangioleiomyomatosis even in the elderly when the condition may have been managed as chronic obstructive pulmonary disease in earlier life.
- Early diagnosis is recommended to anticipate complications especially pneumothoraces and consider anti-lymphangioleiomyomatosis therapy especially sirolimus.
- Even late diagnosis can be helpful as sirolimus treatment may be an option in later life.
- Sirolimus is not suitable in patients with recurrent infection.

Transverse melanonychia

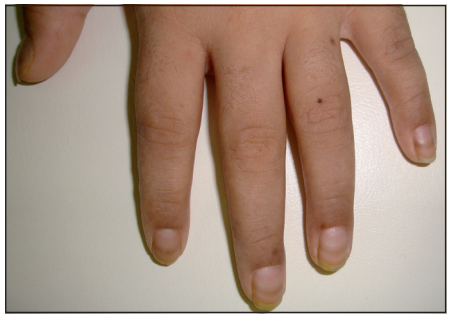
A 16-year-old boy presented to the emergency department with nail discolouration. He had major thalassemia and had undergone allogeneic bone marrow transplantation with an unknown chemotherapy regimen 3 months ago after which the discolouration took place. On physical examination, there were transverse, brown-grayish pigmentations run parallel to the lunula of all the nails (*Figure 1*). The examination was otherwise normal except for chipmunk appearance. The diagnosis of transverse melanonychia following chemotherapy was made.

Dr Hadi Mirfazaelian *is Emergency Physician in the Department of Emergency Medicine, Tehran University of Medical Sciences, Tehran, Iran,* **Dr Ameneh Alaeen** *is Dermatologist in the Department of Dermatology, Arak University of Medical Sciences, Arak, Iran, and* **Dr Yahya Daneshbod** *is Pathologist in the Department of Molecular Pathology, Dr. Daneshbod Pathology Laboratory, Shiraz, Iran*

Correspondence to: Dr H Mirfazaelian (H-mirfazaelian@razi.tums.ac.ir)

Melanonychia is the most frequent form of chromonychia caused by antineoplastic agents and can be seen in diffuse, longitudinal, or rarely transverse band patterns. Melanonychia most often occurs after activation of dormant melanocytes in nail matrix. After that, these cells are transferred to differentiating matrix cells and migrate distally to onychocytes (Andre and Lateur, 2006).

Figure 1. Transverse, brown-grayish bands run parallel to the lunula of all the nails.



Another mechanism of nail pigmentation related to drugs is the storage within the nail plate of systemic drugs that are excreted via the nail unit. This kind of pigmentation moves distally with nail growth (Piraccini and Iorizzo, 2007). Some features such as band breadth greater than 3 mm, variegated borders, change in nail band morphology despite treatment, thumb involvement, extension to adjacent parts, and family history of melanoma warrant concern about the possibility of subungual melanoma (Levit et al, 2000). The patient was referred to the outpatient dermatology clinic. BJHM

Andre J, Lateur N (2006) Pigmented nail disorders. *Dermatol Clin* **24**(3): 329–39
Levit EK, Kagen MH, Scher RK, Grossman M, Altman E (2000) The ABC rule for clinical detection of subungual melanoma. *J Am Acad Dermatol* **42**(2 Pt 1): 269–74
Piraccini BM, Iorizzo M (2007) Drug reactions affecting the nail unit: diagnosis and management. *Dermatol Clin* **25**(2): 215–21, vii