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Progressive cystic lung disease with bullous destruction

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Case presentation

A 62-year-old woman presented with shortness of breath on exertion and reduced exercise tolerance ongoing for several years that had become particularly worse in the previous 3 years. There was no history of extrapulmonary symptoms. She is lifelong non-smoker and there was no history of passive smoking or exposure to industrial dust. She did not have any history of asthma or any other respiratory disease. She was usually independent with activities of daily living (ADLs). Her past medical history included benign ovarian mass diagnosed in 2008 followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy, laparoscopic cholecystectomy, varicose veins and hypertension. Her drug history included atorvastatin, lercanidipine, aspirin, furosemide and a salbutamol inhaler.

She was initially referred to cardiology in February 2019. Electrocardiography (ECG) showed normal sinus rhythm. Echocardiography showed mild aortic stenosis, grade 1 diastolic dysfunction, and normal left and right ventricular size and function. A 24-hour cardiac monitor revealed sinus pauses. She was diagnosed with sinus node dysfunction to be managed conservatively. She was found to have polycythaemia with haemoglobin (Hb) of 200 g/dL (Fig 1; Table 1). An initial chest X-ray showed distended pulmonary vasculature throughout both lungs and at both hilar regions. Atelectasis and focal consolidation can be seen in the right lower zone suggestive of underlying infection (Fig 1). She was treated with a course of antibiotics and referred to respiratory and haematology services for further investigations. In May 2020, she was seen in the haematology clinic and venesection was planned for polycythaemia.

In July 2020, before her respiratory clinic appointment, she presented acutely with worsening shortness of breath and was found to have significant hypoxia with oxygen saturations of 73% on room air. On examination, she had bilateral crackles

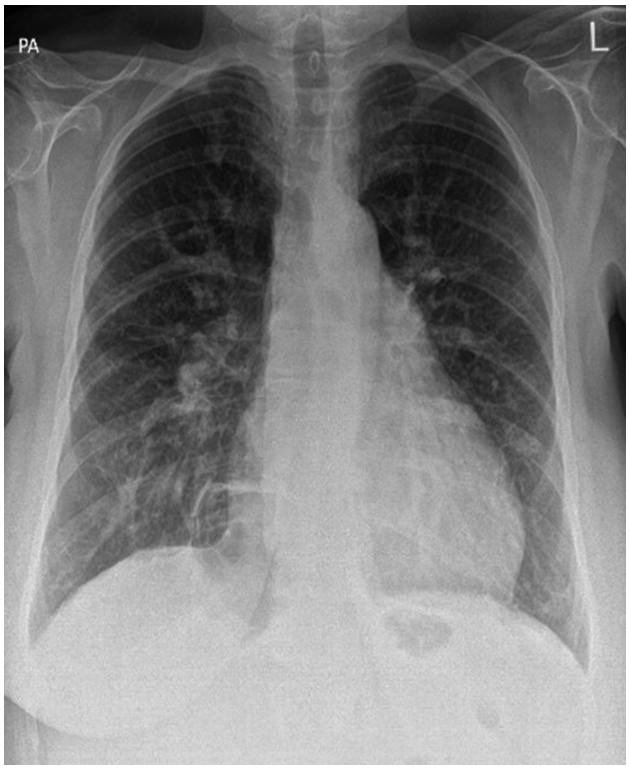

Fig 1. Initial chest X-ray from 2019.

on chest auscultation with pitting oedema on both legs up to her ankles. An arterial blood gas analysis showed compensated type 2 respiratory failure with pH 7.33, partial pressure of carbon dioxide (pCO_2) of 11.1 kPa, partial pressure of oxygen (pO_2) of 8.99 kPa and bicarbonate (HCO_3) of 37.2 mmol/L. An admission chest X-ray (Fig 2) showed dilated pulmonary vasculature throughout both lungs. There was slight blunting of the left costophrenic angle with slight reticular markings in the left lower zone. There was a stable appearance of minimal atelectasis in the right lower zone. The heart, mediastinum and hila were within normal limits.

Her computed tomography (CT) of the chest from 2008 (Fig 3a) showed normal lung parenchyma but her CT pulmonary angiography (CTPA) in 2020 showed bilateral cystic lung disease with bullous destruction with no evidence of pulmonary embolism (Fig 3b–f). A pulmonary function test

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Table 1. Full blood count

	Result	Normal range
White cell count, × 10^9/L	6.9	4–11
Haemoglobin, g/L	200	115–165
Platelets, × 10^9/L	288	150–450
Red blood cels, × 10^{12}/L	6.72	3.5–5.5
Haematocrit, ratio	0.660	037–0.47
Mean corpuscular volume, fL	97.8	75–105
Mean corpuscular haemoglobin, pg	29.7	26–35
Mean corpuscular haemoglobin concentration, g/L	304	290–350
Red blood cell distribution width, %	14.6	11–15
Neutrophils, × 10^9/L	4.7	2–7.5
Lymphocytes, × 10^9/L	1.6	1–4
Monocytes, × 10^9/L	0.4	0.2–0.8
Eosinophils, × 10^9/L	0.1	0–0.4
Basophils, × 10^9/L	0.1	0–0.1

revealed an obstructive picture with forced expiratory volume in the first second (FEV1) of 0.72 L (29% predicted), forced vital capacity (FVC) of 1.53 L (53% predicted), FEV1/FVC of 47%, total lung capacity (TLC) of 106% predicted, reserve volume (RV) of 206% predicted, transfer factor of the lung for carbon monoxide (TLCO) of 47% predicted and transfer coefficient of the lung for carbon monoxide (KCO) of 88% predicted (Fig 4; Table 2). Repeat echocardiography showed normal left ventricular size and function with dilated right ventricle and right atrium with raised pulmonary artery systolic pressure of 64 mmHg. She was discharged home on long-term oxygen therapy.

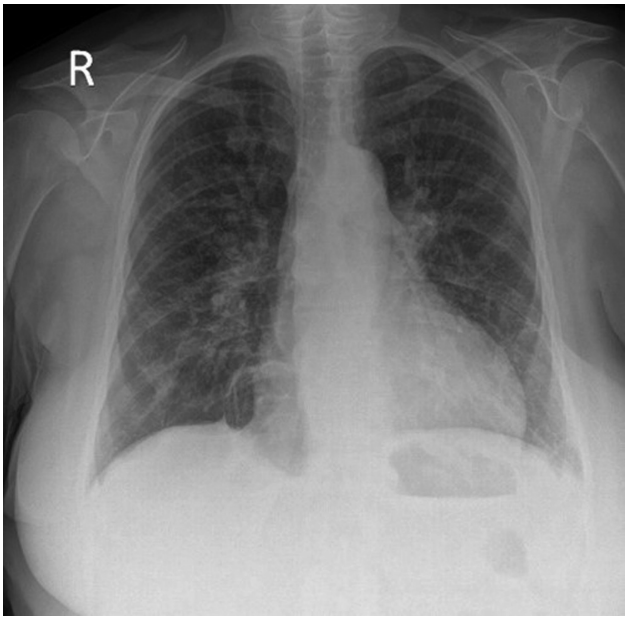

Fig 2. Admission chest X-ray from 2020.

Later, she was reviewed in a specialised tertiary care centre. Alpha-1-antitrypsin and vascular endothelial growth factor–D (VEGF-D) levels came back as normal. Genetic screening for vasculopathy, arteriopathy and familial emphysema were negative. Her case was discussed in a rare lung disease meeting and a decision was made to not proceed with lung biopsy given her poor lung function. Further work up revealed positive polymyositis (PM) / scleroderma (Scl)-100 and anti-Mi-2 antibodies. She was treated for progressive cystic lung disease with bullous destruction on autoimmune background. She was started on prednisolone and mycophenolate mofetil. Unfortunately, she continued to deteriorate and was started on nocturnal non-invasive ventilation (NIV) for type 2 respiratory failure.

Discussion

This is a very unusual presentation of cystic lung disease that had developed more recently. We believe that autoimmunity best explains this disease and the presence of antibodies supports this scenario further. The autoimmunity theory was raised because of the rapidity of disease progression; we have seen non-smokers with autoimmune disorders (such as rheumatoid arthritis, systemic sclerosis or myeloperoxidase (MPO) vasculitis) developing emphysema-like changes in addition to their interstitial lung disease (ILD). The positive antibodies do not confirm a certain autoimmune disease but suggest that there is an autoimmune background to explain this unusual disease.

Idiopathic inflammatory myopathies (IIMs) are a group of systemic diseases involving the skeletal muscle and internal organs classified within the group of connective tissue disorders (CTDs). Other than skin involvement, the lung is the most common extra-muscular target in IIM and the prevalence of ILD in patients with IIMs has been reported to be between 20% to 65%.[1,2] One prospective study has revealed prevalence of ILD in patients with IIMs of 78%.[3] Many patients with myositis and myositis-overlap syndromes have autoantibodies that are associated with distinctive clinical features. The myositis panel consists of 11 myositis-associated autoantibodies (MAAs) or myositis-specific autoantibodies (MSAs). MAAs, which are frequently encountered in rheumatic disorders associated with myositis, include anti-Ro52, anti-U1-ribonucleoprotein (RNP), anti-PM/Scl-100, anti-PM/Scl-75 and anti-Ku. MSAs, which are specific for IIMs, include anti-synthetase autoantibodies, anti-Mi-2 and anti-signal recognition particle (anti-SRP). Anti-synthetase autoantibodies encompass anti-Jo-1 (histidyl-), anti-PL-7 (threonyl-), anti-PL-12 (alanyl-), anti-EJ (glycol-), and anti-OJ (isoleucyl-tRNA synthetase).

Mi-2 antibodies are typically found in patients with steroid responsive dermatomyositis. They are rare in polymyositis. Mi-2 antibodies are invariably of high titre and show no variation during the course of the disease or treatment.

Antibodies to PM-Scl75 and PM-Scl100 antigens are found in 50%–70% of patients with the polymyositis/scleroderma-

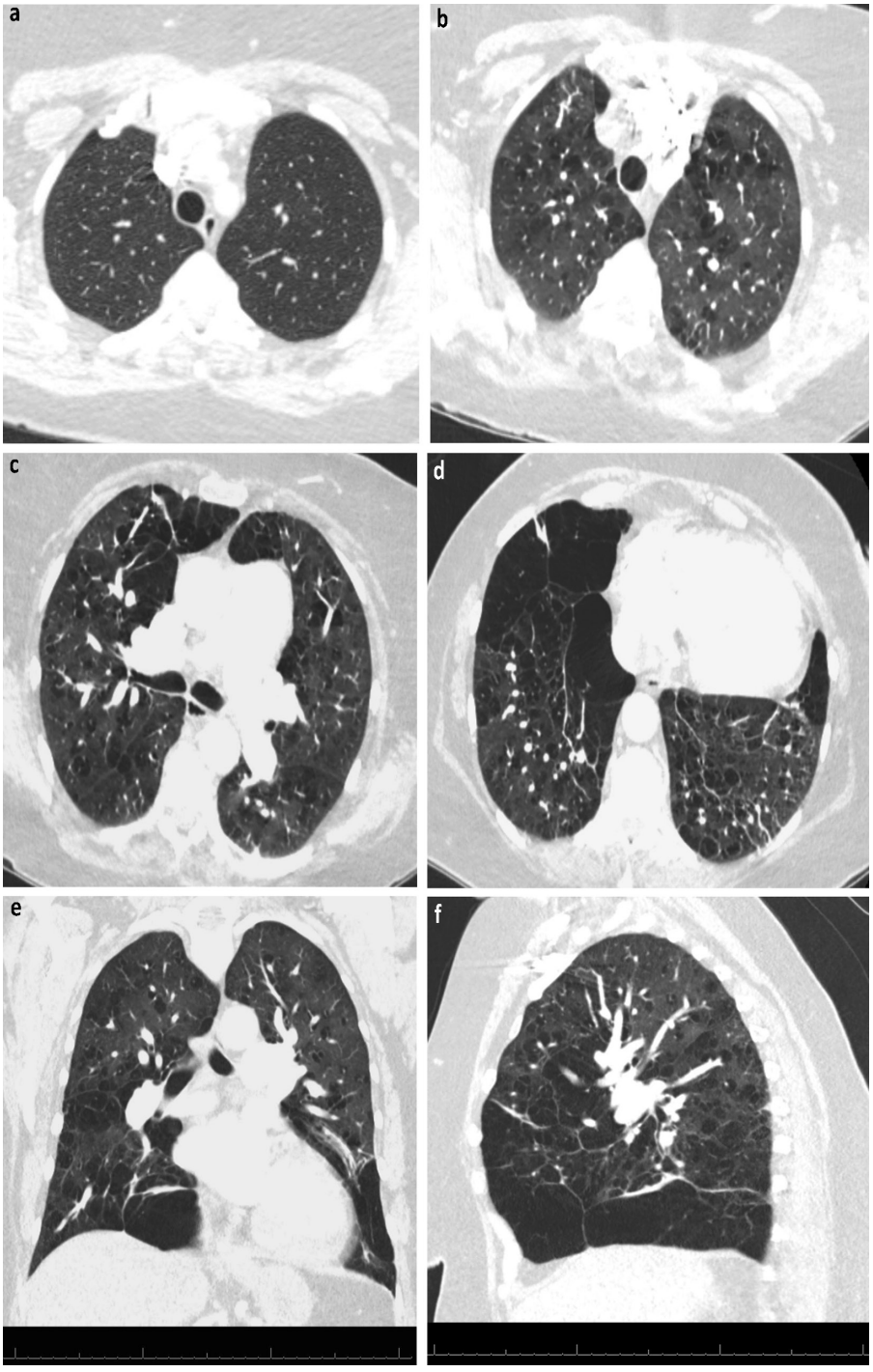

Fig 3. Computed tomography. a) Axial plane from 2008. b, c and d) Axial plane from 2020. e) Coronal plane from 2020. f) Sagittal plane from 2020.

overlap syndrome. PM-Scl100 is not as closely associated with systemic sclerosis as PM-Scl75. Strong nucleolar staining with weak, fine speckled, nucleoplasmic staining can be seen on HEp-2 immunofluorescence.

Despite the fact that myopathic manifestations of IIMs frequently precede lung involvement, in one series, 18% of patients diagnosed with IIM-associated ILD did not have muscle-related symptoms at the time of radiological or clinical diagnosis of lung involvement and may have been misdiagnosed as idiopathic ILD.[4] Song *et al* have reported that, among idiopathic ILD patients, 38% were found to have myositis autoantibodies.[5]

Although there is a well-established link between myositis autoantibodies and idiopathic interstitial pneumonias (IIP; such as fibrosing alveolitis, interstitial pneumonia and desquamative interstitial pneumonia or diffuse alveolar haemorrhage), no

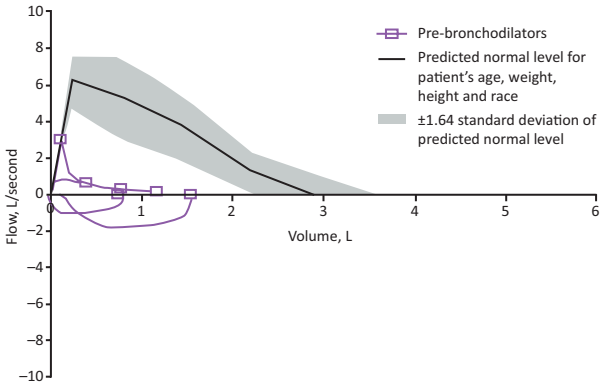

Fig 4. Flow volume loop.

Table 2. Pulmonary function test

	Measured	Predicted	% of predicted	Pre-Z score
FVC, L	1.53	2.90	52.9	–3.17
FEV1, L	0.72	2.45	29.3	–4.55
FEV1/FVC, %	46.81	77.32	60.5	–4.69
PEF, L/s	2.98	6.22	48.0	–3.59
MEF25, L/second	0.13	1.31	9.7	–1.72
MEF50, L/second	0.30	3.70	8.1	–3.09
MEF75, L/second	0.68	5.43	12.5	–3.52
PIF, L/second	1.96	n/a	n/a	n/a
VC_{max}, L	1.53	3.01	50.8	–3.53
IC, L	1.23	2.23	55.1	n/a
ERV, L	0.30	0.79	38.6	n/a
FET, seconds	8.16	n/a	n/a	n/a
TLC, L	5.55	5.23	106	0.53
RV, L	2.01	4.15	206	6.09
TLCOcSB, mmol/min/kPa	7.88	3.83	48.6	–3.47
KCOcSB, mmol/min/kPa/L	1.51	1.33	88.2	–0.63

ERV = expiratory reserve volume; FET = forced expiratory time; FEV1 = forced expiratory volume in the first second; FVC = forced vital capacity; IC = inspiratory capacity; KCOcSB = single breath transfer coefficient for carbon monoxide; MEF25 = maximal expiratory flow at 25% of FVC; MEF50 = maximal expiratory flow at 50% of FVC; MEF75 = maximal expiratory flow at 75% of FVC; PEF = peak expiratory flow; PIF = peak inspiratory flow; RV = residual volume; TLC = total lung capacity; TLCOcSB = single breath transfer capacity of lung for carbon monoxide; VC = vital capacity.

previous case of cystic lung disease with bullous destruction has been reported.

Conclusion

We suggest that in cases of idiopathic ILD, myositis antibody panel evaluation should be considered as antinuclear antibody-negative patients could still present with autoantibodies to cytoplasmic antigens.

Key points

- The lung is the most frequent extra-muscular target in IIMs.
- Eighteen per cent of patients diagnosed with IIM-associated lung disease did not have muscle-related symptoms at the time of radiological or clinical identification of lung involvement.
- In cases of idiopathic interstitial pulmonary disease, a myositis antibody panel assessment should be considered, as individuals with negative antinuclear antibodies may still have autoantibodies to cytoplasmic antigens. ■

References

1 Saketkoo LA, Ascherman DP, Cottin V *et al*. Interstitial lung disease in idiopathic inflammatory myopathy. *Curr Rheumatol Rev* 2010;6:108–19.
2 Chen IJ, Jan Wu YJ, Lin CW *et al*. Interstitial lung disease in polymyositis and dermatomyositis. *Clin Rheumatol* 2009;28:639–46.
3 Fathi M, Vikgren J, Boijsen M *et al*. Interstitial lung disease in polymyositis and dermatomyositis: longitudinal evaluation by pulmonary function and radiology. *Arthritis Rheum* 2008;59:677–85.
4 Fathi M, Dastmalchi M, Rasmussen E, Lundberg IE, Tornling G. Interstitial lung disease, a common manifestation of newly diagnosed polymyositis and dermatomyositis. *Ann Rheum Dis* 2004;63:297–301.
5 Song JS, Hwang J, Cha HS *et al*. Significance of myositis autoantibody in patients with idiopathic interstitial lung disease. *Yonsei Medical Journal* 2015;56:676–83.
6 Paul N, Avalos C, Estifan E, Swyden S. Interstitial lung disease in dermatomyositis complicated by right ventricular thrombus secondary to macrophage activation syndrome- a case report. *AME Case Rep* 2020;4:18.

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