metastases, pneumatoceles and *Pneumocystis carinii* pneumonia [7]. Physicians should also consider the possibility of collagen vascular diseases, especially SS. Additionally, the differential diagnosis of pulmonary involvement in SS includes lymphoma and amyloidosis, and thoracoscopic lung biopsy can be required to obtain a definitive diagnosis.

In conclusion, this is the first case of pneumothorax as a presenting manifestation of SS. This case emphasizes the importance of a careful clinical history and examination in the evaluation of pneumothorax. Although rare, SS should be considered in the patient presenting with pneumothorax and multiple lung cysts.

### Rheumatology key message
- SS should be considered as a cause of spontaneous pneumothorax.

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**Hyperferritinaemia and macrophage activation in a patient with interstitial lung disease with clinically amyopathic DM**

Sir, Clinically amyopathic DM (C-ADM) is characterized by typical skin lesions with amyopathy or hypomyopathy and was recently reported to be complicated by rapidly progressive interstitial lung disease (RP-ILD), especially in those patients who express the anti-C-ADM-140 antibody [1]. RP-ILD with a fatal outcome is commonly associated with hyperferritinaemia [2–4]. However, it has not been clarified as yet why hyperferritinaemia was present in patients with C-ADM-related RP-ILD. In the present study we demonstrated the presence of systemic ferritin-producing macrophages in a C-ADM-related RP-ILD autopsy case.

A 58-year-old Japanese man was admitted with a heliotrope rash and Gottron’s papules of the MCP, elbow and knee joints. Laboratory investigations revealed that the level of serum creatine kinase was 70 IU/l, which is within normal limits, and that the KL-6 and ferritin levels were 735 U/ml (normal value <500 U/ml) and 2100 ng/ml (normal value <261 ng/ml), respectively. Although tests for both ANA and anti-aminocarboxy tRNA synthetase antibodies were negative, the anti-C-ADM-140 antibody was detected by an immunoprecipitation assay and an ELISA using a recombinant MDA5 as the antigen, as described previously [5]. He complained of dyspnoea on exertion. High-resolution CT of the chest demonstrated consolidation in the bilateral lower lobes. The patient was diagnosed with C-ADM-related RP-ILD. We selected combination therapy consisting of prednisolone, tacrolimus and i.v. CYC therapy. However, the RP-ILD had progressed, accompanied by elevation of the serum ferritin level to 4730 ng/ml. The patient died from respiratory failure due to RP-ILD ~5 months after admission.

In the autopsy, the histology of the ILD tissue revealed diffuse alveolar damage (DAD) in the proliferative/organizing phase. The accumulated cells detected in the alveoli were predominantly CD68 positive (Fig. 1). In addition, CD68-positive cells were observed diffusely in the bone marrow, liver and spleen (Fig. 1). Staining detected both heavy-chain ferritin (H-ferritin), which is associated with detoxification of iron and inflammation, and light-chain ferritin (L-ferritin), which is associated with iron storage,
in most CD68-positive cells in each organ (Fig. 1). To analyse isoferritin, the serum ferritin level was investigated via western blot analysis. A higher concentration of serum H-ferritin was observed in the investigated C-ADM-related RP-ILD case than in a healthy donor. However, the concentration of serum L-ferritin did not differ between the two individuals. Taken together, these results indicate that H-ferritin rather than L-ferritin was produced in the patient with C-ADM-related RP-ILD, although systemic macrophages synthesize both L-ferritin and H-ferritin.

We demonstrated the presence of systemic ferritin-producing macrophages in a hyperferritinaemic C-ADM-related RP-ILD autopsy case. Our previous reports demonstrated that the level of serum ferritin correlates with the activity of C-ADM-related RP-ILD, suggesting that serum ferritin can be a valuable biomarker for C-ADM-related RP-ILD [3, 4, 6]. Serum ferritin is delivered primarily from macrophages, although ferritin can also be secreted by numerous cell types, such as T lymphocytes [7, 8]. Ferritin is composed of 24 subunits of two...
functionally distinct subunits: H-ferritin and L-ferritin [9]. H-ferritin plays the major role in the rapid detoxification of iron and intracellular iron transport, whereas L-ferritin is involved in iron nucleation, mineralization and long-term storage. The expression of ferritin is regulated at both the transcriptional and post-transcriptional levels by iron, hormones, cytokines, including IL-1α and TNF-α, and oxidative stress. Ferritin protects cells against damage due to oxidative stress [8–10]. In the present study, the high level of serum ferritin may be attributable to the level of the hypoxia and inflammation caused by systemic activated macrophages in patients with C-ADM-related RP-ILD.

In general, DAD is not always associated with significant macrophage presence. However, it has been reported that DAD with a pronounced increase in macrophages was seen in the alveoli and the interstitium of the lung in severe acute respiratory syndrome (SARS) and that direct injury of virus on alveolar epithelium, prominent macrophage infiltration and distinctive fibroblast proliferation may play major roles in the pathogenesis of SARS. We speculated that increasing alveolar macrophages could be found specifically in some kind of DAD, such as SARS and C-ADM-related RP-ILD. We hypothesized that the regulation of activated macrophages may represent a potent therapy for C-ADM-related RP-ILD.

Rheumatology key message

- A high level of serum ferritin is attributable to systemic activated macrophages in C-ADM-related RP-ILD.

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