An unusual lung involvement in scleroderma: lipoid pneumonia

Sirs,

We report a case of a 75-year-old woman affected by systemic sclerosis (SSc) with limited cutaneous variant and anti-centromere antibody positivity since 2007, who developed an unusual lung involvement. She manifested symptoms of acral vascular involvement, dysphagia, heartburn and constipation over the years. In 2016 she underwent a partial intestinal resection due to volvulus. She never presented overt lung, cardiac, renal involvement or relevant comorbidities. She was on statins, antiplatelet and antacid therapy. In January 2017 she developed pneumonia, requiring hospitalisation and antibiotic therapy with clinical resolution. The scan performed at that time was not available. The discharge indication was to repeat a chest computed tomography (CT) scan after three months, which showed initial interstitial lung involvement (Fig. 1A). Pulmonary function tests (PFTs) were stable compared to those previously performed, with normal static volumes and a mild reduction of both standard DL_{CO} and DL_{CO}/VA. Laboratory inflammation markers were negative. She was asymptomatic for dyspnea or cough, with normal respiratory examination and oxygen peripheral saturation. Exposure history resulted negative.

Due to the disease subset (*i.e.* limited SSc) – she had low risk of SSc-related interstitial lung involvement– we initially attributed the radiological findings to her slow recovery from the recent pneumonia, and in the absence of clinical symptoms, specific therapy was not started.

A second lung CT scan, six months after hospitalisation, showed an increase of the interstitial involvement (Fig. 1B), however, the patient did not report any respiratory symptoms and the PFTs were stable. Resistant infectious processes were excluded by bronchoscopy and the cellular analysis was inconclusive. Suspecting an autoimmune inflammatory process triggered by the recent infection, immunosuppressive therapy was started: prednisone 50mg daily for one month, with subsequent tapering, plus mycophenolate mofetil 2000 mg daily, in order to extinguish the possible self-sustained inflammatory response.

After three months of treatment, unexpectedly, the CT scan showed a further increase in the extension of the multiple areas of ground-glass (Fig. 1C).

The case was examined during the weekly multidisciplinary team meeting involving rheumatologists, radiologists and pulmonologists. Radiologists detected the presence of a crazy-paving pattern, characterised by ground-glass opacities, with superimposed inter-and intra-lobular septal thickening, which could be due to many causes, such as usual or non-specific interstitial pneumonia, alveolar proteinosis, organising or eosinophilic pneumonia, lymphangitic spread of cancer, sarcoidosis or, as in our case, lipoid pneumonia (LP). Taking into account the clinical and radiological information, it was very probable. The patient was specifically asked about possible aetiologies and she admitted to have overused vaseline-oil as a laxative since the volvulus episode for fear of constipation. A bronchoscopy was then performed. Because of spontaneous bleeding during the procedure, it was not possible to make a cellular examination and biopsy. The available literature data show that most cases are self-limited (1), so mycophenolate mofetil was stopped. After eight and sixteen months from the discontinuation of vaseline-oil, the CT scans showed an improvement of lung involvement (Fig. 1D).

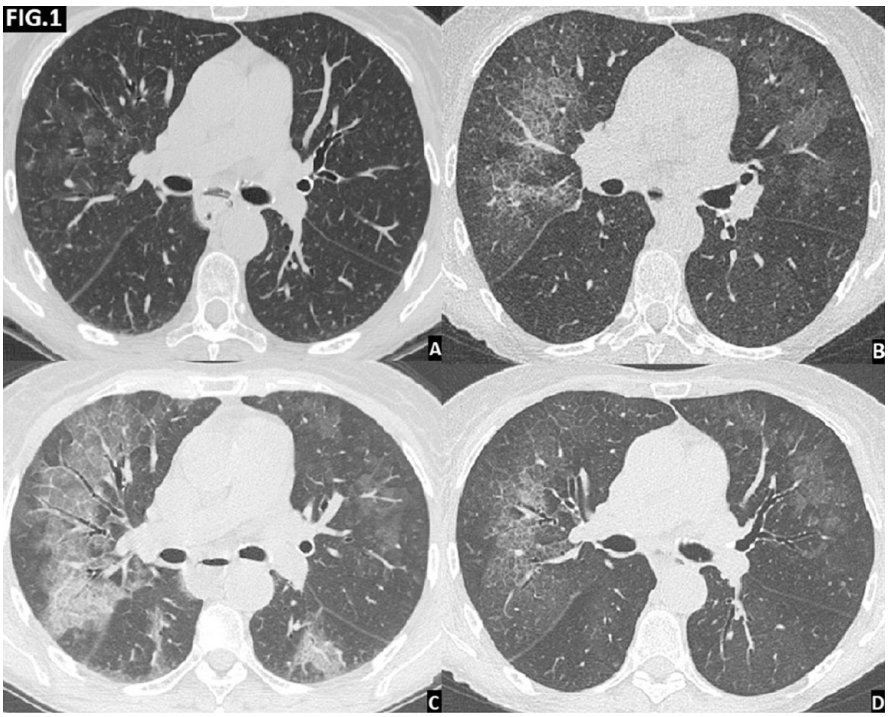

Fig. 1. High resolution chest tomography images.
A. Three months from acute pneumonia. Areas of ground-glass mainly located in right-upper-lobe.
B. Six months from acute pneumonia. Increased extension and density of the ground-glass areas in the right-upper- and in the left-upper-lobe, with superimposed inter-and intra-lobular septal thickening ("crazy paving" pattern).
C. Three months from the beginning of specific therapy. Further increase in the extension of the ground-glass areas, with involvement of both lower lobes. "Crazy-paving" pattern is more evident in right-upper- and left-lower-lobe.
D. Eight months from vaseline-oil discontinuation. Residual areas of "crazy-paving" in the right-upper-lobe and of ground-glass in the left-upper-lobe. Almost complete normalisation of the findings in the lower-lobes.

LP is an uncommon condition that results from the accumulation of lipids in the alveoli. The use of oil-based laxatives is the first cause of the chronic form, and oesophageal reflux is a major risk factor because of microaspiration episodes (1-3). Our patient exhibited both these aspects and the vaseline-oil discontinuation was associated with the dramatic radiological improvement, therefore the final diagnosis of LP was confirmed.

This case highlights the importance of recognising an atypical organ involvement for a disease subset, considering differential diagnoses. Since gastrointestinal dysmotility and constipation are very common in SSc, and the lungs may be affected in the majority of cases, with varying degrees of severity, we think that this case may help rheumatologists' daily clinical practice, identifying LP as possible differential diagnosis. A multidisciplinary approach enables a thorough investigation and allows a broader appraisal of risk-benefit evaluation before initiating therapy.

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References

1. BETANCOURT SL, MARTINEZ-JIMENEZ S, ROSSI SE, TRUONG MT, CARRILLO J, ERASMUS JJ: Lipoid pneumonia: spectrum of clinical and radiologic manifestations. *AJR Am J Roentgenol* 2010; 194: 103-9.
2. MARCHIORI E, ZANETTI G, MANO CM, HOCHHEGGER B: Exogenous lipoid pneumonia. Clinical and radiological manifestations. *Respir Med* 2011; 105: 659-66.
3. JEELANI HM, SHEIKH MM, SHEIKH B, MAHBOOB H, BHARAT A: Exogenous lipoid pneumonia complicated by mineral oil aspiration in a patient with chronic constipation: a case report and review. *Cureus* 2020; 12: e9294.