IL-6 blockade in paraneoplastic interstitial pneumonia with autoimmune features

Sirs,

Paraneoplastic interstitial lung disease (ILD) is an uncommon manifestation of solid tumours, most frequently associated with lung cancer and haematological malignancies, and rarely with gastrointestinal malignancies such as colon adenocarcinoma (1, 2). We report a case of anti-Ro52-positive paraneoplastic interstitial pneumonia with autoimmune features, presenting a severe fibrosing NSIP pattern and favourable therapeutic response to tocilizumab over a 12-month period

A 74-year-old woman with a 36 pack-year smoking history, hypertension, dyslipidaemia and coronary atherosclerosis presented with progressive dyspnoea since April 2024. High-resolution CT (November 2024) revealed new bilateral fibrosing ILD consistent with NSIP: subpleural and peribronchovascular reticular opacities, ground-glass changes and traction bronchiectasis, predominantly affecting the lower lobes, lingula and middle lobe. Hepatic lesions prompted abdominal CT (December 2024), which confirmed hepatic metastases and ascending colon wall thickening with locoregional adenopathy. Colonoscopy with biopsy confirmed infiltrating adenocarcinoma. Tumour markers were elevated (CEA 76.1 ng/mL; CA 19-9 4001 U/mL). Immunological workup showed isolated anti-Ro52 positivity with negative ANA, anti-Ro60, anti-ENA, and scleroderma-specific antibodies (via immunoblotting). Bronchoalveolar lavage demonstrated eosinophilia (32–35%) and lymphocytosis with inverted CD4/CD8 ratio (0.28); cytology was negative for malignancy. Capillaroscopy revealed a scleroderma-like pattern (neoformations, ramifications, avascular zones, haemorrhages), interpreted as cancer-associated (Fig. 1A). Electromyography showed chronic, non-progressive myopathic changes. PET-CT demonstrated hepatic hypermetabolism but no pulmonary uptake, supporting an immune-mediated rather than tumour-infiltrative pulmonary process.

FOLFOX plus bevacizumab was initiated in January 2025, with 50% fluoropyrimidine dose reduction for heterozygous DPYD variant (c.1129-5923C>G). Baseline pulmonary function tests (PFTs) showed FVC 88% predicted. Oxaliplatin was discontinued in March 2025 due to suspected pulmonary toxicity. Despite its withdrawal and a brief prednisone taper, ILD continued to progress: PFTs worsened (FVC 83%, DLCO 42%) and CT (April 9, 2025) showed increased fibrosis with greater architectural distortion (Fig. 1B). Notably, this pulmonary worsening occurred while hepatic metastases were already showing partial response in CT (April 5, 2025), demonstrating a temporal dissociation between oncological improvement and ILD progression. The patient received IV methylprednisolone 250 mg daily for 3 days, with symptomatic improvement. Oral prednisone was initiated with biweekly taper. Given progression, the multidisciplinary team initiated tocilizumab 162 mg subcutaneously weekly on June 9, 2025, three months after oxaliplatin discontinuation.

Tocilizumab was selected based on efficacy in systemic sclerosis-associated ILD, in the focuSSced trial (3), meta-analyses (4), and conditional recommendation in ACR/CHEST 2024 and ATS 2024 guidelines (5, 6). Alternative agents were less suitable: mycophenolate and azathioprine raised interaction concerns with concurrent chemotherapy; rituximab posed humoral immunosuppression risk; nintedanib was contraindicated given diarrhoea risk from colonic malignancy and hepatic metastases (ALT 124, AST 138, ALP 459 U/L) (5, 6). Clinical pharmacology confirmed no interactions between tocilizumab and 5-FU/bevacizumab.

Follow-up through January 2026 (12 months) demonstrated favourable response. Serial CTs (July, September 2025) showed ILD stabilisation for the first time since diagnosis (Fig. 1B). PFTs stabilised (FVC 82%, FEV1 85%, DLCO 38%). Dyspnoea resolved, Raynaud's phenomenon disappeared and capillaroscopy normalised (Fig. 1A). The tumour maintained sustained partial response. No serious adverse events attributable to tocilizumab occurred.

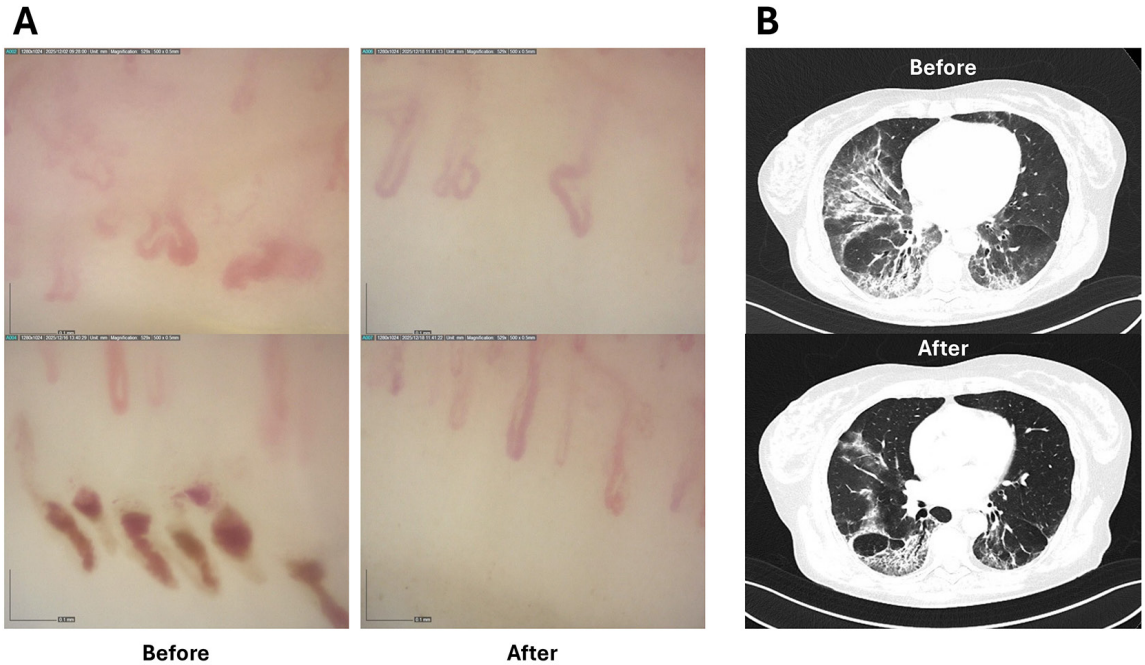

Fig. 1. Two-panel composite showing videocapillaroscopy with abnormal microvasculature normalising after treatment, and chest computed tomography scans demonstrating bilateral interstitial lung disease stabilisation following tocilizumab therapy.
Videocapillaroscopy (**A**) and chest CT (**B**) before and after tocilizumab treatment.
A: Baseline capillaroscopy showing scleroderma-like pattern with giant capillaries, prominent ramifications/neoangiogenesis, haemorrhages, avascular areas, and disorganised architecture (left panels); after IL-6 blockade, improvement with normalised capillary density and reduced ramifications (right panels).
B: Chest CT demonstrating fibrosing NSIP pattern with peribronchovascular consolidations, ground-glass opacities, and architectural distortion without honeycombing (top); stabilisation after 6 months of tocilizumab (bottom).

Tumour burden reduction is the cornerstone of paraneoplastic syndrome management (7, 8). However, the temporal dissociation between emerging oncological response and continued ILD progression until tocilizumab addition provides circumstantial evidence for a contributory role of IL-6 blockade. Additionally, ILD progression persisting one month after oxaliplatin withdrawal argues against drug toxicity as the primary driver. Tocilizumab is established for autoimmune CTD-ILD (3-6), and its application to paraneoplastic ILD represents an incremental extension of known mechanisms (9, 10). Nevertheless, this observation provides practical guidance for multidisciplinary teams facing progressive paraneoplastic ILD where conventional immunosuppression is contraindicated, demonstrating feasibility and safety of combining IL-6 blockade with active chemotherapy.

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