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Therapeutic Limitations of Nintedanib in Connective Tissue Disease–Related Interstitial Lung Disease with Severe Oesophageal Dysmotility: A Case Report

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Abstract

Systemic sclerosis is frequently complicated by interstitial lung disease, which represents one of the leading causes of morbidity and mortality in this multisystem disorder. Progressive fibrosing phenotypes of connective tissue disease–related interstitial lung disease increasingly qualifies for antifibrotic therapy following evidence from trials such as SENSCIS and INBUILD. However, gastrointestinal involvement in systemic sclerosis, particularly severe oesophageal dysmotility and stricturing disease, may impose practical barriers to treatment delivery. We report the case of a 79-year-old woman with Scl-70–positive systemic sclerosis complicated by connective tissue disease–associated interstitial lung disease demonstrating a definite usual interstitial pneumonia pattern and progressive fibrosing behaviour meeting Pharmaceutical Benefits Scheme criteria for antifibrotic therapy. Although antifibrotic treatment with nintedanib was approved following multidisciplinary review, therapy could not be continued because severe oesophageal dysfunction rendered safe oral administration impossible. Tablet modification was contraindicated, and no alternative PBS-funded antifibrotic therapy was available. This case highlights a clinically important yet under-recognised treatment gap in connective tissue disease–related interstitial lung disease management, where eligibility for therapy does not necessarily guarantee feasibility of drug administration in patients with severe systemic involvement.

Keywords: Systemic sclerosis; Connective tissue disease–associated interstitial lung disease; Progressive fibrosing interstitial lung disease; Nintedanib; Usual interstitial pneumonia; Oesophageal dysmotility; Antifibrotic therapy limitation

Introduction

Systemic sclerosis is an autoimmune connective tissue disease characterised by immune dysregulation, vasculopathy, and progressive fibrosis affecting skin and internal organs. Interstitial lung disease occurs in approximately 40–60% of patients and remains the principal cause of mortality in systemic sclerosis worldwide. Radiological manifestations vary, although nonspecific interstitial pneumonia and usual interstitial pneumonia patterns are most common. Recognition of progressive fibrosing behaviour across multiple forms of interstitial lung disease has shifted therapeutic paradigms, extending antifibrotic therapy beyond idiopathic pulmonary fibrosis. Nintedanib is a multi-target tyrosine kinase inhibitor that reduces fibroblast proliferation and extracellular matrix deposition. Randomised trials have demonstrated its ability to slow forced vital capacity decline in systemic sclerosis–associated interstitial lung disease as well as in progressive fibrosing interstitial lung diseases of other etiologies. Consequently, antifibrotic therapy is increasingly incorporated into management guidelines for selected patients with connective tissue disease–related interstitial lung disease. Systemic sclerosis frequently produces gastrointestinal complications, including severe oesophageal dysmotility, reflux disease, and strictures. These complications may substantially influence medication tolerability and delivery. Despite this, treatment guidelines rarely address

practical drug administration challenges posed by systemic disease manifestations. This case demonstrates how real-world clinical complexity may render evidence-supported therapies impractical despite clear therapeutic indication [1-15].

Case Presentation

A 79-year-old woman presented with progressive exertional dyspnoea and systemic manifestations consistent with systemic sclerosis. She was Scl-70 antibody positive and had established connective tissue disease-associated interstitial lung disease with a definite usual interstitial pneumonia pattern on high-resolution computed tomography.

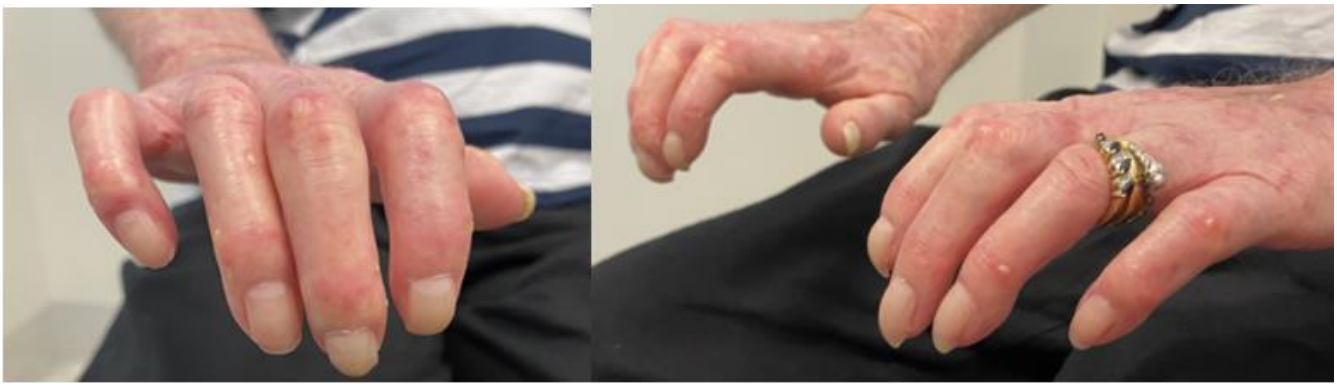

***Figure 1*:** *Systemic sclerosis of the knuckles and visible clubbing.*

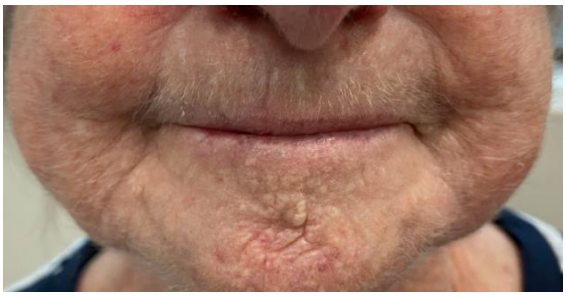

Figure 2: *Visible perioral fibrosis.*

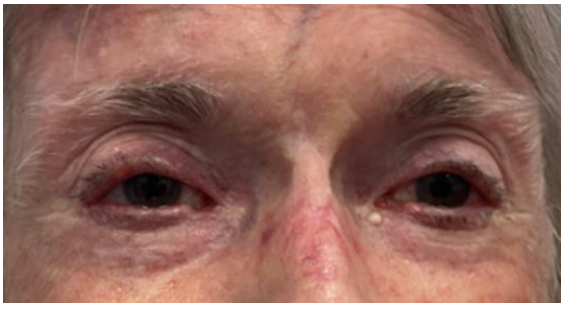

Figure 3: *keratoconjunctivitis sicca, visible telangiectasia and eyelid tightening.*

Test1 18.08.2025 10:31

Parameter	Best	LLN	Z-sc.	%Pred	Pred	Trial1	Trial3	Trial2
FVC[L]	↓1.11	1.58	-2.82	49.3	2.25	↓1.11	↓1.10	↓1.08
FEV1[L]	↓0.96	1.22	-2.46	55.6	1.73	↓0.96	↓0.95	↓0.95
FEV1/FVC	0.87	0.63	1.02		0.78	0.87	0.87	0.88
FEF2575[L/s]	1.57	0.62		107.7	1.46	1.57	1.40	1.44
PEF[L/s]	4.41	–		–	–	2.55	3.61	4.41
FET[s]	19.61					5.10	19.61	4.29
FIVC[L]	↓0.93	1.58		41.3	2.25	↓0.93	↓0.81	↓0.79
PIF[L/s]	1.10	–		–	–	1.05	0.87	1.10

FEV1 Var = 12mL 1.3%, FVC Var = 12mL 1.1%
Test quality FEV1 - A, FVC - A
Possible restriction

Figure 4: *Pulmonary function test conducted on the 18/08/2025.*

Her medical history included chronic type 2 respiratory failure, bronchiectasis, heart failure with preserved ejection fraction, type 2 diabetes mellitus, severe gastro-oesophageal reflux disease, oesophageal stricture requiring prior dilatation procedures, and progressive systemic sclerosis manifestations affecting peripheral tissues. She was an ex-smoker with remote tobacco exposure. Her case was reviewed at a lung fibrosis multidisciplinary meeting, which confirmed progressive connective tissue disease–related interstitial lung disease. Progressive physiological decline satisfied PBS eligibility criteria for antifibrotic therapy, and treatment with nintedanib was recommended. Although treatment approval was obtained, therapy was discontinued shortly after initiation because severe oesophageal dysmotility and reflux created substantial aspiration risk and prevented safe swallowing of medication. Pharmacy consultation confirmed that nintedanib capsules could not be crushed or altered due to occupational exposure risks and unpredictable pharmacokinetic changes. No alternative antifibrotic therapy was available under PBS eligibility criteria. The patient remains under ongoing follow-up with persistent exertional limitation and progression of peripheral systemic sclerosis manifestations (Figures 1-3).

Investigations

Pulmonary function testing demonstrated severe restrictive physiology with marked reduction in forced vital capacity and total lung capacity. Diffusing capacity was significantly reduced, while transfer coefficient was relatively preserved, suggesting fibrotic lung volume loss rather than primary pulmonary vascular disease. Serial high-resolution computed tomography imaging demonstrated established fibrotic usual interstitial pneumonia changes characterised by honeycombing, traction bronchiectasis, and architectural distortion without evidence of new pulmonary nodules. Imaging findings were broadly stable compared with prior scans, although physiological decline persisted. Echocardiography demonstrated preserved left ventricular systolic function, although pulmonary artery pressures could not be reliably estimated. Pulmonary hypertension therefore remains a potential contributor to symptoms and requires ongoing surveillance (Figure 4).

Management

Management decisions were guided by multidisciplinary team consensus, which confirmed connective tissue disease–associated interstitial lung disease with progressive fibrosing behaviour and recommended antifibrotic therapy. Although treatment approval was secured, therapy could not be continued due to severe oesophageal dysfunction preventing safe oral administration. Ongoing management focuses on symptom optimisation, management of comorbidities, pulmonary rehabilitation, reflux control, and surveillance for pulmonary hypertension and respiratory failure progression.

Discussion

This case highlights a clinically significant limitation in interstitial lung disease management whereby therapeutic eligibility does not necessarily translate into treatment deliverability. Clinical trials frequently exclude patients with severe systemic disease manifestations, meaning gastrointestinal complications common in systemic sclerosis are underrepresented in treatment outcome data. Severe oesophageal dysmotility increases the risk of pill retention, aspiration, and medication intolerance. Nintedanib capsules cannot be crushed because modification may create occupational hazards and unpredictable drug absorption. As no parenteral or alternative antifibrotic formulations currently exist, patients unable to swallow oral medication may remain without disease-modifying options. This case underscores the importance of early assessment of gastrointestinal involvement in systemic sclerosis and highlights the need for alternative antifibrotic delivery systems, expanded real-world trial inclusion, and policy flexibility to address treatment feasibility barriers.

Conclusion

This case demonstrates a real-world therapeutic limitation in systemic sclerosis–associated interstitial lung disease in which evidence-supported antifibrotic therapy could not be administered due to severe oesophageal dysfunction. As gastrointestinal involvement is common in systemic sclerosis, clinicians should recognise that medication delivery feasibility may limit treatment even when disease qualifies for therapy. Future therapeutic strategies should address formulation accessibility to ensure equitable treatment availability in patients with multisystem disease.

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