Systemic sclerosis-interstitial lung disease with coexistent subacute invasive pulmonary aspergillosis: a rare association

Benhur Joel Shadrach¹, Kunal Deokar¹, Vikrant Agarwal², Anukool Jain³, Rishabh Goel⁴

¹Pulmonary, Critical care & Sleep Medicine, Department of Pulmonary Medicine, All India Institute of Medical Sciences (AIIMS), Jodhpur

²Aryavart MRI Centre, Gorakhpur, India

³Department of Pulmonary Medicine, Pushpanjali Hospital, Agra, India

⁴Department of Pulmonary Medicine, Shahi Global Hospital, Gorakhpur, India

A 55-year-old female complained of recurrent haemoptysis, low-grade fever, cough, and worsening dyspnoea for three months. She was a diagnosed case of systemic sclerosis-interstitial lung disease for which she was on tapering doses of prednisolone and Mycophenolate Mofetil for past 2 years. On admission, she was febrile, had tachycardia, tachypnoea and pallor was present. Bilateral fine velcro crepitations were present on auscultation of the chest. Arterial blood gas (ABG) revealed acute respiratory alkalosis and hypoxemic respiratory failure. Chest radiograph showed bilateral interstitial shadows and cavitation in right upper zone. Computerised tomography (CT) of the thorax revealed a fibrotic interstitial lung diseases (ILD) with multiple cavities, fungal ball, pericavitary infiltrates, and pleural thickening (Figure 1). Transbronchial lung biopsy (TBLB) disclosed acute angled branching septate hyphae invading lung parenchyma with surrounding necrotic inflammation. Fungal culture grew *Aspergillus fumigatus*. *Aspergillus fumigatus*-specific IgG was elevated. She was labelled as subacute invasive aspergillosis (SAIA) and initiated on voriconazole 200mg twice a day. She responded to treatment and haemoptysis subsided. Oral voriconazole was continued and she was kept under close follow-up.

Pulmonary infections are the most common causes of morbidity and mortality in fibrotic ILD. Parenchymal fibrosis (cysts, traction bronchiectasis, and honeycombing) combined with immunosuppressive therapy predispose to chronic infections, such as tuberculosis and aspergillosis. Spectrum of aspergillus infections include pulmonary aspergilloma, chronic pulmonary aspergillosis (CPA), and invasive pulmonary aspergillosis (IPA).

Figure 1. CT thorax lung window axial sections showing fungal ball with air crescent sign (blue arrow), cavity (red asterisk), and pericavitary infiltrates on background of fibrotic interstitial lung diseases

Address for correspondence: Rishabh Goel, Department of Pulmonary Medicine, Shahi Global Hospital, Gorakhpur, India; e-mail: rishabhgoel1905@gmail.com

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Table 1. Association of fibrotic ILD with pulmonary aspergillosis and their outcomes

Author	Type of study	Year	Fibrosing ILD	Aspergillus spectrum	Treatment	Outcome
Liu C, <i>et al.</i> [2]	Case report	2019	IPF	CNPA	Itraconazole	Progression
Mochizuki E, <i>et al.</i> [3]	Case report	2015	DM-ILD	CPA	Voriconazole	Responded
Nandi, <i>et al.</i> [4]	Case report	2015	Ssc-ILD	Aspergilloma	Itraconazole	Progression
Kurosaki F, <i>et al.</i> [5]	Retrospective study (15 cases out of 539 ILD had pulmonary aspergillosis)	2014	IPF, RA-ILD, PPFE	CPA-14 IPA-1	Itraconazole: 7 Voriconazole: 7 Micafungin: 1	Responded: 6 Progression: 8 No response: 1
Present case	Case report	2020	Ssc-ILD	SAIA	Voriconazole	Responded

DM — dermatomyositis; ILD — interstitial lung diseases; IPF — idiopathic pulmonary fibrosis; PPFE — pleuroparenchymal fibroelastosis; RA — rheumatoid arthritis

CPA can be either chronic cavitary pulmonary aspergillosis (CCPA) or subacute invasive aspergillosis (SAIA). The diagnostic criteria of CPA include one or more cavities with or without a fungal ball or nodules on thoracic imaging, direct evidence of *Aspergillus* infection (microscopy or culture from biopsy) or an immunological response to *Aspergillus* spp. and exclusion of alternative diagnoses, all present for at least 3 months [1]. SAIA previously known as chronic necrotising pulmonary aspergillosis is a form of CPA occurring in mildly immunocompromised patients and has a rapid progression. Although aspergillus infection is usually seen in those with underlying lung diseases, their association with fibrotic ILD's is rare, limited to a single observational study and few case reports [2–5] (Table 1).

Management of CPA includes initiation of antifungal therapy, lowering doses of immunosuppression, intracavitary instillation of antifungal agents, surgical resection, and control of haemoptysis [1]. Itraconazole or voriconazole for a minimum of 4 to 6 months is preferred. Micafungin, caspofungin, amphotericin B lipid complex (ABLC) and posaconazole are used as salvage therapy. Surgery aids in improved control of infection and is curative in few cases. Indications for surgery include localised disease, life-threatening haemoptysis, and lack of response to medical therapy [1]. However, surgery is usually precluded by the lack of adequate pulmonary reserve in chronic fibrosing ILD. Finally, despite best management, prognosis of CPA is less favourable, especially in the background of ILD.

Our case report highlights this rare life-threatening complication of fibrotic ILD and alerts the clinician to the importance of early diagnosis and definitive management. SAIA is rapidly progressive and if not intervened timely, leads to morbidity and mortality.

References:

1. Denning DW, Cadranel J, Beigelman-Aubry C, et al. Chronic pulmonary aspergillosis: rationale and clinical guidelines for diagnosis and management. *Eur Respir J.* 2016; 47(1): 45–68, doi: [10.1183/13993003.00583-2015](https://doi.org/10.1183/13993003.00583-2015), indexed in Pubmed: [26699723](https://pubmed.ncbi.nlm.nih.gov/26699723/).
2. Liu C, Yang J, Lu Z. Idiopathic pulmonary fibrosis with chronic necrotizing pulmonary aspergillosis: a case report. *Int J Clin Exp Pathol.* 2019; 12(7): 2653–2656, indexed in Pubmed: [31934094](https://pubmed.ncbi.nlm.nih.gov/31934094/).
3. Mochizuki E, Furuhashi K, Fujisawa T, et al. A case of treatment with voriconazole for chronic progressive pulmonary aspergillosis in a patient receiving tacrolimus for dermatomyositis-associated interstitial lung disease. *Respir Med Case Rep.* 2015; 16: 163–165, doi: [10.1016/j.rmcr.2015.10.008](https://doi.org/10.1016/j.rmcr.2015.10.008), indexed in Pubmed: [26744690](https://pubmed.ncbi.nlm.nih.gov/26744690/).
4. Nandi S, Santra A, Ghoshal L, et al. Interstitial lung disease in systemic scleroderma, complicated with bilateral pulmonary aspergilloma: an unusual association. *J Clin Diagn Res.* 2015; 9(12): OD11–OD13, doi: [10.7860/JCDR/2015/15340.6926](https://doi.org/10.7860/JCDR/2015/15340.6926), indexed in Pubmed: [26816937](https://pubmed.ncbi.nlm.nih.gov/26816937/).
5. Kurosaki F, Bando M, Nakayama M, et al. Clinical features of pulmonary aspergillosis associated with interstitial pneumonia. *Intern Med.* 2014; 53(12): 1299–1306, doi: [10.2169/internalmedicine.53.1578](https://doi.org/10.2169/internalmedicine.53.1578), indexed in Pubmed: [24930648](https://pubmed.ncbi.nlm.nih.gov/24930648/).