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A brief overview of IPF and NSIP

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The diffuse parenchymal lung diseases (DPLDs), also called interstitial lung diseases (ILDs), are a heterogeneous group of rare disorders that cause expansion of the interstitial compartment by varying degrees of inflammation and fibrosis, resulting in parenchymal damage. This group of lung diseases is subdivided into four categories, one of which is the idiopathic interstitial pneumonias (IIPs) (Table 1).[1] The IIPs account for 25 - 30% of all DPLDs, each with distinct clinicopathological and radiological features. Within this subgroup, idiopathic pulmonary fibrosis (IPF) and idiopathic nonspecific interstitial pneumonia (iNSIP) account for 55% and 25% of cases, respectively.[2-4]

Table 1. Classification of diffuse parenchymal lung diseases (DPLDs)[1]

Category	Examples
1. DPLD of known cause or association	Drug toxicity
	Associated connective tissue disease (CTD)
	Hypersensitivity pneumonitis
	Pneumoconiosis
2. Granulomatous DPLD	Sarcoidosis
3. Rare DPLD with well-defined features	Lymphangioleiomyomatosis (LAM)
	Langerhans' cell histiocytosis (LCH)
4. Idiopathic interstitial pneumonia (IIP)	Idiopathic pulmonary fibrosis (IPF)
	Nonspecific interstitial pneumonia (NSIP)
	Cryptogenic organising pneumonia (COP)
	Acute interstitial pneumonia (AIP)
	Desquamative interstitial pneumonia (DIP)
	Lymphocytic interstitial pneumonia (LIP)
	Respiratory bronchiolitis interstitial lung disease (RBILD)

Accurate diagnosis determines both the appropriate management and the prognosis of DPLDs, and is based on an integrated assessment of clinical, radiological and histological data, preferably by a team experienced in the evaluation of these disorders.[1,3,5]

Other conditions associated with similar pathoradiological patterns must be excluded (Table 2), especially in patients presenting with an NSIP pattern, as 39% are subsequently found to have an underlying condition, usually connective tissue disease (CTD).[6] In addition, human immunodeficiency virus (HIV) infection is an important consideration in the work-up of NSIP.[7] A thorough history and clinical examination, together with judicious use of laboratory investigations (e.g. full blood count, electrolytes and renal function, urinalysis, antinuclear antibody and rheumatoid factor), are invaluable in excluding these associated disorders.[1-3,8]

Table 2. Clinical conditions associated with UIP and NSIP patterns[1]

UIP	NSIP
Connective tissue disease	Connective tissue disease
Drug toxicities	Drug toxicities
Occupational exposures (e.g. asbestos)	HIV infection
Chronic hypersensitivity pneumonitis	Hypersensitivity pneumonitis
Familial idiopathic pulmonary fibrosis	Idiopathic NSIP
Idiopathic pulmonary fibrosis	

UIP = usual interstitial pneumonia; NSIP = nonspecific interstitial pneumonia.

Epidemiology

IPF is a progressive, fibrotic lung disease, which carries a distinctly poor prognosis with a 5-year mortality of 50 - 80%.[2] It typically affects older patients (age range 55 - 75 years), with a male predominance. Cigarette smoking has been implicated in its development.[4,5] In contrast, iNSIP usually occurs among non-smoking women in the sixth decade of life (median age of onset 52 years).[9] Although the course of iNSIP is variable, the long-term outcome is more favourable than for IPF, with a 5-year mortality <20%.[2,10]

Clinical presentation

Classically, patients report a chronic, non-productive cough and exertional dyspnoea that progresses over months. Fever and weight loss are unusual in IPF, but are seen in a minority of iNSIP patients who follow a subacute course with prominent constitutional symptoms.[1]

Digital clubbing is found more commonly in IPF (25 - 66%) than iNSIP (8%).[1,11] Although they are nonspecific, bibasilar crackles are the cardinal feature on respiratory examination.[1,3]

The chest X-ray usually reveals nonspecific changes, including reduced lung volumes and bilateral, predominantly lower-zone, reticular opacities.[1,3]

During early disease, lung function tests may be normal, but with disease progression

Table 3. UIP and NSIP patterns on HRCT scan[1-3]

UIP	NSIP
Bilateral reticular opacities	Bilateral reticular opacities
Ground-glass opacities *not* prominent	Bilateral ground-glass opacities
Basal and subpleural predominance	Basal predominance, diffuse or subpleural
Fibrosis and honeycombing	Honeycombing minimal or absent
With or without traction bronchiectasis	With or without traction bronchiectasis

UIP = usual interstitial pneumonia; NSIP = nonspecific interstitial pneumonia; HRCT = high-resolution computerised tomography.

restriction develops. Among smokers and ex-smokers, IPF and chronic obstructive pulmonary disease may co-exist (combined pulmonary fibrosis and emphysema (CPFE)). In patients with CPFE, lung volumes are typically preserved compared with non-smokers with IPF.[1] Most patients demonstrate impaired gas exchange, as evidenced by low oxygen-haemoglobin saturation at rest or on exercise; hypoxaemia on arterial blood gas sampling; or impaired diffusing capacity (DLCO).[1] Serial lung functions are used to monitor IPF and iNSIP, with a declining forced vital capacity (FVC), DLCO and exercise capacity reflecting disease progression.[12]

Diagnosis

Identification of a characteristic usual interstitial pneumonia (UIP) or NSIP pattern on high-resolution computerised tomography (HRCT) scan is the initial step in making a definitive diagnosis of IPF and iNSIP, respectively (Table 3).[1-3,11]

Lung biopsy is not required in patients with a typical clinical picture and a definite UIP pattern on HRCT. However, unless specifically contraindicated, surgical lung biopsy (SLB) is recommended for patients with atypical features of IPF (e.g. extensive ground-glass opacities, nodules, consolidation and discrete cysts) or an NSIP pattern on imaging, as radiological and pathological correlation is inconsistent in these situations.[1,3,4,9]

Bronchoalveolar lavage and/or transbronchial biopsies are not required for the diagnosis of an IIP, but may be helpful in excluding differential diagnoses under consideration.[13]

Clinical course and management

Most patients with IPF follow a chronic course, steadily declining over several years. However, subgroups of patients experience either rapid progression or acute exacerbations – defined as periods of rapid deterioration without an identifiable precipitant – both of which portend a poor prognosis.[5]

Unfortunately, despite active research, there is currently no pharmacotherapy with proven benefit in the management of IPF. Consequently, supportive measures (vaccination against pneumococcus and influenza, domiciliary oxygen therapy, pulmonary rehabilitation, management of right heart failure and treatment of gastro-oesophageal reflux) form the mainstay of therapy. However, lung transplantation may offer improved survival for appropriately selected patients.[14]

Although the course of iNSIP differs among individuals, it is generally more responsive to pharmacotherapy than IPF, especially for patients with predominantly inflammatory disease (cellular NSIP), as opposed to predominant fibrosis (fibrotic NSIP).[1,3,10] Since prospective, randomised, controlled data in iNSIP are lacking, the therapeutic approach is largely extrapolated from studies of ILD complicating CTD. It employs immunosuppression with corticosteroids, alone or in combination with steroid-sparing cytotoxic agents, such as azathioprine, cyclophosphamide and mycophenolate mofetil.[9] For the minority of iNSIP patients who progress despite pharmacotherapy, supportive measures, similar to those employed in the management of IPF, can be used.

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