Review

Detecting and Dealing with IPF

Geetika Verma, MD, FRCPC; and Charles K. N. Chan, MD, FRCPC, FCCP, FACP

Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic lung disease with a grim prognosis in most cases. IPF is more common in males and two-thirds of patients who present are > 60-years-of-age.[1] Challenges to making the diagnosis include the:

- insidious onset,
- non-specific presentation and
- broad differential diagnosis for the clinical and chest x-ray features.

The decision to treat IPF is complex and requires an assessment of the risks and benefits on an individual basis.

Who should be treated?

Those who should be treated include younger patients with fewer comorbidites and, potentially, patients with earlier disease or ground glass opacities on high-resolution computed tomography (HRCT).

Presentation

In addition to exertional dyspnea, most patients report a paroxysmal dry cough. A history of cigarette smoking is commonly associated with IPF. Clinical signs include bibasilar end-inspiratory, or "velcro"-type crackles and digital clubbing in approximately 40% of patients.[1]

Disease course

The disease course is usually characterized by relative stability of lung function in spite of progressive dyspnea, with episodic rapid deterioration attributable to:

- infection,
- pulmonary embolus, or
- acute exacerbation of IPF.

Differential diagnosis

A detailed history should focus on exclusion of causes that are treatable or modifiable. These include exposures to:

- metal or rock dusts,
- farms,
- birds/feathers and, among others,
- moulds.

Drug history

A detailed drug history is essential, with common culprits including:

- amiodarone,
- bleomycin,
- methotrexate, or
- nitrofurantoin.

Other

Suspicion of connective tissue disease should prompt serologic screening. A history of

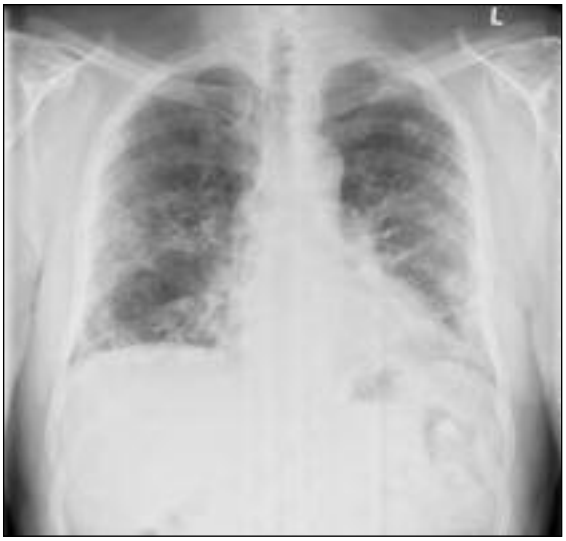

Figure 1. The high resolution computed tomography (HRCT) scan provides more detailed information that may rule in the diagnosis of idiopathic pulmonary fibrosis (IPF) and evaluate severity. The characteristic HRCT findings include basal and peripheral-predominant fibrotic changes, possibly including traction bronchiectasis and honeycombing, with minimal ground glass opacification.

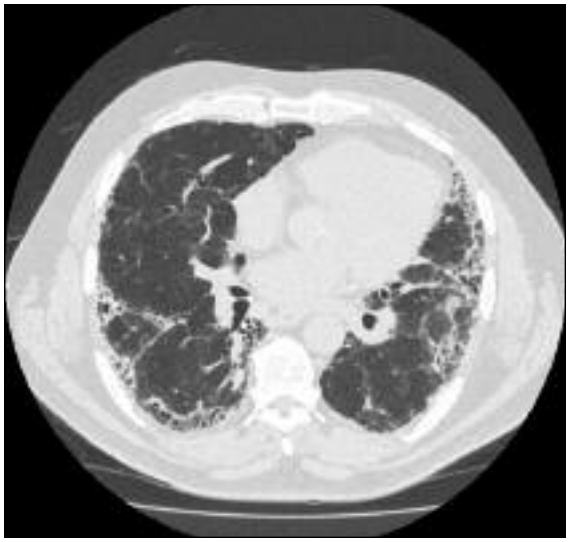

Figure 2. Lung biopsies are generally performed in patients < 50-years-of-age, who exhibit atypical radiographic or clinical features, or who have a history suspicious for another form of interstitial lung disease (hypersensitivity pneumonitis, sarcoidosis, or interstitial lung disease associated with connective tissue disease).

asbestos exposure may entitle patients to workers' compensation for disability.

Investigations

Pulmonary function test

Full pulmonary function tests demonstrate restriction (reduced total lung capacity and forced vital capacity). Early on, there may only be reduced diffusing capacity and residual volume. As disease progresses, patients exhibit oxygen desaturation during a six-minute walk test.

Chest x-ray

Plain chest x-ray findings include:

- increased reticular markings with basal predominance and
- reduced lung volumes.

Prognosis

The mean survival from time of diagnosis is 2.5 to 3.5 years.[2] Poor prognostic factors include:

- age at presentation,
- extent of smoking history,
- finger clubbing,
- degree of fibrosis on imaging,
- severity of spirometric and lung volume impairment,
- exercise desaturation and
- pulmonary hypertension.

Dr. Verma is a Respirology Fellow, University of Toronto, Toronto, Ontario.

Dr. Chan is a Respirologist, Department of Medicine, University Health Network and Mount Sinai Hospital and Professor, University of Toronto, Toronto, Ontario.

Frequently Asked Questions

1. **In whom should I suspect IPF?**

   IPF should be suspected in patients > 50-years-of-age who present with insidious onset of dyspnea on exertion, typically over six months or more.

2. **Who should be treated?**

   Younger patients with fewer comorbidites and, potentially, patients with earlier disease or ground glass opacities on HRCT.

3. **How is the diagnosis made?**

   Characteristic clinical, HRCT and pulmonary function test findings usually suffice to diagnose IPF. In patients with atypical features, a lung biopsy should be pursued.

Treatment

The therapeutic options available for IPF have limited efficacy and often significant toxicity. Though corticosteroids have been a hallmark of treatment, they have demonstrated minimal benefit in clinical trials. There is evidence that the combination of prednisone and azathioprine has an advantage over prednisone alone. N-acetyl cysteine (NAC) has been studied in conjunction with these medications and has shown some benefit. While the evidence of its efficacy is limited, NAC has minimal side-effects and therefore, little downside.

Therapies that are currently under investigation include:

- γ interferon (IFN-), a T-helper Type 1 cytokine and
- pirfenidone, an anti-inflammatory, anti-oxidant and anti-fibrotic compound.

Both may impact on progression of fibrosis and mortality, though this remains to be seen.

Take-home message

- The management of IPF patients includes addressing factors that may aggravate cough, such as postnasal drip and concomitant chronic obstructive pulmonary disease
- Gastro-esophageal reflux disease should be treated aggressively, as it is common in IPF and may aggravate both cough and fibrosis
- Treatment for hyperlipidemia with statins may have particular impacts on patients with IPF due to their anti-oxidant properties
- IPF patients should receive annual influenza vaccinations and the pneumonia vaccine
- Infections should be treated early and aggressively to prevent morbidity and mortality
- As disease progresses, physicians should evaluate patients for home oxygen requirements, at rest and with exercise
- Primary care physicians should refer patients to a respirologist early in the course of disease for potential enrollment in clinical trials, further investigations if there is diagnostic uncertainty, or for transplant referral

Finally, patients who are potential lung transplant candidates should be referred early, as deterioration or death may occur suddenly and unpredictably. Dx

References

1. American Thoracic Society. Idiopathic pulmonary fibrosis: Diagnosis and treatment. International consensus statement. American Thoracic Society (ATS) and the European Respiratory Society (ERS). Am J Respir Crit Care Med 2000; 161(2 Pt 1):646-64.
2. King TE, Tooze JA, Schwarz MI, et al: Predicting survival in idiopathic pulmonary fibrosis: Scoring system and survival model. Am J Respir Crit Care Med 2001; 164(7):1171-81.