Case 11
To treat or not to treat? IPF and preserved lung function

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Overview

• Idiopathic Pulmonary Fibrosis is an unpredictable disease.\textsuperscript{1,2}

• Acute IPF exacerbations can occur at any time of the disease and are often fatal.\textsuperscript{2,3}

• In this case, the history of an IPF patient is presented from her first presentation with mild lung function impairment to her death after an acute exacerbation.

Medical History and Tests

- 64 year-old female
- Ex-smoker, 30 pack-years, stopped smoking 2007
- 3-month history of mild breathlessness when playing golf
- No extra-thoracic symptoms
- No past medical history of note
- No medications
- No exposures
Medical History and Tests

Clinical Examination:
• No clubbing or lymphadenopathy
• Very occasional fine basal crepitations
• Normal cardiovascular examination
Laboratory

• Normal inflammatory markers
• Rheumatoid factor negative
• Negative autoimmune panel
## Lung Function

<table>
<thead>
<tr>
<th>Value</th>
<th>Absolute</th>
<th>% of predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>2.80</td>
<td>90%</td>
</tr>
<tr>
<td>FEV$_1$ (L)</td>
<td>2.25</td>
<td>92%</td>
</tr>
<tr>
<td>FEV$_1$/ FVC (%)</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>DL$_{CO}$ (ml/min/mmHg)</td>
<td></td>
<td>63%</td>
</tr>
<tr>
<td>K$<em>{CO}$ (DL$</em>{CO}$/VA)</td>
<td></td>
<td>92%</td>
</tr>
</tbody>
</table>
Imaging

Computed tomography (CT) at presentation:
• Subtle, sub-pleural reticulation with basal predominance
• No honeycombing or ancillary features
Imaging

Subtle, sub-pleural reticulation with basal predominance
Expert opinion

Multidisciplinary Team (MDT) discussion of the baseline CT:
• Subtle sub-pleural disease with reticulation but no honeycombing
• No ancillary features

Based on current international consensus criteria, CT appearances most closely resemble possible UIP but given age of patient it was felt surgical lung biopsy was necessary to confirm diagnosis.
Biopsy

Surgical Lung Biopsy – Left Lower and Upper Lobes
Pathology

Summary of Pathologic Findings

The patient exhibits a typical UIP pattern with the following characteristics:

- Established fibrosis with a sub-pleural distribution
- Temporal and spacial heterogeneity
- Microcystic honeycomb destruction
- Occasional fibroblastic foci
Pathology
Diagnosis

- Radiological appearance = possible UIP
- Histological appearance = UIP
- Clinical history – no identifiable cause for UIP pattern

This leads to the MDT conclusion that the diagnosis is IPF.
Question 1

How would you treat this patient? (multiple entries possible)

1. Pirfenidone*
2. Nintedanib*
3. No treatment (observation)
4. N-acetyl cysteine
5. Enter into clinical trial
Answer 1

Author’s Solution: Initiate Anti-fibrotic Therapy

Data presented at the ATS 2015 support the notion that patients with marginally impaired lung function might benefit from anti-fibrotic therapy.

- Same effect of nintedanib (post hoc subgroup analyses of INPULSIS) in patients with “mild/early” IPF (FVC >90% predicted) vs patients with more advanced lung function impairment\(^1\)

- The treatment effect with pirfenidone was similar in patients with “mild/early” IPF (FVC ≥ 80% or GAP 1) compared to those with more advanced IPF in a subgroup analysis of pooled ASCEND and CAPACITY data\(^2\)

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Medical History and Tests

Six Months Later

• Reports a two-week history of rapidly worsening breathlessness
• Now shortness of breath when climbing one flight of stairs
• Dry cough
• No fever, well in self
• No other new symptoms

Clinical examination:
• Afebrile
• Crepitations to mid zones
• Blood test: Normal inflammatory markers
Imaging

HRCT: 6 months later

- Coarsening of sub-pleural reticulation
- Increase in ground glass attenuation
- Subtle inter-lobular septal thickening
Imaging

Coarsening of sub-pleural reticulation, increase in ground glass attenuation, subtle inter-lobular septal thickening
Ward

- Presumed acute exacerbation
- Admitted
- Supportive care
- Intravenous methylprednisolone and intravenous antibiotics
- Worsening respiratory failure
Imaging

HRCT: 1 week later

Dense, dependant consolidation throughout all lobes of the lung
Imaging

Dense, dependant consolidation throughout all lobes of the lung
Pathology

The post mortem histology showed

- Patchy established fibrosis in sub-pleural distribution typical of UIP
- Diffuse alveolar damage with sloughing off of epithelial cells, fluid in alveolar space and hyaline membranes
- Negative Gram stain and culture

Cause of death: **Acute exacerbation of IPF**
Pathology

Patchy established fibrosis in sub-pleural distribution typical of UIP (Low Power Magnification)
Diffuse alveolar damage with sloughing off of epithelial cells, fluid in alveolar space and hyaline membranes
Learnings From the Case

The most important take home messages of the case are:

1. Acute exacerbations are catastrophic life-threatening episodes which may occur in early disease
2. It is impossible to predict disease course at diagnosis
3. Treatment, had it been available, may have prevented the acute exacerbation