UIP OR NOT UIP PATTERN: THAT IS NOT THE ONLY QUESTION!

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CASE OVERVIEW

This case highlights how a usual interstitial pneumonia (UIP) pattern may be caused by a number of different pathologies, not just idiopathic pulmonary fibrosis (IPF). In order to make an accurate diagnosis of IPF, it is important to conduct a rigorous clinical primary examination to exclude other pathophysiological causes.
MEDICAL HISTORY AND TESTS

Initial visit (July 2012)
• Male, 67 years old
• 90 kg, 175 cm
• Ex-smoker:
  – 15 pack-years
• Occupation:
  – Former commercial delegate who travelled regularly to USA, China and North Africa; no history of environmental exposures
MEDICAL HISTORY AND TESTS

Initial visit (July 2012)

• Comorbidities:
  – Arterial hypertension, type 2 diabetes, coronary heart disease (stent in 2004), mesenteric infarction (1995) and arthrosis

• Current medications:
  – Esomeprazole 20 mg, ramipril 5 mg, ASA 75 mg, metoprolol 200 mg, metformin 850 mg, gliclazide 60 mg and simvastatin 20 mg
MEDICAL HISTORY AND TESTS

Initial visit (July 2012)

- **Physical examination:**
  - Chronic productive cough (with mucopurulent sputum) and mild dyspnoea (New York Heart Association Stage I) but no asthenia, anorexia or fever
  - Patient had a history of recurrent lower respiratory tract infections in the past 2 years
  - Blood pressure 120/60 mmHg
  - Heart rate 56 beats per minute
  - $\text{SpO}_2$ (room air) = 98%
  - Bibasilar crackles on lung auscultation
  - Hypereosinophilia = 1700/mm$^3$
HRCT scan (August 2012)

- Pattern recognised:
  - Subpleural, basal predominance
  - Reticular abnormality
  - Honeycombing
  - Absence of features listed as inconsistent with UIP pattern

- Conclusion = definite UIP pattern
Definite UIP pattern with reticular abnormalities with a subpleural, basal predominance (arrows)
Honeycombing with a subpleural, basal predominance (circles)
IMAGING – HRCT (IMAGE 3)

HRCT (August 2012)

Reticular abnormalities (arrows) and honeycombing (circles) with a subpleural, basal predominance
IMAGING – HRCT (IMAGE 4)

HRCT (August 2012)

Reticular abnormalities (arrows) and honeycombing (circles)
IMAGING – HRCT (IMAGE 5)

HRCT (August 2012)

Reticular abnormalities (arrows) and honeycombing (circles)
IMAGING – HRCT (IMAGE 6)

HRCT (August 2012)

Reticular abnormalities (arrows) and honeycombing (circles)
QUESTIONS

Question 1

- If a patient with the signs shown in the photo and a definite UIP pattern on chest CT-scan presents at the clinic complaining of bilateral joints and muscles pains, following a recent occurrence of Raynaud syndrome, what is the most probable diagnosis?
  - Idiopathic pulmonary fibrosis
  - Rheumatoid arthritis with ILD
  - Diffuse erythematous lupus with ILD
  - Anti-synthetase syndrome with ILD [correct answer]
ANSWERS

Answer 1
Although there is a high variability in symptoms and severity, the presence of a number of extra-thoracic manifestations, such as myalgia or muscular deficit, Raynaud’s phenomenon, polyarthritis, fever, or mechanics hands in association with interstitial lung disease are all suggestive of antisynthetase syndrome.\(^1,2\) However, positive anti-RNA synthetase antibodies (anti-Jo1, anti-PL7, and anti-PL12) are required to confirm the diagnosis.\(^1,2\)

LUNG FUNCTION

Lung function measurements (August 2012)

- Overall, lung function/gas exchange appeared to be good
- There were no signs of infection or connective tissue disease
- Results of bronchoalveolar lavage appeared normal; however, additional blood tests revealed an increasing eosinophil count
- A 6-minute walk test was not performed
### Lung Function Measurements (August 2012)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (% of predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁/FVC</td>
<td>89% predicted</td>
</tr>
<tr>
<td>FEV₁</td>
<td>117% predicted</td>
</tr>
<tr>
<td>FVC</td>
<td>98% predicted</td>
</tr>
<tr>
<td>DLCO</td>
<td>62% predicted</td>
</tr>
</tbody>
</table>
Laboratory results

- **Blood eosinophil count:**
  - 2200/mm³ in August 2012; 2700/mm³ in September 2012

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antinuclear antibody</td>
<td>Negative</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-cyclic citrullinated peptide antibodies</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-neutrophil cytoplasmic antibodies</td>
<td>Negative</td>
</tr>
</tbody>
</table>
BRONCHOSCOPY

Bronchoscopy results
- Normal bronchial tree with no macroscopic anomalies observed

- BAL differential cell count:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cell count</td>
<td>$3.4 \times 10^6$ cells/mL</td>
</tr>
<tr>
<td>Alveolar macrophages</td>
<td>87%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>12%</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>1%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0%</td>
</tr>
</tbody>
</table>

- Normal BAL differential count, no hypereosinophilia on BAL
QUESTIONS

Question 2

• What would make you suspect another diagnosis other than IPF?
  – Possible UIP pattern on chest CT-scan
  – Probable UIP pattern on pulmonary histology
  – Numerous long-term medications
  – 42 year-old patient [correct answer]
Because IPF is rare before the age of 50, the index of suspicion for an underlying connective tissue disease should be high.\(^1\) In such a young patient, you have to be very careful with the diagnosis of IPF. The patient should be promptly referred to a lung transplant centre and evaluated for specific telomerase mutations ie, SFPC, SFPB, GATA-2.\(^2\)

MEDICAL HISTORY AND TESTS

Follow-up (July 2013)

- Similar to on first presentation; however, the patient’s dyspnoea had worsened (New York Heart Association Stage II)

- Laboratory findings were also similar to those observed on initial presentation with the exception of the patient’s eosinophil count, which had increased
  - 3500/mm$^3$ in July 2013
  - 5700/mm$^3$ in September 2013

- Raised suspicion of possible Churg-Strauss syndrome or parasitic infection such as aspergillosis, ascaridosis, lymphatic filariasis, distomatosis, trichinosis, toxocarisis, strongyloides

- Also possibility of other connective tissue diseases e.g. rheumatoid arthritis or systemic lupus erythematosus
IMAGING

HRCT scan (July 2013)
Consistent with a definite UIP pattern, including
• Reticular abnormalities
HRCT (July 2013)
Reticular abnormalities
IMAGING – HRCT (IMAGE 2)

HRCT (July 2013)
Honeycombing
IMAGING – HRCT (IMAGE 3)

HRCT (July 2013)

Reticular abnormalities (arrows) and honeycombing (circles)
IMAGING – HRCT (IMAGE 4)

HRCT (July 2013)

Reticular abnormalities (arrows) and honeycombing (circles)
IMAGING – HRCT (IMAGE 5)

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Reticular abnormalities (arrows) and honeycombing (circles)
IMAGING – HRCT (IMAGE 6)

HRCT (July 2013)

Reticular abnormalities (arrows) and honeycombing (circles)
LUNG FUNCTION

Lung function measurements (July 2013)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (% of predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV$_1$/FVC</td>
<td>86% predicted</td>
</tr>
<tr>
<td>FEV$_1$</td>
<td>105% predicted</td>
</tr>
<tr>
<td>FVC</td>
<td>90% predicted</td>
</tr>
<tr>
<td>TLC</td>
<td>86% predicted</td>
</tr>
<tr>
<td>DLCO</td>
<td>57% predicted</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (absolute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.48</td>
</tr>
<tr>
<td>PaO$_2$</td>
<td>92 mmHg</td>
</tr>
<tr>
<td>PaCO$_2$</td>
<td>35 mmHg</td>
</tr>
<tr>
<td>CO$_2$</td>
<td>24%</td>
</tr>
<tr>
<td>SaO$_2$</td>
<td>97%</td>
</tr>
</tbody>
</table>

- Slight decline in lung function from previous visit
LUNG FUNCTION

Lung function measurements (July 2013)
• Results of 6-minute walk test (room air):
  – 480 m without pause, no desaturation (100% → 99%); Borg 2 → 3
Haematology results (September 2013)

- To exclude other causes such as Churg–Strauss syndrome or parasitic infections a myelogram, osteomedullar biopsy and medullary karyotyping were conducted
  - All tests appeared normal

- Furthermore, and because there was a suspicion of hypereosinophilic syndrome the patient was genotyped
  - Genotyping identified an FIP1L1-PDGFRα fusion gene
1. HRCT scans revealed a UIP pattern suggestive of IPF; however, the patient’s lung function remained relatively stable throughout.

2. Laboratory tests revealed an increasing eosinophil count.

3. Following genotyping an FIP1L1-PDGFRα fusion gene was identified.

→ The patient was diagnosed as having either IPF and hypereosinophilic syndrome or hypereosinophilic syndrome with lung fibrosis.

→ Imatinib was initiated.
LEARNINGS FROM THE CASE

1. Demonstrates the importance of a thorough clinical examination, including physical examination, laboratory tests and blood work-up, and HRCT in the diagnosis of interstitial lung diseases

2. Highlights that, in complex cases, a pulmonologist must also think like an internist and consider pulmonary manifestations of other diseases