CASE OF COMBINED PULMONARY FIBROSIS AND EMPHYSEMA (CPFE)

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MEDICAL HISTORY AND TESTS

Patient history (66-year-old male)

Symptoms at first presentation:

- Increasing dyspnoea on exertion starting 6 months ago (1/2 stairs possible)
- No angina pectoris
- No dyspnoea attacks at night
- Persistent productive cough in the morning

Medication at initial visit:

- Simvastatin 20mg/d
- Acetylsalicylic acid 100mg
- Inhaled therapy with ICS/LABA (formoterol/beclomethasone) combination
MEDICAL HISTORY AND TESTS

Patient history
• Electrician
• No familial disposition for ILDs
• No allergies
• Current smoker with 30 pack-years

Pre-existing conditions:
• Coronary artery disease with stenting 10 years ago
• Mild left ventricular impairment
• Arterial hypertension
• Childhood: meningitis, suspicion of tuberculosis
Physical examination
At first presentation
• Body weight 82 kg; height 177 cm
• Bibasiliary velcro crackles
• Heart rate 88 beats/min
• No heart murmurs
• Mild leg oedema
Pulmonary function tests
First presentation
LUNG FUNCTION

Pulmonary function tests
First presentation

<table>
<thead>
<tr>
<th>Value</th>
<th>Absolute</th>
<th>% of predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>( VC_{\text{MAX}} ) (L)</td>
<td>2.1</td>
<td>80</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.0</td>
<td>79</td>
</tr>
<tr>
<td>FEV(_1) (L)</td>
<td>1.8</td>
<td>83</td>
</tr>
<tr>
<td>( \frac{\text{FEV}<em>1}{\text{VC}</em>{\text{MAX}}} )</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>RV (L)</td>
<td>1.8</td>
<td>100</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>3.9</td>
<td>85</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>( \text{DL}_{\text{CO}-\text{SB}} )</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>( \text{DL}_{\text{CO}/\text{VA}} )</td>
<td></td>
<td>36</td>
</tr>
<tr>
<td>( Pa_{\text{O}_2} ) (mmHg)</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>( Pa_{\text{CO}_2} ) (mmHg)</td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>
Laboratory results

- Autoantibody testing negative for
  - Extractable nuclear antigens (ENA) including JO-1, scl-70
  - Rheumatoid factor (RF)
  - Anti-CCP

- Anti-nuclear antibodies (ANA): 1:160

- Laboratory profile: uneventful

BAL: mixed cell pattern with predominant neutrophils
MEDICAL HISTORY AND TESTS

Echocardiography
- Borderline to mild impaired left ventricular function
- Diastolic dysfunction
- Enlarged right ventricle (42mm diameter, 28cm²)
- Mild impairment of right ventricular function (TAPSE: 15mm)
- No pericardial effusion
- Tricuspid insufficiency
- Pulmonary artery systolic pressure (PASP): 45mmHg
LUNGFUNCTION

Cardio pulmonary exercise testing (CPET)

<table>
<thead>
<tr>
<th>Value</th>
<th>Absolute</th>
<th>% of predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing reserve (%)</td>
<td>-22</td>
<td></td>
</tr>
<tr>
<td>$V_{O2Peak}$ (ml/min)</td>
<td>810 (= 9.6 ml/min/kg)</td>
<td>38</td>
</tr>
<tr>
<td>Work rate ($WR_{MAX}$; Watts)</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>$Pa_{O2rest}$ (mmHg)</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>$Pa_{O2max}$ (mmHg)</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>$V_D/V_{I_{max}}$ (%)</td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>$O2 puls$ ($V_{O2}/HR; ml$)</td>
<td>6.6</td>
<td>46</td>
</tr>
<tr>
<td>$Eq_{O2}$</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>$Eq_{CO2}$</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

- The patient shows a restrictive breathing pattern and pulmonary limitation (breathing reserve at maximal load is below 20%, namely -22%)
- Decrease of $Pa_{O2max}$ under exertion
- Pathological $Eq_{O2}$ and $Eq_{CO2}$
LUNG FUNCTION

Cardio pulmonary exercise testing (CPET)

Combined pulmonary and cardiac limitation with suspicion of pulmonary hypertension

Panel 8  Panel 3  Panel 2
MEDICAL HISTORY AND TESTS

Right heart catheter

- Pulmonary artery pressure: 67/23(38)mmHg
- Pulmonary artery wedge pressure: 12mmHg
- Cardiac output: 4.4l/min
- Cardiac index: 2.21l/min/m²
- Pulmonary vascular resistance: 473dyn*s/cm⁵ or 5.91 WU
- Transpulmonary pressure gradient: 26mmHg
IMAGING

HRCT scan
Images were obtained by thin section multislice CT (MSCT).

<table>
<thead>
<tr>
<th>Scan</th>
<th>Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-enhanced scan</td>
<td>Window level: 1600/-600</td>
</tr>
<tr>
<td>64-line scanner</td>
<td>Slice thickness: 1mm</td>
</tr>
<tr>
<td>Inspiratory breath-hold</td>
<td>Increment: 0.7mm</td>
</tr>
<tr>
<td></td>
<td>Scan time: 5s</td>
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</tbody>
</table>

The MSCT shows the following patterns:
- Centrilobular emphysema
- Paraseptal emphysema
- Traction bronchiectasis (minimal)
- Reticulation (only around emphysema)
IMAGING-HRCT

Please note:
Images will be cropped
Colors will be adapted to guidelines

Emphysema
Emphysema

The area marked on the upper left side (dark blue) of the image can only be recognised as emphysema in combination with the other regions of emphysema. Viewed alone, it would not be distinguishable from honeycombing.
IMAGING-HRCT

Please note:
Images will be cropped
Colors will be adapted to guidelines

Emphysema
IMAGING-HRCT

Please note:
Images will be cropped
Colors will be adapted to guidelines

Traction bronchiectasis
IMAGING-HRCT

Traction bronchiectasis

Please note:
Images will be cropped
Colors will be adapted to guidelines
IMAGING-HRCT

Please note:
Images will be cropped
Colors will be adapted to guidelines

Reticulation
Reticulation

Please note:
Images will be cropped
Colors will be adapted to guidelines
Question: Which of the following features can you see on this scan?

- Traction bronchiectasis
- Honeycombing
- Emphysema*
- Reticulation*
QUESTION

Author’s solution:
Emphysema (in blue) and reticulation (in green) can be seen on this scan.
Question: What is the most dominant feature in this scan?

- Honeycombing
- Emphysema*
- Reticulation
- Traction bronchiectasis
QUESTION

Author’s solution:
In this image, emphysema (marked in blue) is the dominant feature.
DIAGNOSIS

The MSCT shows signs of emphysema and pulmonary fibrosis with possible UIP pattern, i.e. combined pulmonary fibrosis and emphysema.

The differential diagnosis includes the following:

• Idiopathic interstitial pneumonia with emphysema, ie. CPFE
• Connective tissue disease-associated CPFE

The patient’s history, clinical and radiological findings were discussed in our multidisciplinary ILD Board meeting and the diagnosis of idiopathic combined pulmonary fibrosis (IPF) and emphysema was made.


Question: Which of the following statements is true?

a) FVC is often more compromised in CPFE than in IPF alone
b) There is a gap between preserved lung function and significantly comprised DL$_{co}$*
c) CPFE is a syndrome usually found in non-smokers
d) Pulmonary hypertension is a rare finding in CPFE

* (b) is the correct answer
Lung function values, especially FVC, are preserved in CPFE. This is thought to be the consequence of two counteracting disease patterns: pulmonary fibrosis restricts the lung volumes while emphysema hyperinflates them. The gas exchange, however, is significantly decreased in CPFE patients compared to IPF patients due to the combination of fibrotic and emphysematous lung disease and in some cases also due to PH.

OUTPATIENT CLINIC

Treatment and follow-up

The following therapies were recommended:

• Smoking cessation
• Ambulatory rehabilitation (“lung sports”)
• Vaccination against pneumococci and influenza
• Long-term oxygen therapy
• Discontinuation of ICS/LABA and initiation of symptomatic treatment with LAMA due to own positive case experience in CPFE patients
• Antioxidative therapy with N-acetyl cysteine after thorough discussion with the patient of treatment options for IPF including pirfenidone
• Provisional pulmonary hypertension therapy with sildenafil and spironolactone

Under this combination therapy, the patient’s symptoms (dyspnoea and coughing) decreased, pulmonary function tests have remained stable for 6 months.
LEARNINGS FROM THE CASE

Radiologist

HRCT shows a possible UIP pattern with

• Traction bronchiectasis (minimal)
• Centrilobular emphysema
• Paraseptal emphysema / DD honeycombing
• Reticulation (only around emphysema)

The differential diagnosis of a UIP pattern remains difficult and sometimes cannot be “solved”.

In some situations a paraseptal emphysema is very difficult to distinguish from honeycombing. In these cases searching for coincidence with centrilobular emphysema could be helpful.

LEARNINGS FROM THE CASE

Pulmonologist (Diagnosis)

- CPFE is a distinct and still under-recognised syndrome with a characteristic presentation on HRCT. Until today, it has been described in combination with idiopathic fibrotic lung disease and in CTD-ILD patients.
- Patients are most often current or ex-smokers.
- Data on prognosis are conflicting, with some showing worse prognosis than IPF alone and vice versa.
- Pulmonary hypertension in these patients is relatively common, being the major determinant of morbidity and mortality.
- Pulmonary function testing reveals preserved vital capacity, only in rare cases an obstructive pattern, and this is contrasted by significantly impaired diffusion capacity.
- The incidence of CPFE is still unknown, but studies suggest that up to 35% of patients with IPF may have CPFE.
- The diagnosis of this syndrome is based on HRCT with emphysema in the upper zones (mainly centrilobular and/or paraseptal emphysema), and basal fibrotic lung disease.


LEARNINGS FROM THE CASE

Pulmonologist (Treatment)

Data on therapy of CPFE are limited and patients may be treated for both diseases, i.e. fibrosis (in this case IPF) and emphysema. Smoking cessation in current smokers may be the mainstay of therapy. Oxygen therapy should be prescribed according to international guidelines, especially with regards to pulmonary hypertension. Inhaled bronchodilators are often prescribed but data are lacking. It is a point for discussion if the treatment for fibrosis could be similar to that used for fibrotic lung disease, e.g. N-acetylcysteine or novel drugs such as pirfenidone in IPF, but no clinical trials have been published to date. Immunosuppressive therapy is discouraged when a diagnosis of IPF has been made. The treatment of pulmonary hypertension in these patients has been a matter of debate and been addressed at the update discussion in Nice (Fifth World Symposium on Pulmonary Hypertension, Nice, 2013). However, no results of clinical trials have been published to date in this patient population and it has to be kept in mind that vasodilator drugs can worsen hypoxaemia.