Combined pulmonary fibrosis and emphysema (CPFE): an increasingly diagnosed condition

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Note for MLR:

This case will be published in ePatCare and Images of ILD
# Patient case details

<table>
<thead>
<tr>
<th>Title of the case</th>
<th>CPFE: an increasingly diagnosed condition</th>
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</thead>
<tbody>
<tr>
<td>Lung disease type</td>
<td>CPFE</td>
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<tr>
<td>Radiologic pattern</td>
<td>Usual Interstitial Pneumonia (UIP)</td>
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<tr>
<td>Authors</td>
<td>Giovanna Elisiana Carpagnano Ennio Vincenzo Sassani</td>
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<tr>
<td>Language of the case</td>
<td>English</td>
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<tr>
<td>Diagnostic or Treatment case?</td>
<td>Diagnostic</td>
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</tbody>
</table>
A 69-year-old man presented with cough and exertional dyspnoea and a long history of smoking. Lung volumes were preserved as shown by lung function tests, but carbon monoxide diffusing capacity (DL\textsubscript{CO}) was strongly impaired. High resolution computed tomography (HRCT) scans showed a clear UIP pattern. Further testing included volume and endoscopic imaging and transthoracic echocardiography. After a multidisciplinary discussion between pneumologists and radiologists a consensus on the final diagnosis of CPFE was reached.
Medical history and tests

Date of first visit: November 2013
Male, 69 years, ex-smoker (>40 pack-years)
Symptoms on presentation: cough and exertional dyspnoea for 6 months, poor exercise tolerance
Comorbidities: COPD, diabetes, hypertension
Medication:
- Inhaled corticosteroids (ICS) and Long Acting Beta 2 Agonists (LABA)
- Diuretic
- Insulin

PB 130/80 mmHg; HR 80 beats/minute
Physical examination: Finger clubbing
Lung auscultation: Bibasilar crackles and wheezing
Medical history and tests

Personal exposure investigation

- Exposure to birds: NO
- Exposure to moulds: NO
- Exposure to mineral dust: NO
- Exposure to asbestos: NO
- Exposure to pro-fibrotic drugs: NO
Medical history and tests

6-minute walking test (November 2013)

- 63 meters
- $\text{SaO}_2$ at rest: 100%
- $\text{SaO}_2$ post 6 MWDT: 80%
Imaging

HRCT

- Honeycombing consisting of multi-layered thick-walled cysts
- Architectural distortion with traction bronchiectasis due to fibrosis
- Predominance in basal and sub-pleural region
- Paraseptal emphysema at upper lobes
- UIP pattern at lower lobes

→ Radiological conclusions: CPFE syndrome
Imaging

HRCT

Scan specifications:
Inspiratory HRCT scan
Scanner: 16-LINE

Scan settings:
W/L:1500/-500
Slice thickness: 0.5mm; Increment: 1mm
Scan Time: 50 sec
Imaging

HRCT

Sub-pleural honeycombing

Traction bronchiectasis
Imaging

HRCT

Sub-pleural micro-honeycombing (circle); Traction bronchiectasis (arrow)
Imaging

HRCT

Paraseptal emphysema (coronal plane)

Traction bronchiectasis (axial plane by minimum intensity projection reconstruction)
Imaging

Volume and endoscopic images

A volume rendering image that shows multiple areas of architectural subversion, more extended to the right lung

A virtual endoscopic image of bronchial tree at the carina without lesions
Imaging

HRCT Image stack
Question 1

Question: CPF is characterised by:

Answer 1: Only basal honeycombing
Answer 2: Centrilobular and/or paraseptal emphysema in upper zone and predominant pulmonary fibrosis of the lower lobes (UIP or NSIP pattern possible)
Answer 3: NSIP pattern
Answer 4: Centrilobular nodules with emphysema at upper lobes

Correct answer: 2
The HRCT diagnosis of CPF may be possible only if there is an association of UIP or NSIP with emphysema.

The major difficulty is to distinguish between small bubbles from UIP cysts, especially when the distribution is not uniform and typical.

The honeycombing appearance of the cysts is helpful.
## Lung function

18/11/2013

<table>
<thead>
<tr>
<th>Value</th>
<th>Absolute</th>
<th>% of predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>1.77</td>
<td>84</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>2.38</td>
<td>84</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>4.14</td>
<td>73</td>
</tr>
<tr>
<td>RV (L)</td>
<td>1.45</td>
<td>56</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>35</td>
<td>78</td>
</tr>
<tr>
<td>DL\textsubscript{CO} (mmol/kPa.min)</td>
<td>1.5</td>
<td>22</td>
</tr>
<tr>
<td>K\textsubscript{CO} (DL\textsubscript{CO}/VA)</td>
<td>0.50</td>
<td>44</td>
</tr>
</tbody>
</table>
Laboratory

Blood gas analysis (November 2013)

- pH: 7.41
- $P_{O_2}$: 76 mmHg
- $P_{CO_2}$: 39 mmHg
- $HCO_3^-$: 24.7 mEq/L
- $SaO_2$: 97.5 %
## Laboratory

### Autoimmune diseases assessment

- **ESR, CRP**
- **ANA, ENA**
- **ANCA, ASMA, ASCA,**
- **Anti-CCP Anti-B2 GPI, Anticardiolipin**
- **C3/C4**
- **IgG4, IgG/IgA/IgM, IgG classes**
Bronchoscopy

Bronchoalveolar lavage (BAL) (November 2013)

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>BAL differential cell count</th>
<th>BAL differential lymphocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar macrophages</td>
<td>93%</td>
<td>CD3+ 65%</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>2%</td>
<td>CD3+/HLA-RD+ 36%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>5%</td>
<td>CD4+ 34%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0%</td>
<td>CD8+ 28%</td>
</tr>
</tbody>
</table>

Conclusion: Normal BAL except for a slightly reduced CD4/CD8 ratio.
Imaging

Transthoracic echocardiography

Mild mitral and moderate tricuspid valves regurgitation (PAPs = 45 mmHg)

(Apical 4 rooms image with continuous Doppler recording trans-tricuspid blood speed)
Question 2

Question: What did the echocardiography indicate?

Answer 1: Cardiac failure
Answer 2: Precapillary pulmonary hypertension
Answer 3: Both
Answer 4: None

Correct answer: 2
Echocardiography revealed precapillary pulmonary hypertension, which is common in patients affected by pulmonary fibrosis. The symptoms and morbidity in patients with CPFE are largely attributable to the development of severe precapillary pulmonary hypertension (PH). The risk of the development of PH is elevated (about 50%) in patients with CPFE than either IPF or emphysema alone, and its onset heralds a poor prognosis and increased mortality.¹

Diagnosis

Radiologic discussion

The presence of characteristic imaging features in the correct clinical context is very suggestive of the diagnosis of CPFE.

HRCT typically show:
• Centrilobular and paraseptal emphysema
• Pulmonary fibrosis of the lower lobes typical of UIP
Diagnosis

Pneumological discussion

This was a typical case of CPFE.

The clinical data were suggestive of the diagnosis:

1. Male
2. Ex-smoker (of >40 pack-years)
3. Severe dyspnoea
4. Functional airway obstruction with preserved lung volumes
5. Impaired carbon monoxide diffusing capacity
6. Hypoxaemia at exercise
7. Indirect signs of pulmonary hypertension
Diagnosis

Multidisciplinary discussion (November 2013)

The multidisciplinary discussion considered:

• Smoking history
• Hypoxaemia during exercise and poor exercise tolerance
• FVC, FEV₁ and TLC mildly affected with significantly reduced DL_{CO}
• Coexistence of centrilobular and paraseptal emphysemas in upper lung zones and interstitial fibrosis in lower lobes at chest HRCT
• Indirect signs of pulmonary hypertension

Based on the multidisciplinary discussion, the diagnosis was CPFE.
Question 3

Question: CPFE is characterised by:

Answer 1: Combined emphysema of the upper lobes and fibrosis of the lower lobes on HRTC

Answer 2: Preserved lung volumes

Answer 3: Impaired carbon monoxide diffusing capacity

Answer 4: All of the above

Correct answer: 4
Question 3 - Answer

Author’s solution:

CPFE, also known as Cottin syndrome, is characterised by the following:

- Combined emphysema of the upper lobes and fibrosis of the lower lobes on chest computed tomography

- Preserved lung volumes

- Strongly impaired carbon monoxide diffusing capacity of the lung and hypoxaemia at exercise
Learnings from the case

This was a very clear case of CPFE with:

1. Combined emphysema of the upper lobes and fibrosis of the lower lobes on chest computed tomography
2. Preserved lung volumes
3. Strongly impaired carbon monoxide diffusing capacity of the lung and hypoxaemia at exercise
Combined pulmonary fibrosis and emphysema (CPFE) is a possible new addition to a growing list of smoking-related lung diseases characterised by the coexistence of UIP or NSIP with emphysema in smokers.

The association described in 2005 by Cottin comes as no surprise since both diseases are associated with a history of exposure to cigarette smoke.

Although the pathogenesis and exact association is yet to be elucidated in larger studies, it is important to be aware of probable inherent susceptibility of some patients to pulmonary fibrosis from cigarette smoking.

For further reading:

Draw a circle question 1

Draw circles around the areas of traction bronchiectasis (turquoise) and emphysema (yellow):

Circle the area of honeycombing (red):
Draw a circle question 2

Please mark all areas showing reticulation (turquoise):
Draw a circle answer

Mark all the areas showing emphysema (turquoise):

Mark all the areas showing honeycombing (turquoise):