nasal and oral breathing while the oronasal mask was used. It is possible that this is a major determinant of how the oronasal interface will impact on the distribution of pressures in the nasal and oral segments. There is evidence that upper airway resistance during sleep and the propensity to obstructive sleep apnoea are significantly lower while breathing nasally rather than orally [7].

TEO *et al.* [3] have recently reported the first randomised trial that compared CPAP titration with nasal and oronasal masks in patients with newly diagnosed OSA. While the CPAP pressures achieved by nasal and oronasal interfaces was similar (~ 11 cmH₂O) the AHI was significantly lower on nasal mask (5.3 ± 3.4 versus 11.0 ± 10.4 events per h, respectively; $p=0.01$). Moreover, the high AHI standard deviation while on oronasal mask indicates a wide effectiveness variability. In the study of TEO *et al.* [3] the use of oronasal mask was also associated with worse sleep quality, higher air leak and poorer patient satisfaction. We speculate that the observed mechanisms in our patient may help to explain why several patients are not effectively treated while on oronasal CPAP. These mechanisms may contribute to higher air leak and poorer treatment satisfaction.

In conclusion, our case report is in line with recent studies suggesting that CPAP delivered by oronasal interface may not be effective in a subgroup of patients with OSA [3, 4]. Our case report suggests that CPAP delivered through an oronasal interface may push the tongue backwards in some patients. Therefore, a nasal mask should be preferred as the first option as a CPAP interface. Patients on an oronasal mask should be carefully followed. The low compliance to CPAP when an oronasal interface is used may be partially explained by suboptimal therapeutic effectiveness.

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Combined pulmonary fibrosis and emphysema associated with microscopic polyangiitis

To the Editors:

Microscopic polyangiitis (MPA) is a necrotising multiorgan vasculitis associated with a variety of circulating autoantibodies, such as anti-neutrophil cytoplasm antibodies (ANCA) against myeloperoxidase (MPO) [1]. Typical and most common pulmonary involvement comprises of alveolar haemorrhage secondary to pulmonary capillaritis as well as interstitial lung fibrosis [2] and progressive obstructive lung disease [1, 3, 4].

The combination of pulmonary fibrosis and emphysema (CPFE) is a recently defined syndrome, encompassing a distinct radiology, revealing both upper-lobe emphysema and lower-lobe fibrosis on high-resolution computed tomography (HRCT) of the chest, as well as lung function profile, with apparently preserved lung volumes contrasting with disproportionately impaired gas exchange, as assessed by reduced diffusing capacity of the lung

for carbon monoxide [5, 6]. CPFE has been recently described in the context of connective tissue diseases [7]. Nevertheless, it is still debatable whether CPFE represents a distinct syndrome or it is just a phenotype of pulmonary fibrosis with coincidental emphysema. Here, we describe for the first time, in a male patient, a novel type of pulmonary manifestation of MPA, the combination of pulmonary fibrosis and emphysema.

In 2008, an 80-yr-old Greek-Caucasian male, heavy ex-smoker (80 pack-yrs), ex-farmer and coal worker with a history of idiopathic pulmonary fibrosis, based on the absence of other underlying conditions and the presence of a histopathological and radiological pattern of usual interstitial pneumonia combined with upper-lobe emphysema (fig. 1a and b) since 2005, was referred to the emergency department of the University Hospital of Alexandroupolis (Alexandroupolis, Greece) due to

FIGURE 1. High-resolution computed tomography of the patient at the same level of the a, e) upper and b, f) lower lobes at diagnosis of idiopathic pulmonary fibrosis, and at 5-yr follow-up and when microscopic polyangiitis was diagnosed in the setting of alveolar haemorrhage: c) upper lobe; d) lingula. There is paraseptal emphysema in the upper lobes (a and e), and an extensive subpleural reticular pattern characterised by traction bronchiolectasis and bronchiectasis, ground-glass opacity, and minimal subpleural honeycombing at the lung bases (b and f). Note the presence of segmental and lobar areas of ground-glass opacity and peribronchovascular consolidation in the c) right and left upper lobes and d) lingula consistent with alveolar haemorrhage.

haemoptysis, progressive breathlessness on mild exertion and low-grade fever (37.5°C) for the previous 4 days.

On physical examination he was *in extremis*, with tachypnoea (respiratory rate $24\text{ breaths}\cdot\text{min}^{-1}$) and tachycardia (heart rate $100\text{ beats}\cdot\text{min}^{-1}$). Arterial blood gas analysis demonstrated respiratory failure (arterial oxygen tension 55 mmHg , arterial carbon dioxide tension 39 mmHg and pH 7.42 while breathing room air). He also had clubbing with no skin lesions, cervical lymphadenopathy or joint swelling. Auscultation of the lungs revealed bibasal inspiratory crackles. The rest of the physical examination was unremarkable. On admission, laboratory findings revealed an elevated erythrocyte sedimentation rate ($65\text{ mm}\cdot\text{h}^{-1}$), with mild leukocytosis (1.124×10^4 white blood cells per μL), anaemia with a significant decline of the haematocrit (Ht) levels from baseline values (Ht 42.5% , haemoglobin (Hb) $14.1\text{ g}\cdot\text{dL}^{-1}$ versus Ht 28.5% , Hb $9.5\text{ g}\cdot\text{dL}^{-1}$), elevated C-reactive protein ($12.86\text{ mg}\cdot\text{dL}^{-1}$) abnormal serum creatinine concentrations ($116\text{ }\mu\text{mol}\cdot\text{L}^{-1}$), elevated 24-h urine protein levels ($1400\text{ mg}\cdot\text{dL}^{-1}$) and haematuria with red blood cell renal casts in microscopic urine analysis. His tuberculin skin test was negative. Functional assessment showed a moderate restrictive pattern that was significantly deteriorated compared with baseline values (table 1). Chest radiography (not shown) followed by HRCT revealed diffuse ground-glass opacities and areas of peribronchovascular consolidation consistent with alveolar haemorrhage (fig. 1c and d). On day 2, flexible bronchoscopy followed by bronchoalveolar lavage (BAL) was undertaken and revealed findings compatible with alveolar haemorrhage, with a red macroscopic appearance and $>40\%$ siderophages. No endobronchial lesion was detected. BAL specimens were smear and culture negative for common

bacteria and acid-fast bacilli. Immunological testing revealed increased titres of antinuclear antibody ($1/160$), and anti-MPO antibodies estimated by ELISA ($14\text{ ELISA units (EU) per mL}$, normal range $<9.0\text{ EU}\cdot\text{mL}^{-1}$) and immunofluorescence analysis (perinuclear pattern ANCA $1/20$). His immunoglobulin levels were slightly elevated $3.1\text{ mg}\cdot\text{dL}^{-1}$ (normal range $2.5\text{--}3.0\text{ mg}\cdot\text{dL}^{-1}$). While the patient was experiencing a rapid deterioration of his renal function (serum creatinine levels $255\text{ }\mu\text{mol}\cdot\text{L}^{-1}$), he underwent renal biopsy showing necrotising glomerulonephritis and capillaritis, which constitute evidence compatible with necrotising MPA.

The patient was commenced on 3-day pulses of 1 g methylprednisolone followed by 60 mg of oral cyclophosphamide per day, with improvement of his renal (serum creatinine levels $177\text{ }\mu\text{mol}\cdot\text{L}^{-1}$) and general clinical condition. The patient was discharged on day 21 with *N*-acetylcysteine (1800 mg daily) coupled with 60 mg of oral cyclophosphamide per day for 6 months and 60 mg oral prednisolone per day for 6 months, gradual tapering (overall 7 months). 2 yrs after treatment completion, his serum creatinine levels dropped to $88\text{ }\mu\text{mol}\cdot\text{L}^{-1}$, his 24-h urine protein levels were within the normal range and his anti-MPO levels were undetectable. A stabilisation of lung involvement, as assessed by both functional (table 1) and radiological status (fig. 1e and f) was also reported.

CPFE occurring in the context of autoimmune disorders, such as MPA, may provide a common pathogenetic mechanism for both emphysema and pulmonary fibrosis. Recent data give credence to the view that circulating neutrophils, through exogenous stimulation such as cigarette smoke and/or occupational

TABLE 1 Summary of pulmonary function tests, 6-min walk distance (6MWD), systolic pulmonary artery pressure (sPpa) and arterial blood gases

	Time after MPA diagnosis		
	-12 months	0 months	36 months
FEV1 % pred	69.2	59.6	60.9
FVC % pred	70.1	63.6	67.7
FEV1/FVC	73.7	70.8	66.2
FEF25–75% %pred	44	40	33
TLC % pred	73	58.5	53.3
DLCO %pred	43.4	25.7	30.2
6MWD m	380	NA	370
sPpa [#] mmHg	25	35	35
PaO ₂ mmHg	66	55	60
PaCO ₂ mmHg	40	39	46

MPA: microscopic polyangiitis; FEV1: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; FEF25–75%: forced expiratory flow at 25–75% of FVC; TLC: total lung capacity; DLCO: diffusing capacity of the lung for carbon monoxide; PaO₂: arterial oxygen tension; PaCO₂: arterial carbon dioxide tension; NA: not available. [#]: measured by echocardiography.

exposure, become primed and express MPO on their surfaces [8]. Increased circulating levels of MPO on activated neutrophils for prolonged periods of time, especially in heavy smokers, may lead to loss of immune tolerance and acceleration of autoimmunity phenomena, including production of MPO-ANCA. The latter may promote degranulation of reactive oxygen species located within the neutrophilic cytoplasmic domain, resulting in an uncontrolled oxidative burst within the pulmonary interstitium that could promote fibroblast proliferation as well as alveolar epithelial and endothelial cell apoptosis, leading to fibrosis and emphysema development [9].

In line with this hypothesis, it is conceivable to speculate that in our case study, MPA followed an inconspicuous clinical course with low titres of MPO antibodies, undetectable using the conventional immunoassays but enough to trigger the pathogenetic cascade of emphysema and fibrosis. The latter became clinically prominent when MPO antibodies reached a critical level sufficient to cause renal dysfunction, alveolar haemorrhage and progression of fibrosis and emphysema, as indicated by clinical, functional and radiological deterioration.

Larger studies screening, on a repetitive basis, patients with CPFE for circulating autoantibodies are sorely needed to exclude the possibility of clinically inconspicuous autoimmune disorders.

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