CASE REPORT

Pleuroparenchymal fibroelastosis with positive MPO-ANCA diagnosed with a CT-guided percutaneous needle biopsy

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SUMMARY

A 67-year-old woman was referred to our hospital because of gradually increasing dyspnoea on exertion for 6 months. Chest CT scan showed subpleural parenchymal fibrotic opacities with traction bronchiectasis in the bilateral upper lung fields. Serum rheumatoid factor and myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) were positive. There was no evident reason to suspect connective tissue disease such as ANCA-associated vasculitis or rheumatoid arthritis. We performed a CT-guided percutaneous needle biopsy of the subpleural lesion that showed slight uptake on the fluorodeoxyglucose-positron emission tomography (FDG-PET) CT scan. This specimen showed subpleural fibrosis as evidenced by an abnormal increase of elastic tissue and minimal collagen deposition, which indicated pleuroparenchymal fibroelastosis (PPFE). Although PPFE can be associated with a variety of causes, its association with MPO-ANCA is unknown. A CT-guided transthoracic lung biopsy caused no adverse events and was useful in the diagnosis of PPFE in our patient.

BACKGROUND

Pleuroparenchymal fibroelastosis (PPFE) is a rare interstitial pneumonia that consists of fibrosis involving the pleura and subpleural lung parenchyma, predominantly in the upper lobes.¹ Although the cause of PPFE is not clearly known, PPFE has been described in association with drugs, chronic hypersensitivity pneumonia, chronic infection, collagen vascular disease and bone marrow transplantation.² An association between myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA), microscopic polyangiitis (MPA) and pulmonary fibrosis has since been shown.³ However, few studies have reported on an association between MPO-ANCA and PPFE.⁴ Moreover, Esteves *et al* recently reported a useful strategy of a CT-guided transthoracic lung biopsy for the diagnosis of PPFE.⁵

CASE PRESENTATION

A 67-year-old woman, a housewife who had never smoked, presented with a 6-month history of increasing dyspnoea on exertion and was admitted to our hospital. An abnormal shadow had been pointed out on a health examination X-ray obtained 2 years ago, and since then, the shadow had expanded very slowly. She had no known history

of dust exposure (eg, asbestos and aluminium), mycobacterial or fungal infection, lung or bone transplantation, or underlying chemotherapy for malignancies. There was no family history of either interstitial pneumonia or autoimmune disease. She had a medical history of hypertension. Physical examination did not reveal clubbing of the fingers or connective tissue disease (CTD) such as eruptions or swelling of the joints, morning stiffness or superficial lymph nodes. Her oxygen saturation on pulse oximetry was 97%. Chest auscultation revealed no abnormal findings, and heart sounds indicated a regular rhythm with no murmur.

INVESTIGATIONS

Laboratory analysis revealed high levels of KL-6 (607 U/mL) and surfactant protein-D (277.3 ng/mL). Her rheumatoid factor level was elevated at 281 U/mL, as was her MPO-ANCA titre at 49.0 EU. Other autoantibodies were negative. Her urine was slightly positive for occult blood but showed normal sediment and was negative for proteins, crystals and casts. A nephrology consultation indicated a low probability of ANCA-related kidney disease based on these results. A serum T-SPOT. TB test, IgA antibody against *Mycobacterium avium* complex glycopeptidolipid and antigen/IgG antibody of *Aspergillus* were all negative. A chest CT scan revealed subpleural parenchymal fibrotic opacities with traction bronchiectasis in the bilateral upper lung fields (figure 1A,B). Pulmonary function testing showed evidence of restrictive ventilatory impairment with forced vital capacity (FVC) of 1.07 L (41.6% of predicted), forced expiratory volume in 1 s (FEV₁) of 1.07 L (52.7% of predicted), FEV₁/FVC ratio of 91.5%, total lung capacity (TLC) of 2.91 L (72.6% of predicted), residual volume (RV) of 1.74 L (106.7% of predicted), RV/TLC ratio of 59.8% (66.5% of predicted) and diffusing capacity of carbon of carbon monoxide of 9.68 mL/min/mm Hg (66.5% of predicted). A 6-min walking test revealed oxygen desaturation (her minimum oxygen saturation was 90%). An FDG-PET/CT scan showed mild FDG uptake within the subpleural lesion in both upper lobes, but no other suspicious findings of ANCA-related disease (figure 1C). Differential diagnosis of the pulmonary lesions included malignancy, chronic infections (ie, that by mycobacteria or aspergillus), ANCA-related interstitial pneumonia and idiopathic origin. Therefore,

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Figure 1 (A,B) Chest high-resolution CT showing subpleural parenchymal fibrotic opacities with traction bronchiectasis in the bilateral upper lung fields. (C) FDG-PET/CT scan showed slight accumulation (SUV_{max} of 1.4) in the area of subpleural thickening. (D) A CT-guided percutaneous needle biopsy of the subpleural lesion.

a CT-guided percutaneous needle biopsy was performed of the subpleural lesion showing mild uptake on the FDG-PET CT scan (figure 1D). The specimens revealed subpleural fibrosis as evidenced by an abnormal increase of elastic tissue and minimal collagen deposition, which was compatible with the diagnosis of PPFE (figure 2).

TREATMENT

After she was diagnosed as having PPFE, we guided her in respiratory rehabilitation and then closely monitoring her condition while withholding the dosage. If she develops MPA including pulmonary haemorrhage in the future, we plan to start anti-inflammatory therapy promptly.

Figure 2 Histological findings from the CT-guided biopsy specimen showing subpleural fibrosis with an abnormal increase of elastic tissue and intra-alveolar collagen deposition in the limited area. (A) H&E stain, $\times 40$, (B) Elastica van Gieson stain, $\times 40$.

OUTCOME AND FOLLOW-UP

During a 1-year follow-up period from the initial visit, her FVC on pulmonary function testing and radiological fibrotic change have deteriorated slightly, but her pulmonary symptoms have not worsened. Her serum MPO-ANCA titer remained between 28 and 40 EU, and MPA has not developed.

DISCUSSION

PPFE has been identified as a distinct clinicopathological entity in recent years.¹ The most common presenting complaints are those of dyspnoea on exertion, cough, weight loss, pneumothorax and chest pain.⁶ This case highlighted the following clinical implications. First, PPFE may develop in MPO-ANCA-positive patients. Previous reports pointed out that the presence of MPO-ANCA-associated vasculitis in pulmonary fibrosis may simply be coincidental and that the presence of MPO-ANCA positivity is an important unfavourable prognostic factor in patients with pulmonary fibrosis.^{3 7} However, in these reports, the radiopathological pattern of the pulmonary fibrosis in most cases was of usual interstitial pneumonia. In our case, the association between MPO-ANCA and PPFE was unclear and may also have been coincidental. However, pulmonary fibrosis can be associated with all CTDs and present in one setting, that is, pulmonary fibrosis with some autoimmune features but that does not fulfil criteria for a defined CTD, which was recently defined as ‘interstitial pneumonia with autoimmune features’.⁸ Although autoantibodies have demonstrable usage in the diagnosis and management of patients with CTD-associated pulmonary fibrosis, there remains a lack of data to guide clinical practice.⁹ Because testing for MPO-ANCA is not recommended as a routine examination, there may be patients with both PPFE and MPO-ANCA positivity. Additionally, the co-existence of MPO-ANCA and rheumatoid factor was also previously described in the literature with rheumatoid arthritis developing in only a minority of these patients.¹⁰ Pathological features of MPO-ANCA-associated interstitial pneumonia included vasculitis, small airway disease and lymphoid follicles.¹¹ These suspicious findings of MPO-ANCA-related disease were not apparent in our case. Therefore, further studies should focus on the possible correlation between MPO-ANCA and PPFE.

Second, a CT-guided transthoracic lung biopsy can be useful in the diagnosis of PPFE. Although the diagnosis of PPFE is based mainly on surgical lung biopsy (SLB) results, the vast majority of patients have markedly impaired lung function, which makes SLB impossible to perform.¹² Only one report has suggested that a CT-guided biopsy can be a good diagnostic tool and can be considered the first choice for the invasive assessment of PPFE, sparing patients a late SLB.⁵ No serious complications were recognised in the patients in that report, as in our case.

Learning points

- ▶ Pleuroparenchymal fibroelastosis (PPFE) can be associated with autoimmune disease.
- ▶ Rare instances of the possible correlation of myeloperoxidase-antineutrophil cytoplasmic antibody positivity with PPFE in patients with pulmonary fibrosis may exist.
- ▶ CT-guided transthoracic lung biopsy may be an alternative tool for the histological diagnosis of PPFE.

In conclusion, we describe a rare case of PPFE positive for MPO-ANCA. PPFE is a rare disease entity; thus, further studies should focus on the possible correlation of MPO-ANCA positivity with PPFE. Because interstitial pneumonia may precede signs and symptoms of systemic vasculitis if this ever occurs over many years in MPO-ANCA-positive patients, these patients require a close follow-up by both a pulmonologist and a rheumatologist. Moreover, a CT-guided transthoracic lung biopsy may be an alternative tool for the histological diagnosis of PPFE.

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REFERENCES

- 1 Travis WD, Costabel U, Hansell DM, *et al.* An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013;188:733–48.
- 2 Nakatani T, Arai T, Kitaichi M, *et al.* Pleuroparenchymal fibroelastosis from a consecutive database: a rare disease entity? *Eur Respir J* 2015;45:1183–6.
- 3 Arulkumaran N, Periselman N, Gaskin G, *et al.* Interstitial lung disease and ANCA-associated vasculitis: a retrospective observational cohort study. *Rheumatology* 2011;50:2035–43.
- 4 Yamakawa H, Takemura T, Yamanaka Y, *et al.* Useful radio-pathological features for diagnosing ANCA-positive seroconversion in a patient with interstitial pneumonia. *Modern Rheumatology Case Reports* (accessed 31 Jul 2017).
- 5 Esteves C, Costa FR, Redondo MT, *et al.* Pleuroparenchymal fibroelastosis: role of high-resolution computed tomography (HRCT) and CT-guided transthoracic core lung biopsy. *Insights Imaging* 2016;7:155–62.
- 6 Watanabe K. Pleuroparenchymal fibroelastosis: its clinical characteristics. *Curr Respir Med Rev* 2013;9:229–237.
- 7 Homma S, Matsushita H, Nakata K. Pulmonary fibrosis in myeloperoxidase antineutrophil cytoplasmic antibody-associated vasculitides. *Respirology* 2004;9:190–6.
- 8 Fischer A, Antoniou KM, Brown KK, *et al.* An official European Respiratory Society/American thoracic society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J* 2015;46:976–87.
- 9 Jee AS, Adelstein S, Bleasel J, *et al.* Role of autoantibodies in the diagnosis of connective-tissue disease ILD (CTD-ILD) and interstitial pneumonia with autoimmune features (IPAF). *J Clin Med* 2017:6.
- 10 Kagiya N, Takayanagi N, Kanauchi T, *et al.* Antineutrophil cytoplasmic antibody-positive conversion and microscopic polyangiitis development in patients with idiopathic pulmonary fibrosis. *BMJ Open Respir Res* 2015;2:e000058.
- 11 Tanaka T, Otani K, Egashira R, *et al.* Interstitial pneumonia associated with MPO-ANCA: clinicopathological features of nine patients. *Respir Med* 2012;106:1765–70.
- 12 Kushima H, Hidaka K, Ishii H, *et al.* Two cases of pleuroparenchymal fibroelastosis diagnosed with transbronchial lung biopsy. *Respir Med Case Rep* 2016;19:71–3.

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