CASE REPORT

Bronchiolitis obliterans organising pneumonia as an initial manifestation in a patient with systemic lupus erythematosus: a rare presentation

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SUMMARY

Bronchiolitis obliterans organising pneumonia as an initial manifestation of systemic lupus erythematosus (SLE) is a rare and uncommon presentation. We describe a case of SLE presenting with shortness of breath, found to have pneumothorax, bilateral nodular infiltrates along with pleural effusions and pericardial effusion. Work-up suggested a diagnosis of active SLE with anaemia, thrombocytopenia, positive antinuclear antibodies (ANAs) and positive anti-double-stranded DNA. On retrospective review of patient records, from 8 years prior to presentation, lung biopsy histology consistent with bronchiolitis obliterans organising pneumonia with positive ANA serology was found, without any further autoimmune work-up. In our opinion, bronchiolitis obliterans organising pneumonia was the index presentation of SLE. Treatment with steroids and subsequent management with immunosuppressive therapy could have prevented subsequent hospitalisations. Prompt work-up for autoimmune diseases should be considered in patients with positive ANA and histological evidence of bronchiolitis obliterans organising pneumonia.

BACKGROUND

Bronchiolitis obliterans organising pneumonia is characterised by distinct inflammation in the lungs and histopathologically by the formation of plugs of fibrous tissue in alveoli, alveolar ducts and distal bronchioles.¹ It is associated with various disorders including infection, toxins, malignancies and collagen vascular diseases.² Bronchiolitis obliterans organising pneumonia presenting as a manifestation of systemic lupus erythematosus (SLE) has been reported infrequently in current literature.¹⁻⁷ SLE has various pulmonary manifestations including shrinking lung syndrome, acute lupus pneumonitis, cavitary pulmonary nodules, pulmonary vasculitis, pulmonary hypertension, pulmonary embolism, chronic interstitial pneumonitis, alveolar haemorrhage, pleuritis, pleural effusions and bronchiolitis, with or without organising pneumonia as well as various opportunistic infections due to the immunosuppressive effects of various drugs used for the treatment of SLE.⁸ We found only three cases reported in literature where bronchiolitis obliterans organising pneumonia was reported as initial manifestation of SLE.^{3 4 6} We report a case of SLE presenting as bronchiolitis obliterans organising

pneumonia, which being an uncommon initial presentation poses a diagnostic challenge.

CASE PRESENTATION

An 81-year-old man with a biopsy-proven diagnosis of bronchiolitis obliterans organising pneumonia presented to the emergency department with complaints of shortness of breath, pleuritic chest pain and lower extremity swelling. The patient did not report any history of fever, chills, arthralgias, cough, recent travel, alopecia, rash, oral ulcers, seizures, mood changes, vision changes or any history of Raynaud's phenomenon. On physical examination, the patient was found to be tachypnoeic, with absent breath sounds on his right side, distant heart sounds and bilateral lower extremity oedema. Musculoskeletal examination suggested degenerative changes in small joints of hands and feet without evidence of inflammation.

INVESTIGATIONS

ECG showed sinus rhythm and radiological imaging revealed right-sided pneumothorax, airspace opacities and bilateral pleural effusion (figures 1 and 2). Echocardiogram showed an ejection fraction of 15% and mild to moderate circumferential pericardial effusion with no evidence of cardiac tamponade. Blood work showed anaemia and thrombocytopenia. Pleural fluid analysis was exudative (lactate dehydrogenase ratio >0.6 and protein ratio >0.5). Respiratory cultures (including Gram stain, aerobic/anaerobic cultures, fungal cultures, viral cultures and acid-fast bacilli stain/cultures), pleural fluid cultures and blood cultures ruled out an infectious aetiology.

Autoimmune work-up revealed positive antinuclear antibodies (ANAs) (1:320 nucleolar pattern), positive anti-double-stranded DNA (343 IU/mL), low levels of C3 levels (80 mg/dL), positive anti-beta-2 glycoprotein IgA (60 Standard Units) and positive anti-cyclic citrullinated peptide (22 units). Anti-Smith, anti-ribonucleoprotein (anti-RNP), anti-Sjogren's syndrome-related antigens A and B, human leucocyte antigen B27, anti-neutrophilic cytoplasmic antibody (cytoplasmic and perinuclear) and rheumatoid factor (RF) were negative.

On review of prior records, it was found that 8 years ago, the patient presented to the pulmonary outpatient clinic with chronic cough, and initial CT of the chest showed right upper lobe infiltrates

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Figure 1 CT thorax images from the patient's current presentations showing bibasilar consolidation associated with bilateral pleural effusions and right-sided pneumothorax.

along with a pulmonary nodule. Within 4 months of this presentation, the patient was admitted to the hospital with worsening shortness of breath and cough, and repeat CT revealed several

bilateral nodular infiltrates (figures 2 and 3). An ANA done at that hospitalisation was positive, but titres were not checked. The patient underwent video-assisted thoracoscopic surgery

Figure 2 Chest radiography: (A) Old radiographs showing scattered patchy nodular infiltrates. (B) Radiographs at current presentation showing right apical pneumothorax, airspace opacity at the right lung base related to atelectasis, infiltrate and/or pleural effusion.

Figure 3 CT thorax images from old records, when patient was initially diagnosed with bronchiolitis obliterans organising pneumonia, showing bilateral patchy fleeting nodular infiltrates and air bronchograms.

with wedge resection of the superior segment of the left lower lobe. The biopsy was consistent with bronchiolitis obliterans organising pneumonia (figure 4). An excellent response to steroids led to clinical and radiological resolution. For reasons not clear, neither further autoimmune work-up nor rheumatological referral was pursued despite positive ANA, histological evidence of bronchiolitis obliterans organising pneumonia and subsequent recurrent hospitalisations for exudative pleural effusions. Patient was hospitalised at least four times, with similar symptoms, before a rheumatological evaluation was considered by patient's primary physician.

DIFFERENTIAL DIAGNOSIS

With the current presentation of pleural and pericardial effusion, the differentials included congestive heart failure, infections, malignancy and systemic autoimmune diseases like lupus, overlap syndromes and vasculitis. Rheumatoid arthritis and mixed connective tissue disease were also considered as possible differentials, but patient did not have evidence of synovitis, inflammatory myopathy, Raynaud's phenomenon, mechanic hands and serologies were negative for RF and anti-RNP. In the setting of anaemia, thrombocytopenia with positive ANA, positive anti-double-stranded DNA, hypocomplementemia, history of recurrent pleural effusions, current presentation of pericardial effusion and previous diagnosis of bronchiolitis obliterans organising pneumonia, the patient was diagnosed with active SLE.

TREATMENT

It is thought the patient's bronchiolitis obliterans organising pneumonia relapsed with steroid discontinuation after primary presentation. With progression of possible lupus (undiagnosed

after primary presentation), the relapses manifested as recurrent exudative pleural effusions along with nodular infiltrates, requiring therapeutic thoracentesis for symptomatic relief. After the complete rheumatologic work-up during the current presentation, a diagnosis of SLE was established, he was started on steroids, prednisone 60mg daily, with complete resolution of symptoms, with a plan to start mycophenolate mofetil (Cellcept) as steroid sparing during outpatient clinic follow-up.

OUTCOME AND FOLLOW-UP

Follow-up imaging showed improvement in pleural and pericardial effusion, bilateral infiltrates and patient's respiratory status. He was continued on steroids, with a plan to start immunosuppressant at rheumatology outpatient clinic follow-up.

DISCUSSION

Bronchiolitis obliterans organising pneumonia was initially described in 1985 by Epler *et al.*¹ It is a distinct clinical and pathological entity characterised by subacute or chronic respiratory illness. Histopathologically, it is characterised by the presence of granulation tissue in the alveoli, alveolar ducts as well as bronchiolar lumen and is associated with a variable degree of interstitial and airspace infiltration by mononuclear cells.^{1 9} Bronchiolitis obliterans organising pneumonia is considered to be an inflammatory disease of the lung, not a fibrosing process.^{3 9} Bronchiolitis obliterans organising pneumonia is associated with several connective tissue disorders, such as rheumatoid arthritis, SLE, Sjögren's syndrome, dermatomyositis and polymyositis.¹⁰ During our review of the literature, we found only a three cases where bronchiolitis obliterans organising pneumonia was reported as an initial manifestation of SLE.^{3 4 6} Common pulmonary manifestations of SLE include pleuritis (40%–60%), pleural

Figure 4 Histopathology of left lung lower lobe biopsy showing H&E stains (figure A—original magnification $\times 10$ and B—original magnification $\times 40$) and trichome stain (C) with intraluminal organising fibrosis (black arrows), inflammatory infiltrates (red arrows) and foamy macrophages (yellow arrows).

effusion (50%), acute pneumonitis (1%–12%), interstitial lung disease (3%–9%), shrinking lung syndrome (1%–6%), pulmonary hypertension (4%), diffuse alveolar haemorrhage and thromboembolic disease.⁸ In a prospective study over 10 years, Cervera *et al*¹¹ reported lung involvement in only 3% patients at the onset of lupus with 7% patients developing lung manifestations over the period of observation. Castellino and Varga¹² reported an overall incidence of parenchymal lung disease in SLE as 2%–8%. Approximately 50% of the patients with bronchiolitis obliterans organising pneumonia present with persistent non-productive cough, dyspnoea, low-grade fever, malaise and weight loss.⁹ Less common symptoms include chest pain and haemoptysis. Physical examination may reveal fine crackles. Pulmonary function tests may show a restrictive pattern.⁹ Chest imaging in bronchiolitis obliterans organising pneumonia may reveal bilateral patchy infiltrates, small linear opacities or reticulonodular opacities.¹³ On CT, the absence of honeycombing or an irregular reticular pattern can help us differentiate bronchiolitis obliterans organising pneumonia from other interstitial lung diseases. Lung biopsy is the preferred diagnostic method for bronchiolitis obliterans organising pneumonia. Conventional radiography and high-resolution CT serve as guides in determining the biopsy site, and pathological examination is needed to exclude infection and other pulmonary manifestations. A characteristic histologic feature is the presence of granulation tissue plugs within the lumen of small airways. The combination of cytologic bronchoalveolar lavage, which reveals a lymphocyte predominant pattern, and histologic transbronchial lung biopsy helps to diagnose bronchiolitis obliterans organising pneumonia. Differential diagnosis of bronchiolitis obliterans organising pneumonia includes metastatic lung disease, various

complications of collagen vascular disease, Wegener's granulomatosis, bronchogenic carcinoma, eosinophilic pneumonia and tuberculosis.⁹ Therefore, correct diagnosis is paramount in order to treat the disease appropriately. There is a general agreement on treating bronchiolitis obliterans organising pneumonia (irrespective of underlying aetiology) with systemic corticosteroids. Several protocols have been suggested in literature.^{14–16} Lazor *et al* suggested using prednisone for bronchiolitis obliterans organising pneumonia as a tapering regimen of 0.75 mg/kg for 4 weeks, 0.5 mg/kg for 4 weeks and 20 mg for 4 weeks, 10 mg for 6 weeks and 5 mg for 6 weeks.¹⁶ Several immunosuppressant agents, such as azathioprine, mycophenolate mofetil, cyclosporin, cyclophosphamide and plasmapheresis, have studied in various case reports.^{8, 17} Patients usually recover within days or weeks with simultaneous improvement in radiographic findings.⁹ Recurrence rate has been reported between 13% and 58%, dependent on several factors, including underlying systemic connective tissue disease.^{16, 18} Usually a relapse is triggered when steroid therapy or other immunosuppressive therapy used for treating bronchiolitis obliterans organising pneumonia is stopped.⁹

In our case, the patient had a medical history of bronchiolitis obliterans organising pneumonia, which was diagnosed 8 years ago prior to the diagnosis of SLE. The significant relapse rate, despite adequate initial systemic steroid therapy is highly suggestive of causal association with underlying SLE and primary presentation 8 years ago. We strongly believe that it was the patient's initial manifestation of SLE since laboratory work from 8 years ago showed positive results for ANA and patient had several subsequent hospital admissions due to recurrent pleural effusions. At initial presentation, the work-up was not completed, which could have helped to diagnose the patient

Learning points

- Prevalence of parenchymal lung disease (interstitial lung disease) has been reported to be 3%–9% of cases with systemic lupus erythematosus (SLE), and bronchiolitis obliterans organising pneumonia as an initial presentation of SLE has been reported only as few case reports in literature.
- The initial treatment of bronchiolitis obliterans organising pneumonia with steroids, with subsequent management of underlying connective tissue disease (SLE) with immunosuppressive therapy, could have prevented recurrent pleural effusions and the current presentation discussed in this case.
- Prompt work-up for autoimmune diseases and timely involvement of rheumatology should be considered in patients with positive antinuclear antibody and pathological evidence of bronchiolitis obliterans organising pneumonia.

with SLE. His relapses could have been prevented with early evaluation for underlying connective tissue disease if work-up was initiated at primary presentation.

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