Respiratory Medicine Case Reports 8 (2013) 40–42

Contents lists available at SciVerse ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Pulmonary vasculitis as the first manifestation of rheumatoid arthritis

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ARTICLE INFO

Article history:
Received 11 December 2012
Received in revised form
3 January 2013
Accepted 7 January 2013

Keywords:
Vasculitis
Rheumatoid arthritis
Pulmonary
Lungs

ABSTRACT

In this report, we describe a 61-year-old man that presented with isolated pulmonary vasculitis and a positive anti-cyclic citrullinated peptide (CCP) antibody. Within a few months, the patient developed the symmetric polyarthritis consistent with rheumatoid arthritis (RA). Because the anti-CCP antibody is highly specific for RA and vasculitis is a known association of RA, we suspect the pulmonary vasculitis in this patient was the first manifestation of underlying RA. This case extends on previous reports that have shown that lung disease may predate the development of articular RA and that anti-CCP positivity and lung disease may represent a pre-RA phenotype. To our knowledge, this is the first case report of pulmonary vasculitis as the first manifestation of RA.

1. Introduction

Lung disease occurs commonly in rheumatoid arthritis (RA), can involve any of the lung compartments, is associated with significant morbidity and is the second leading cause of RA-associated mortality.[1] Pulmonary vasculitis, a rare manifestation of RA, is typically identified in those with long-standing severe forms of RA.[2] A recent study has demonstrated that anti-cyclic citrullinated peptide (CCP) positive individuals with airways or interstitial lung disease may represent a pre-articular RA phenotype.[3] In this report, we describe a patient that presented with pulmonary vasculitis, and a positive anti-CCP antibody; within a short period of time the patient developed the symmetric polyarthritis of RA.

2. Case presentation

A 61-year-old Caucasian man, with a remote eight pack-year smoking history, seasonal allergies, gastroesophageal reflux disease, obstructive sleep apnea, and dyslipidemia presented with pleuritic chest pain and dry cough of five months duration. There was no improvement with two courses of oral antibiotics. There was no evidence of sinusitis, arthralgias, inflammatory arthritis, rash or other symptoms of connective tissue disease. Physical examination revealed a healthy, obese man with a normal set of vital signs and resting room air pulse oximetry of 97%. Chest auscultation was notable for inspiratory crackles at the right lung base. His musculoskeletal and skin examinations were normal. Laboratory studies demonstrated high-positive anti-CCP and anti-Ro (SSA) antibodies, and a weakly positive rheumatoid factor (Table 1). Latent tuberculosis assessment was negative. Thoracic high-resolution computed tomography (HRCT) imaging revealed several nodules and thick-walled cavities predominantly in the right lung (Fig. 1). The patient had a normal nuclear cardiac stress test, a negative ventilation/perfusion scan and normal pulmonary physiology (Table 1). Surgical lung biopsy revealed necrotizing granulomatous inflammation with geographic necrosis, vasculitis and lymphocytic pleuritis (Fig. 2) most compatible with an autoimmune-mediated vasculitis.

After the lung biopsy, treatment with oral corticosteroids (0.5 mg/kg/day prednisone) was initiated and the patient reported rapid clinical improvement in respiratory symptoms. Two months after lung biopsy, as corticosteroids were tapered; the patient developed symmetric inflammatory polyarthritis involving the small joints of the hands, wrists, and feet. Synovitis was identified on physical examination. Plain radiographs of the hands and feet were normal. Injectable methotrexate was initiated and rapidly titrated to 25 mg weekly. Corticosteroids were gradually tapered off over the subsequent three months, and synovitis symptoms, pleurisy, and cough remained quiescent. No new symptoms or signs of systemic vasculitis have developed. A follow-up HRCT, reflecting three months of therapy with corticosteroids and methotrexate demonstrates that the pulmonary cavitary nodularity is gradually

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2213-0071
http://dx.doi.org/10.1016/j.rmcr.2013.01.003

Table 1
Initial laboratory and pulmonary function test results.

White blood cell count	8.3 K/μL
Hemoglobin	15.0 g/dL
Platelet count	198 K/μL
Serum creatinine	0.9 mg/dL
Albumin	4.5 g/dL
Alanine aminotransferase	28 IU/L
Erythrocyte sedimentation rate	18 mm/h
C-reactive protein	0.03 (normal ≤ 0.4)
Urinalysis	No protein, red blood cells, white blood cells, or casts
Anti-nuclear antibody	Negative
Anti-Ro (SSA) antibody	132 units (negative ≤ 20)
Anti-La (SSB) antibody	Negative
Anti-dsDNA, anti-RNP, anti-Smith	All negative
C-ANCA	Negative
P-ANCA	Negative
Anti-proteinase 3-antibody	Negative
Anti-myeloperoxidase antibody	Negative
Anti-GBM-antibody	Negative
Rheumatoid factor	25 IU/mL (negative ≤ 14)
Anti-cyclic citrullinated peptide antibody	161 Units (negative ≤ 20)
Total lung capacity	8.0 L (125% predicted)
Forced vital capacity	4.4 L (96% predicted)
Forced expiratory volume in 1 s	3.4 L (100% predicted)
Diffusing capacity for carbon monoxide	35.1 ml/min/mmHg (106% predicted)

improving (Fig. 3). Follow-up autoantibody testing three and six months after initiation of methotrexate was notable for persistent high-positive anti-CCP and low-titer positive RF, and negativity to anti-proteinase-3, anti-myeloperoxidase and C- and P-anti-neutrophil cytoplasmic antibody (ANCA).

3. Discussion

Vasculitis is a well recognized extra-articular manifestation of RA; however, it is usually considered to be associated with long-standing, severe, erosive, nodular, and sero-positive disease.[2] RA-vasculitis often manifests in the skin with pyoderma gangrenosum, nervous system with mononeuritis multiplex, or may involve other organs such as the lungs. Because the current era offers more effective disease modifying anti-rheumatic drug therapies, RA-vasculitis is less commonly encountered.[4–6]

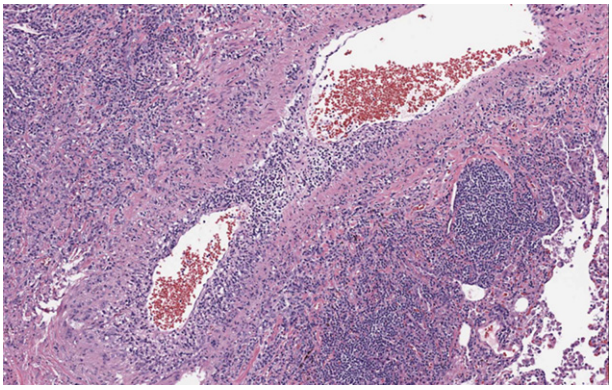

Fig. 2. Photomicrograph (10×) of histopathology specimen demonstrating necrotizing granulomatous inflammation with geographic necrosis, and vasculitis.

We believe this case represents pulmonary vasculitis as the presenting manifestation of RA. A few factors argue in favor of such a diagnosis: the presence of the high-titer anti-CCP; an autoantibody known to be highly specific for RA.[7] The growing body of evidence that anti-CCP antibody positivity and lung disease may predate the articular manifestations of RA, and that such patients may reflect a pre-RA phenotype.[3,8,9] Our patient developed the symmetric inflammatory polyarthritis and synovitis consistent with RA. Finally, pulmonary vasculitis is a well known manifestation of RA. Although the order of presentation – lungs before joints – is atypical, the overall clinical scenario favors anti-CCP positive RA with pulmonary vasculitis as the best unifying diagnosis.

We can not fully discount the possibility that this case represents an atypical presentation of granulomatosis with polyangiitis (GPA) (formerly Wegener's). Indeed, inflammatory polyarthritis is a common finding in patients with GPA.[10] There are several aspects of this case that argue against a diagnosis of GPA: the patient did not have sinusitis or renal involvement; two features commonly encountered in GPA.[10] The patient was ANCA, proteinase-3, and

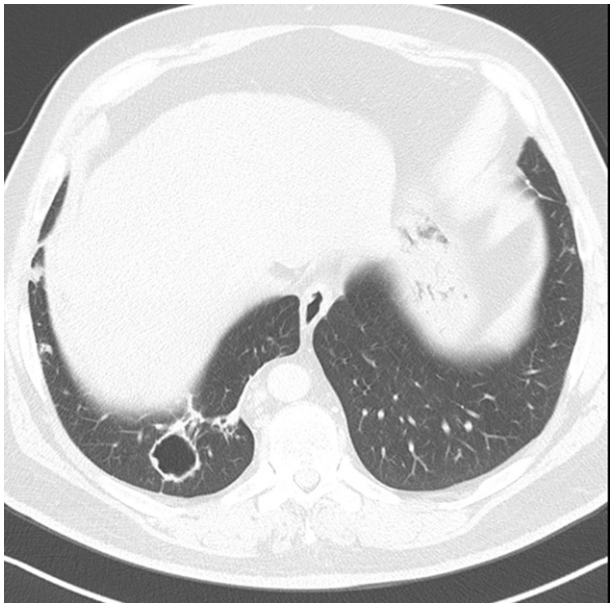

Fig. 1. Initial high-resolution computed tomographic image demonstrating right lower lobe nodular, cavitary lung disease.

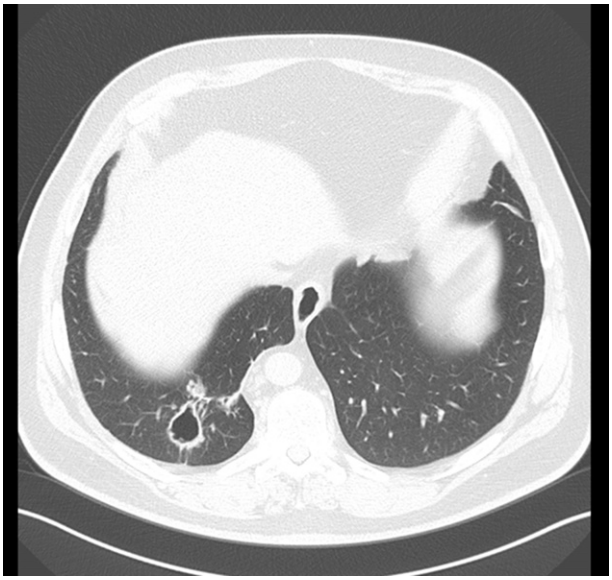

Fig. 3. Follow-up high-resolution computed tomographic image demonstrating mild improvement in right lower lobe nodular, cavitary lung disease.

myeloperoxidase antibody negative. The patient had a high-titer RA specific autoantibody (anti-CCP).

In conclusion, this case reinforces the concept that a wide spectrum of lung disease may be the presenting manifestation of RA – including pulmonary vasculitis.

Conflict of interest statement

None of the authors have any financial interests to disclose.

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