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CASE REPORT

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Bronchiolitis obliterans organizing pneumonia associated with sulfasalazine in a patient with rheumatoid arthritis

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Abstract Pulmonary toxicity and blood dyscrasias are rare side effects of sulfasalazine. Pulmonary pathology is variable, the most common being eosinophilic pneumonia with peripheral eosinophilia, and interstitial inflammation with or without fibrosis. We here present the case of a 68-year-old female patient treated for 6 months with sulfasalazine for rheumatoid arthritis. On laboratory examination, eosinophil count was 97×10^3 mm^3. Thorocoscopic biopsy was performed. Histopathologic diagnosis was bronchiolitis obliterans organizing pneumonia (BOOP). This is the first case in the literature to present with sulfasalazine-induced BOOP in a patient with seronegative RA.

Keywords Bronchiolitis obliterans organizing pneumonia

Abbreviations BOOP: Bronchiolitis obliterans organizing pneumonia · DMARS: Disease-modifying antirheumatic drugs · RA: Rheumatoid arthritis

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Introduction

Pulmonary complications in patients with RA may be due to rheumatic disease and also due to side effects of drugs such as DMARS (disease-modifying antirheumatic drugs) . Pulmonary pathologies such as pleural effüsions, pulmonary rheumatoid nodules and, less frequently, BOOP, may be seen in this group [1]. BOOP has been reported primarily in women with long-standing, seropositive RA in their fifth or sixth decade of life [2].

Sulphasalazine is a disease-modifying antirheumatoid drug that has been used in the treatment of rheumatoid arthritis since 1940, and is also used in several other inflammatory diseases [3].

Case report

A 68-year-old woman was admitted to the hospital with progressive dyspnea lasting 4 months and pruritus. She had been diagnosed as seronegative RA according to American Rheumatology Association (ARA) criteria and been administered sulfasalazine (2×1 g) for 4 months. She was smoking 30 packs per year and had been an exsmoker for the last 6 months.

On physical examination, skin pigmentation was seen on the right suprascapular and left infrascapular areas. Chest auscultation revealed bilateral crackles. On laboratory examination, peripheral eosinophil count was 971×10^3 mm^3, pulmonary function tests were FVC: 75%, FEV1:68%, FEV1/FVC:75% DLCO: 49, DLCO/VA: 40, arterial blood gases (ABG) analysis was pH: 7.39, PCO_2: 38.1, PO_2: 66.8, SaO_2:92.7, HCO_3: 22.5.

Chest radiogram showed diffuse, bilateral reticular, nodular infiltration, mainly in the middle and lower lobes. There was no similar lesion on chest radiology before treatment [1]. CT scans of the thorax revealed extensive bilateral, reticulonodular infiltration and alveolar consolidation, pretracheal, carinal and prevascular bilateral axillar lymphadenopathy (Figs. 1, 2). Thorocoscopic lung biopsy was performed for differential diagnosis. Plugs of granulation tissue within the lumina of obscured small airways were seen on the histopathological sample. There were also focal alveolar accumulations of foamy macrophages, inflammation of the alveolar walls with lymphocytes, and focal interstitial thickening. These findings were diagnosed as BOOP (Fig. 3).

The patient was prescribed prednizolone (60 mg/day) because of her severe symptoms and hypoxemia, and sulfasalazine was withdrawn. Clinical improvement occurred and ABG analysis was

pH: 7.47, PO_2: 87, PCO_2: 26.9, HCO_3: 19.9; the peripheral blood eosinophilia recovered to thebnormal range within a few days. Prednisolone was given for 3 months in tapering doses. After 45 days, radiologic improvement was seen on thorax CT (Fig. 4).

Discussion

The most common side effects of sulfasalazine are nausea and vomiting, skin rashes and pigmentation, arthralgia, fever, and hepatic dysfunction. More serious side effects include pulmonary toxicity and blood dyscrasias [4, 6, 7, 8, 9]. In one study, 50 cases with pulmonary complications of sulfasalazin were reviewed. The daily doses of sulfasalazine reported in this study ranged from 1 to8 g and average duration of exposure was 18.8 months, range 0.5–120 months. The main clinical symptoms were reported as breathlessness (80%), fever (35%) and cough (64%). On laboratory testing, peripheral blood eosinophilia (52%), hypoxemia (90%), restrictive (66%) and obstructive (24%) deficit on pulmonary function tests were reported [5].

The CT finding of BOOP with multifocal consolidations was seen in about 80% of patients. Air-space opacity is usually bilateral (70%–90%), asymmetric, and showed no apical/basal predominance [10].

In this case, extensive bilateral, reticulonodular infiltration and alveolar consolidation, pretracheal, carinal and prevascular bilateral axillar lymphadenopathy were seen on thoracic CT scans. These findings were smiliar to those described in the literature.

In the Pary study, HRCT chest scans were performed on only five patients. In one of these the image was consistent with alveolar and ground glass opacities, with air bronchograms. The second case had multiple bilateral peripheral wedge-shaped infiltrates, with one of the nod-

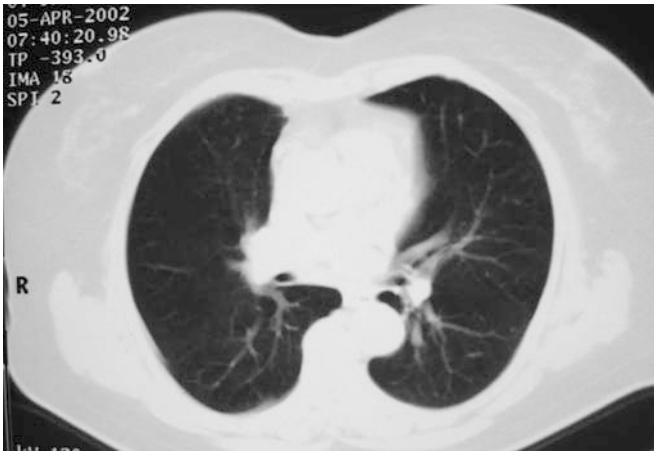

Fig. 1 CT scan shows normal aeration of both lungs without focal lesions

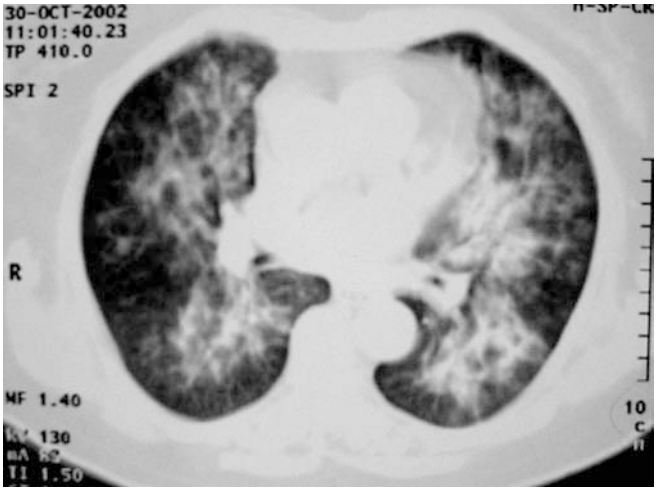

Fig. 2 On CT scan, which was performed 6 months later, bilateral perihilar alveolar infiltrates with air bronchograms are seen

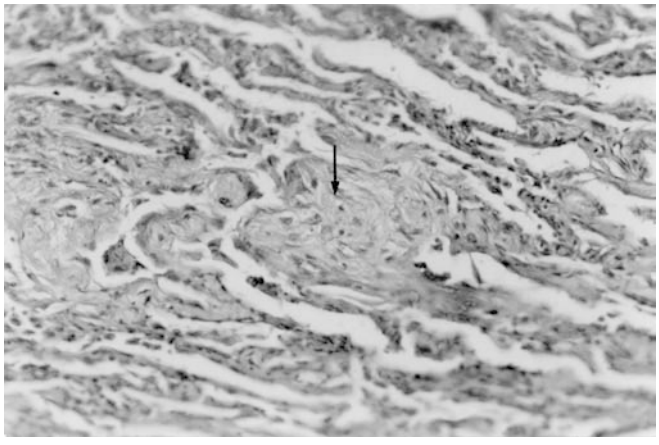

Fig. 3 Loose fibroblastic tissue filling on alveolar duct (*arrow*). There is some chronic inflammation. (H&E x200)

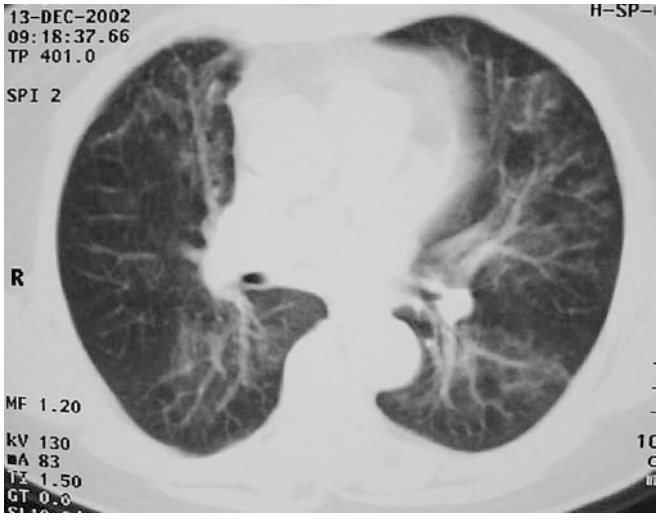

Fig. 4 On control thorax CT scan, which was performed 45 days after the second examination, previously described alveolar infiltrates are seen to regress significantly, but focal ground glass densities are still present

ules showing central cavitation. In the third case, HRCT imaging showed patchy ground glass shadowing, mainly in the middle and upper lobes. The fourth case had interstitial opacities with pleural thickening in the upper lung. Finally, the fifth case had extensive bilateral upper-lobe infiltration with areas of ground glass appearance [5].

Corticosteroid therapy was effective in most cases, and clinical improvement was often dramatic [4].

In the case presented here, chest radiography was normal before the initiation of sulfasalazine therapy. During therapy pulmonary symptoms and eosinophilia developed, and pruritus may also manifest as a side effect of the drug.

To the best of the authors' knowledge, this is the first case in the literature to present with sulfasalazine-induced BOOP in a patient with seronegative RA.

In conclusion, drug side effects should be taken into consideration in the diagnosis of BOOP secondary to RA.

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