

Bronchiolitis obliterans organizing pneumonia and rheumatoid arthritis

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ABSTRACT: Bronchiolitis obliterans, with or without organizing pneumonia, can be a serious and life-threatening complication of rheumatoid arthritis. We describe a case of bronchiolitis obliterans organizing pneumonia in a patient who recently developed rheumatoid arthritis, presenting as a severe respiratory insufficiency. Diagnosis was made by means of open lung biopsy. Treatment with corticosteroids induced a quick response and substantial improvement of the respiratory symptoms.

A simultaneous strong rise in titres of serological tests suggests a relationship between the bronchiolitis obliterans organizing pneumonia and the rheumatoid arthritis.

Eur Respir J., 1991, 4, 905-911.

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Keywords: Bronchiolitis obliterans organizing pneumonia; respiratory insufficiency; rheumatoid arthritis.

Received: June 1990; accepted after revision March 22, 1991.

Bronchiolitis obliterans has recently become a subject of renewed interest [1-3]. Two types can be differentiated on either side of a continuum: a pure bronchiolitis obliterans type, and bronchiolitis obliterans organizing pneumonia (BOOP) [3, 4]. Bronchiolitis obliterans sometimes constitutes a serious complication of rheumatoid arthritis (RA), with an often grave prognosis [1, 5, 6]. We describe a patient with BOOP apparently related to RA, leading to a rapidly progressing respiratory insufficiency, which quickly responded to corticosteroid treatment.

Case report

A 75 yr old male, former post-office employee, was admitted to hospital in the spring of 1988.

There was a history of asthma as a child, hay fever and sinusitis in young adulthood. At the age of 50 yrs he was operated on for a right-sided traumatic hip fracture. From the age of 67 yrs on there were episodes of arthritis in both feet, particularly at the first metatarsophalangeal joints and left knee, presenting as gouty arthritis, which was supported by a left knee aspirate. There was a hyperuricaemia ($0.57 \text{ mmol} \cdot \text{l}^{-1}$). Therapy consisted of non-steroidal anti-inflammatory drugs: indomethacin, naproxen, and at a later stage piroxicam and allopurinol. In December 1986, necrosis of the right femoral head necessitated a total hip arthroplasty.

Six months later, because of recurrent arthritis, this time with a polyarthritic presentation, the possibility of rheumatoid arthritis, as of then seronegative, was

seriously considered. Hydroxychloroquine sulphate was added to the medication.

In December of that same year, five months before the present admission, a left total hip arthroplasty was performed for a traumatic hip fracture. Arthritic complaints of shoulders, wrists, hands, and ankles restricted mobility thereafter.

On admission the patient complained of progressive dyspnoea on exertion, a cough productive of brownish sputum with bloodstreaks, a sense of reduced chest expansion, sharp chest pains, and general malaise.

Physical examination revealed a gaunt male with an evident exertional dyspnoea. Body temperature was 37.6°C . An early systolic murmur was present at the apex cordis, as were crepitations over the right dorsal lower lung zones, and a pleural rub over the left infrascapular region.

Thickened wrists, metacarpophalangeal and proximal interphalangeal joints of both hands, as well as thickened ankle joints were noted.

Laboratory investigations

Erythrocyte sedimentation rate $140 \text{ mm} \cdot \text{h}^{-1}$; Haemoglobin $94 \text{ gm} \cdot \text{l}^{-1}$; Haematocrit 31%; platelets $840 \times 10^9 \cdot \text{l}^{-1}$; leucocytes $14.0 \times 10^9 \cdot \text{l}^{-1}$; differential count: 82% segmented neutrophils, 1% band forms, 1% eosinophils, 14% lymphocytes, 2% monocytes.

Immunoglobulin E $110 \text{ kU} \cdot \text{l}^{-1}$ (normal: <50); immunoglobulin G 18.6; immunoglobulin A 4.7; immunoglobulin M $0.9 \text{ g} \cdot \text{l}^{-1}$.

Serological tests for RA, previously negative, had become positive one month earlier: latex fixation test 1:160; immunoglobulin M-rheumatic factor (enzyme linked immunosorbent assay): 30 IE; peri nuclear factor positive; anti nuclear antigen negative; C-reactive protein $17 \text{ mg} \cdot \text{l}^{-1}$.

Alkaline phosphatase $118 \text{ U} \cdot \text{l}^{-1}$ (normal. 30–100); serum protein $63 \text{ g} \cdot \text{l}^{-1}$; urea $7.2 \text{ mmol} \cdot \text{l}^{-1}$; creatinine $110 \text{ } \mu\text{mol} \cdot \text{l}^{-1}$; uric acid $0.21 \text{ mmol} \cdot \text{l}^{-1}$; urine analysis was negative.

In spite of oxygen supplementation by nasal catheter, there was a progressive partial respiratory insufficiency. Blood gas analysis on the third hospital day with oxygen $4 \text{ l} \cdot \text{min}^{-1}$ arterial oxygen tension (Pao_2) 5.1 kPa ; arterial oxygen saturation (Sao_2) 74%; arterial carbon dioxide tension (Paco_2) 4.5 kPa ; pH 7.45.

The chest roentgenogram (fig. 1) showed reticulo-nodular opacities, most pronounced in the right upper and lower regions, locally conflating to ground glass densities, with a right sided basal pericardial consolidation. Left upper and lower lung fields were affected to a lesser extent. Lung volumes appeared to be reduced.

Lung perfusion scan revealed no segmental defects, but there was diminished activity in the region of the consolidation.

Hand films demonstrated juxta-articular demineralization and erosions in the wrists, consistent with RA.

Flexible fiberoptic bronchoscopy disclosed no endobronchial lesions, although white frothy secretions

originating from the right lower lobe were seen. In biopsies taken from the superior and posterior basal segmental bronchi of the right lower lobe, microscopy demonstrated bronchial epithelium with acute and chronic inflammatory infiltrations.

Cytological examination of both bronchial secretions obtained during bronchoscopy, and expectorated sputum showed only neutrophils and lung macrophages.

Cultures for various organisms including *Legionella* sp., respiratory viruses and mycobacteria remained negative.

Because of clinical and roentgenological deterioration (fig. 2), and progression of the respiratory insufficiency, an open lung biopsy was performed on the third day.

At operation the lung was found to be firm with little ventilatory movement; a biopsy was taken from the right lower lobe. Postoperatively, mechanical ventilation was instituted.

Microscopy revealed a mixed pattern of bronchiolitis obliterans with organizing pneumonia, with plugs of oedematous granulation-tissue extending into distal alveolar ducts, and a patchy interstitial infiltrate accompanied by accumulated alveolar macrophages distal to the plugged alveolar ducts (figs 3 and 4). There was no evidence of vasculitis.

Prednisolone was started at a dose of $80 \text{ mg} \cdot \text{day}^{-1}$ and was decreased by 10 mg every week.

The densities on the chest films steadily diminished (fig. 5), and artificial ventilation was discontinued on the seventh postoperative day.

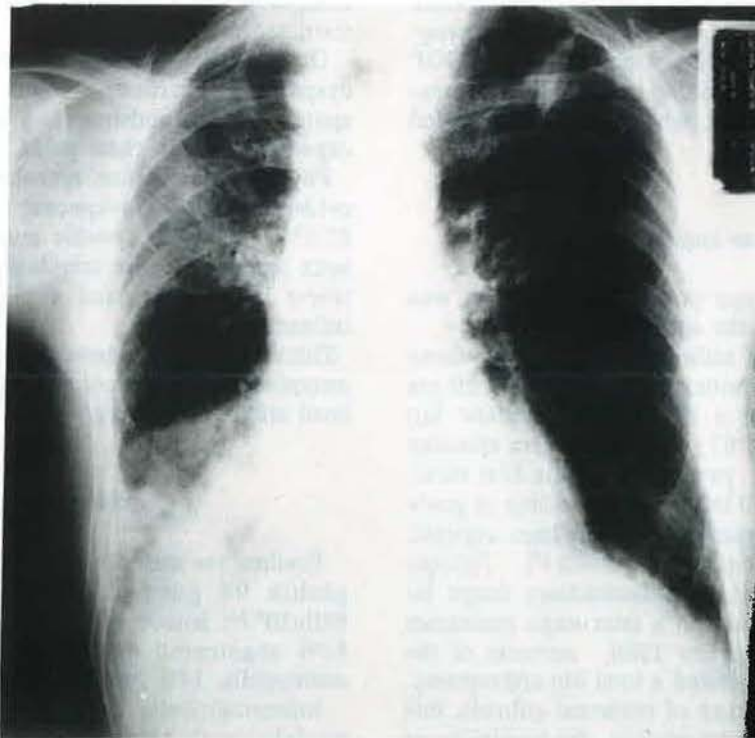


Fig. 1. — Chest radiograph on admission.

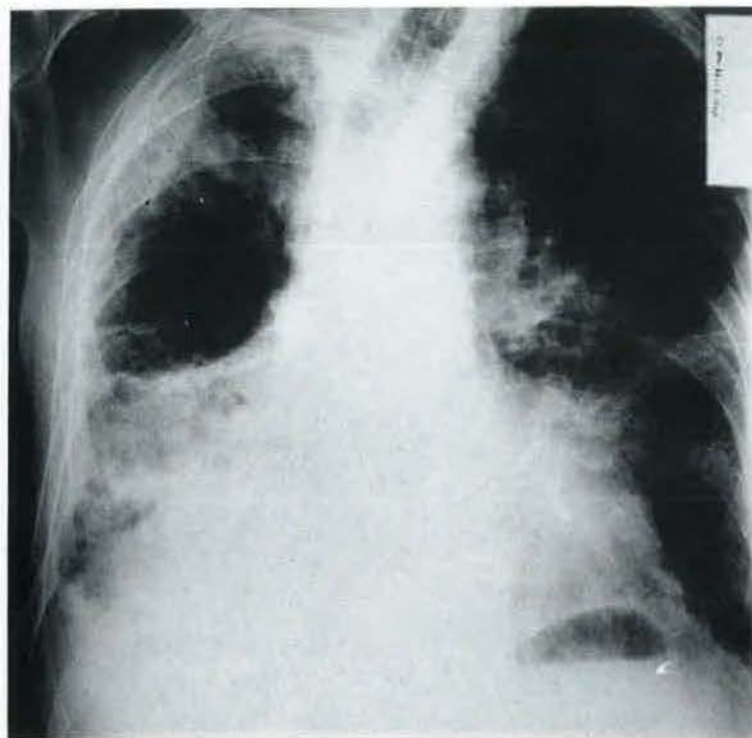


Fig. 2. - Progression of opacities just before open lung biopsy.



Fig. 3. - Plug of granulation tissue, extending into alveolar ducts and alveoli.

Various complications delayed convalescence: suspected left heart failure, urinary tract infections (*Escherichia coli*), oropharyngeal candidiasis, pneumothoraces on the right side, for which pleurodesis was

attempted, gastrointestinal blood loss, a bilateral peroneus palsy, and impending sacral decubitus.

Repeated chest roentgenograms showed continuing improvement with residual basal linear opacities in the

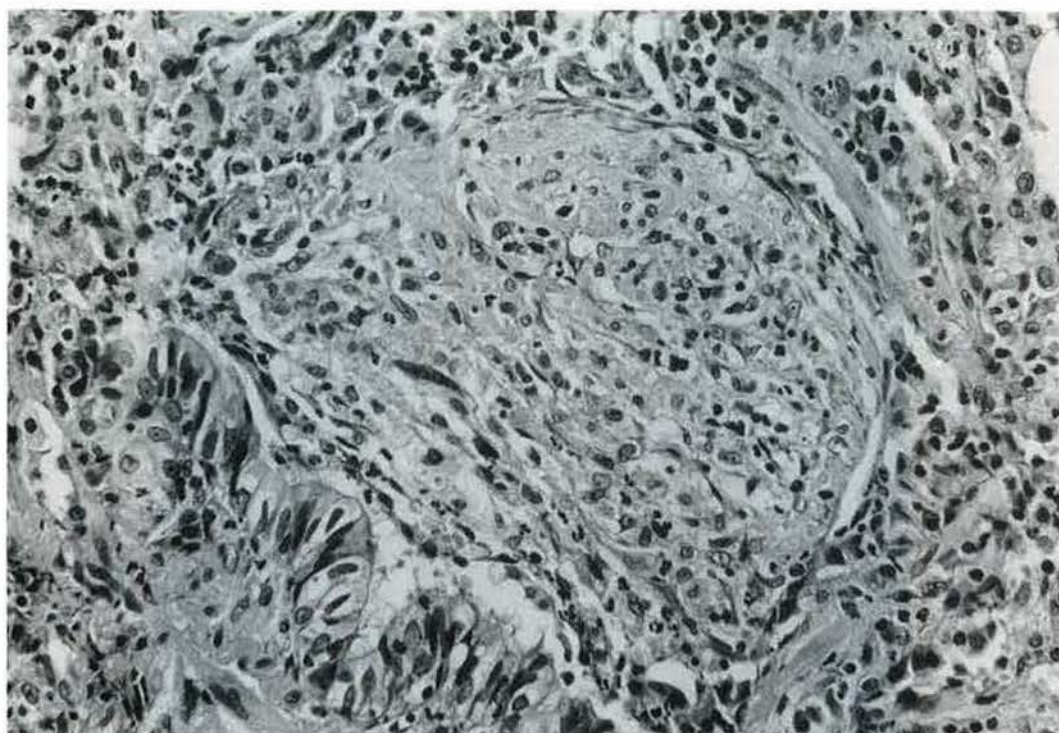


Fig. 4. - Bronchus obliterated by granulation tissue.

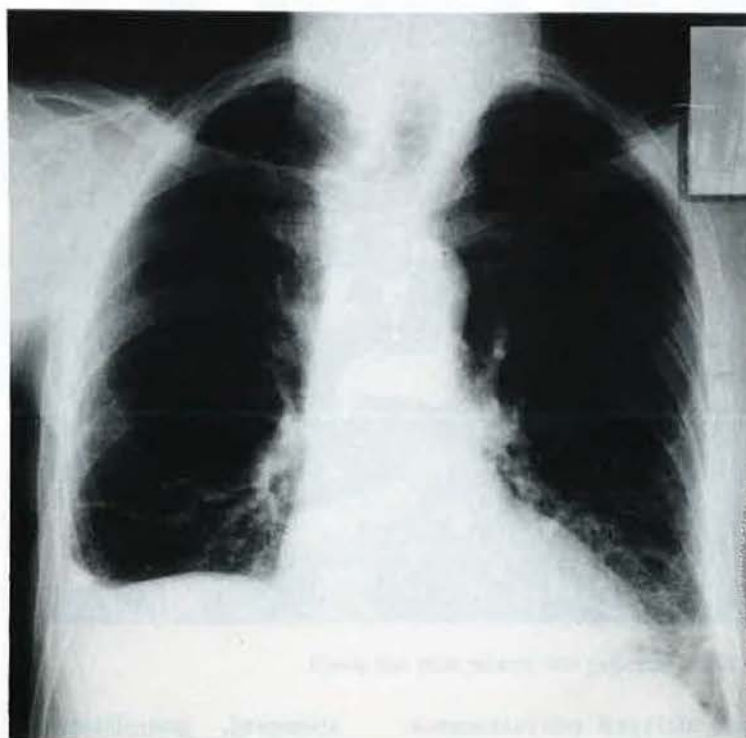


Fig. 5. - Chest radiograph after two months of therapy.

Table 1. - Pulmonary function tests

	Pred.	On Admission	After 5 months	After 8 months	After 1 year
IVC	3.87 l	2.46	2.39	2.28	2.29
FEVC	3.72 l	2.53	2.65	2.46	2.39
FEV ₁	2.85 l	1.64	1.98	1.58	1.77
FEV ₁ /VC	74%	61*	79	66	78
TLC	6.83 l	5.12	4.66	4.47	3.67
FRC(He)	3.67 l	2.79	3.05	3.00	2.10
RV	2.70 l	2.59	2.01	2.01	1.41
DLco	25.0**	12.4	13.2	12.8	11.2
DLco/VA	4.80†	3.10	3.49	3.14	3.72
Pao ₂	8.0-13.3 kPa	5.1††	13.1‡	11.5‡‡	9.9
Paco ₂	4.7-6.0 kPa	4.5	4.3	4.5	4.7
Sao ₂	95%	74	98	97	95
pH	7.35-7.45	7.45	7.46	7.44	7.42
HCO ₃ ⁻	22-28 mmol·l ⁻¹	NA	21.9	NA	22.5
Height	m	1.74	1.74	1.74	1.74
Weight	Kg	64	58	57	68

*: Reversible to 84% with salbutamol; **: ml·min⁻¹·mmHg⁻¹; †: min⁻¹·mmHg⁻¹; ††: with oxygen 4 l·min⁻¹ by nasal catheter; ‡: measured after 6 months; ‡‡: measured after 7 months; IVC: inspiratory vital capacity; FEVC: forced expiratory vital capacity; FEV₁: forced expiratory volume in the first second; TLC: total lung capacity; FRC (He): functional residual capacity measured with helium; RV: residual volume; DLco: pulmonary diffusing capacity measured with single breath carbon monoxide; VA: alveolar volume; Pao₂: arterial oxygen tension; Paco₂: arterial carbon dioxide tension; Sao₂: arterial oxygen saturation.

Serologic tests, ESR and CRP

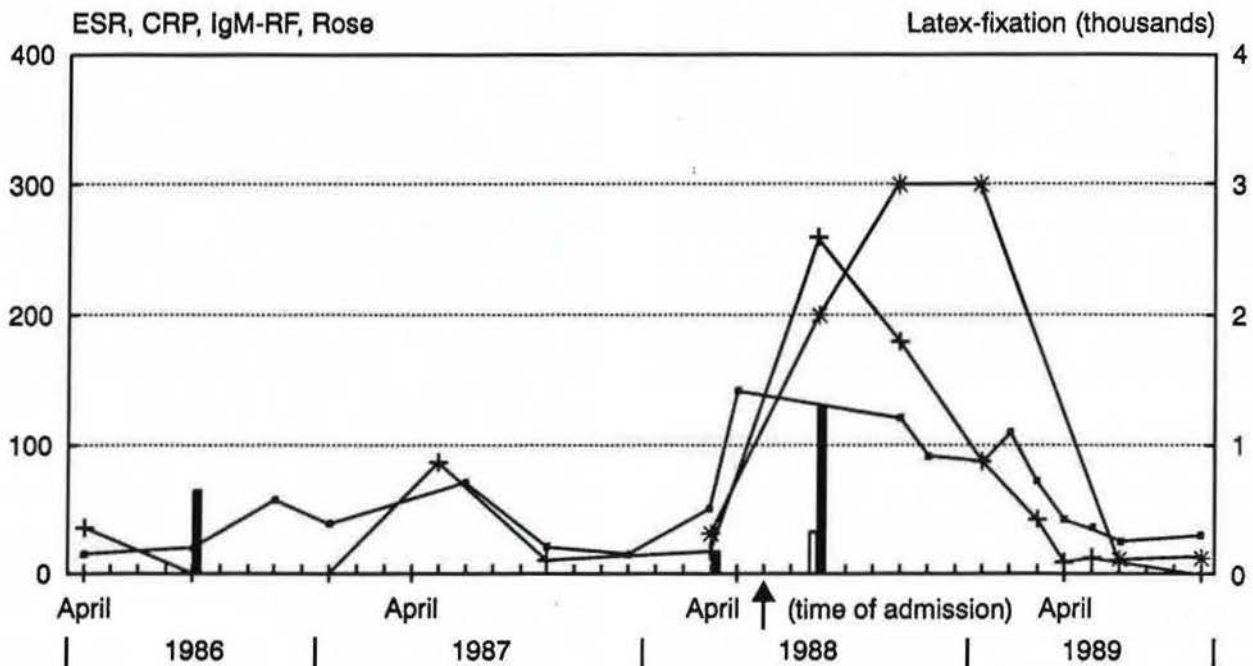


Fig. 6. - Serologic tests, ESR and CRP. —•—: ESR mm·h; —+—: CRP mg·l; —*—: IgM-RF IE; ■: Latex-Fixation; □: Rose Waaler.

right lower region. Blood gas values virtually normalized (table 1).

After three and a half months of hospitalization the patient was discharged. One and a half years later, the patient is doing well; he is still receiving 15 mg prednisolone, and gold salts have been added to the regime.

Discussion

Bronchiolitis obliterans, with or without organizing pneumonia, has recently often been described as a complication of rheumatoid arthritis (RA) [4, 7], sometimes apparently related to D-penicillamine therapy [1, 8–10].

The predominant interstitial and organizing pneumonia in this case is fairly unusual in cases related to, or coincidental with RA: more often the constrictive pattern of bronchiolitis obliterans prevails [1, 8, 9, 11, 12]. The roentgenological findings are also more consistent with reports concerning BOOP: bi- or unilateral ground glass opacities, without predilection for specific areas, lobar in distribution; sometimes a coarse reticular pattern [3, 13, 14]. In contrast to other reports [13, 14] lung volumes appeared decreased.

Unlike the often described airflow obstruction in pulmonary function tests of patients with RA [15], or bronchiolitis obliterans associated with RA [1, 10], our patient had a predominantly restrictive pattern with a slight reversible obstructive component, as in other cases of BOOP [3].

On the basis of clinical and radiological information one should be able to suspect the diagnosis in typical cases [3]. Definite diagnosis, however, requires a lung biopsy [16–18]. Because of the focal nature of the lesions an open lung biopsy is preferable [3, 18, 19]; morbidity and mortality are relatively low, whilst diagnostic accuracy is high when compared to other methods [20].

As in cases of idiopathic BOOP [3], our patient quickly responded to corticosteroid treatment, whilst in other cases related to RA response has been less favourable [1, 6, 11, 12]. The so-called "midinspiratory squeak" [1] was heard once, only after therapy had long been instituted. During this admission the patient definitely fulfilled the criteria for rheumatoid arthritis [21].

Although rheumatic factor levels do not necessarily equal disease activity [22, 23], in this case there was a strong temporal relationship (fig. 6). Therefore, we consider a causal relationship between the RA, and the BOOP conceivable. Before his presentation with BOOP this patient had never received D-penicillamine or gold therapy.

The apparent relationship between the BOOP and the RA in this patient, and the atypical presentation, more consistent with idiopathic BOOP than with bronchiolitis obliterans in other cases of RA, could point toward a modifying effect which medication such as gold salts or D-penicillamine may have on the course of this complication in RA.

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Observation clinique. Bronchiolite oblitérante avec pneumonie fibrosante et arthrite rhumatoïde. R.J. Van Thiel, S. van der Burg, A.D. Groote, G.D. Nossent, S.H. Wills.

RÉSUMÉ: La bronchiolite oblitérante, accompagnée ou non d'une pneumonie fibrosante, peut être une complication sérieuse et létale de l'arthrite rhumatoïde. Nous décrivons un cas de bronchiolite oblitérante avec pneumonie fibrosante, chez un patient dont l'arthrite rhumatoïde était apparue récemment et qui a développé une insuffisance respiratoire sévère. Le diagnostic a été assuré par une biopsie pulmonaire à ciel ouvert. Le traitement aux corticostéroïdes a entraîné une réponse rapide et une amélioration substantielle des symptômes respiratoires. Une augmentation importante et simultanée des titres des tests sérologiques suggère une relation entre la bronchiolite oblitérante avec pneumonie fibrosante et l'arthrite rhumatoïde.

Eur Respir J., 1991, 4, 905-911.