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Case of severe treatment resistant cryptogenic organising pneumonia

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Abstract

English:

Cryptogenic organising pneumonia (COP) is a rare interstitial lung disease with different onset of symptoms, which responds rapidly to glucocorticoid treatment. We present a case of COP which manifested as progressive 3-year dyspnoea that has led ultimately to acute respiratory failure. Moreover, treatment with prednisone for this patient exhibits slow onset of the effect.

Keywords

organising pneumonia • acute respiratory failure • prednisone therapy

Un caz de pneumonie cu organizare criptogenică severă, rezistentă la tratament

Rezumat

Romanian:

Pneumonia criptogenică organizată este o boală interstițială rară cu manifestări clinice variate și care răspunde rapid la terapia cu glucocorticozi. Prezentăm un caz de pneumonie criptogenică organizată ce a debutat cu o dispnee progresivă (aproximativ 3 săptămâni) care s-a soldat cu insuficiență respiratorie. Mai mult tratamentul cu prednison în acest caz a început târziu să își facă efectul.

Cuvinte-cheie

Pneumonie crpitogenica organizata • insuficienta respiratorie acuta • esec tratament prednison

Introduction

Organising pneumonia (OP) is a rare diffuse interstitial lung disease characterised by mesenchymal proliferates (Masson body) in the lung tissue histopathology (1). There are no specific clinical and radiological findings attributed for this disease (2). Aetiologically OP can be either secondary (secondary to a lung injury such as infection, drug and pathogen toxicity, gastroesophageal reflux, or radiotherapy and pulmonary lesions of another nature such as vasculitis, lymphoma, lung cancer, hypersensitivity pneumonitis, eosinophilic pneumonia, acute interstitial pneumonia (3)) or cryptogenic (2). Although the exact prevalence of cryptogenic organising pneumonia (COP) is not known, some studies present estimated incidence of 1–3/100,000 hospital admissions (4). Men and women are affected equally (4). COP typically occurs in patients aged between 50 years and 60 years (4), who are usually non-smokers (3). Patients with cryptogenic OP usually present with acute or subacute (days to weeks in duration) respiratory symptoms and rarely develops a progressive disease

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with severe dyspnoea and hypoxaemia (4,5). Moreover, majority of symptoms are considerably improved short after glucocorticoids therapy (4,6). We introduce an unusual case, in which the patient presents with chronic progressive and severe dyspnoea leading to acute respiratory failure, and the disease itself responding vaguely to glucocorticoid therapy.

Case report

We present a case of 54 years-old women whose main complaint is shortness of breath. Dyspnoea started 3 years ago and progressed from symptoms limited only to physical activity to dyspnoea in rest. There were at least two acute viral respiratory infection episodes during this 3-year period. Patient is a non-smoker, has no comorbidities and no exposition to respiratory toxins or to professional hazards.

Thoracic Computer Scan was conducted to specify/find possible causes of these symptoms ,and it showed multiple bilateral confluent irregular foci mostly in the lower lobes, ground glass appearance and traction bronchiectasis, all suggesting interstitial lung disease (Figure 1).

Due to progressive dyspnoea, patient was hospitalised in our department for further management. Physical examination revealed respiratory rate of 19 times/min at rest and tachypnoea during light physical activity (respiratory rate greatly elevated and was immeasurable). In auscultation no audible rales and normal vesicular breathing were inspected. Peripheral blood oxygen saturation (SpO_2) on room was 95% at rest and 82–85% during light physical activity, with oxygen supply SpO_2 increased to 90–92%. Pulmonary function assessment demonstrated low grade restriction and minor gas diffusion impairment (FVC (Forced Vital Capacity) 72%, FEV_1 (forced expiratory volume in 1 second) 69%, FEV_1/FVC 82%, TLC (Total Lung Capacity) 70%, VC (Vital Capacity) 72%, DLCO (diffusing capacity for carbon monoxide) 62%). Control chest roentgenography showed remaining signs of interstitial disease mostly in the lower lobes (Figure 2).

Further diagnostics included bronchoscopy with lung cryobiopsy and bronchoalveolar lavage (BAL). Histology confirmed interstitial lymphocytic infiltration with OP (Figure 3). BAL microscopic and microbiologic examination showed no pathological changes: cancerous cells, acid resistant bacteria, *Mycobacterium tuberculosis* complex DNA, viruses were not detected. The growth of bacteria, fungi, or *M. tuberculosis* was not observed. Patient tested negative for ANA and ANCA. Based on radiological findings, histology results and absence of aetiologic factors, the patient was diagnosed with COP and was

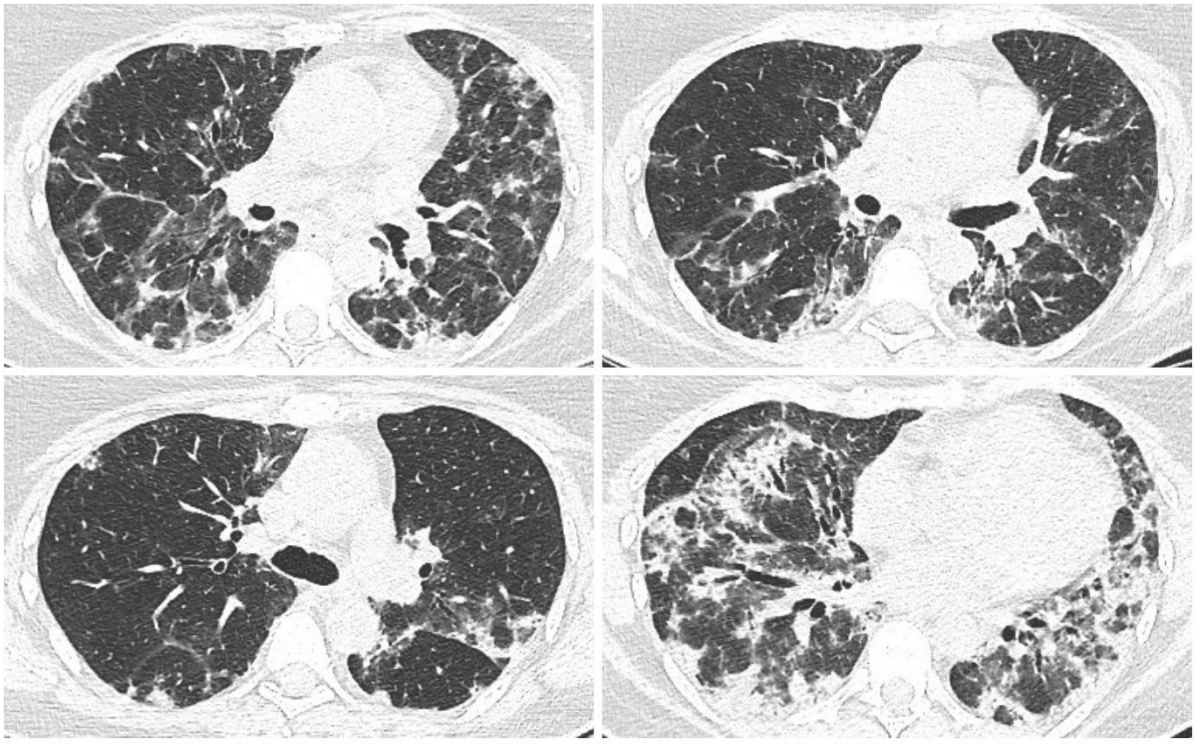

Figure 1. Chest CT showing multiple bilateral confluent irregular foci mostly in the lower lobes, ground glass appearance and traction bronchiectasis.

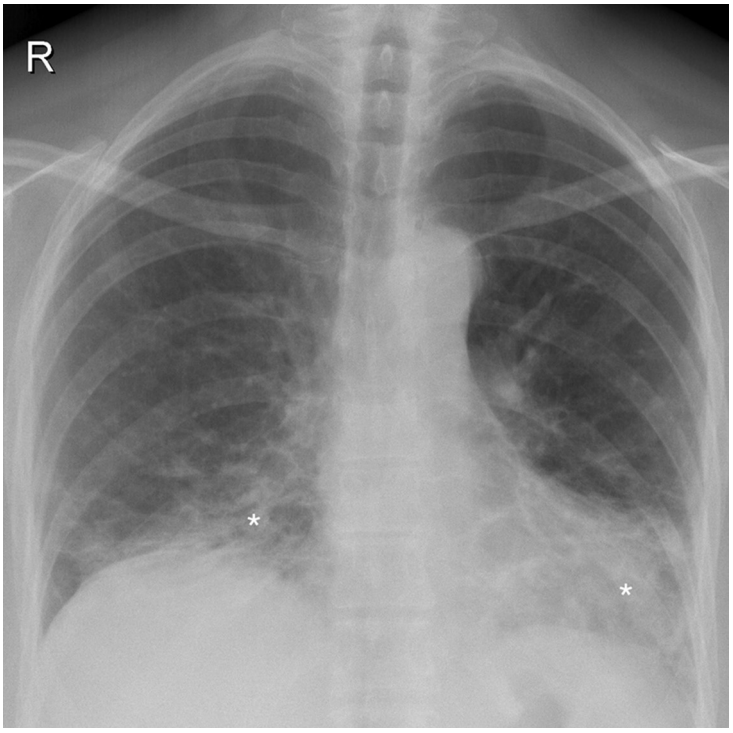

Figure 2. Control chest-X-ray showing remaining signs of interstitial disease mostly in the lower lobes.

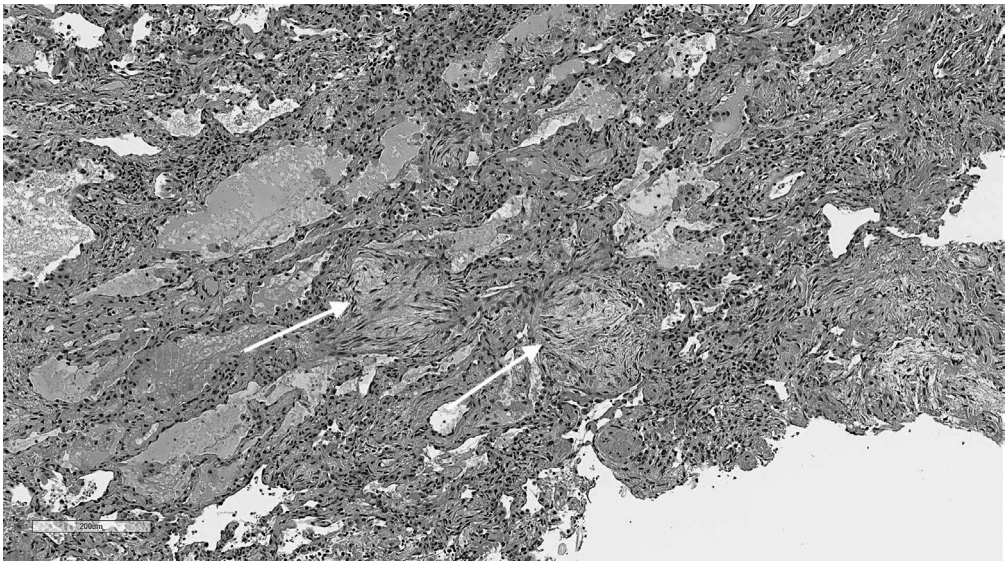

Figure 3. Histopathological examination showing interstitial lymphocytic infiltration with OP. OP, organising pneumonia.

treated with initial oral dose of 30 mg/day of prednisolone for 1 month, and gradually downgraded to 20 mg/day for 2 months. After 3 months, patient revisited for treatment control. Subjective patient symptoms relieved and exercise tolerance increased slightly. Chest roentgenography, in comparison with previous roentgenogram, showed minor positive dynamics mostly in the basal segments, although signs of interstitial disease remain (Figure 4).

In pursuance to avoid adverse events, oral dose of prednisone was gradually reduced to 15 mg/day for another 3 months.

In the next follow-up, normopnoea (respiratory rate of 16 times/min) at rest and normal lungs auscultation were observed.

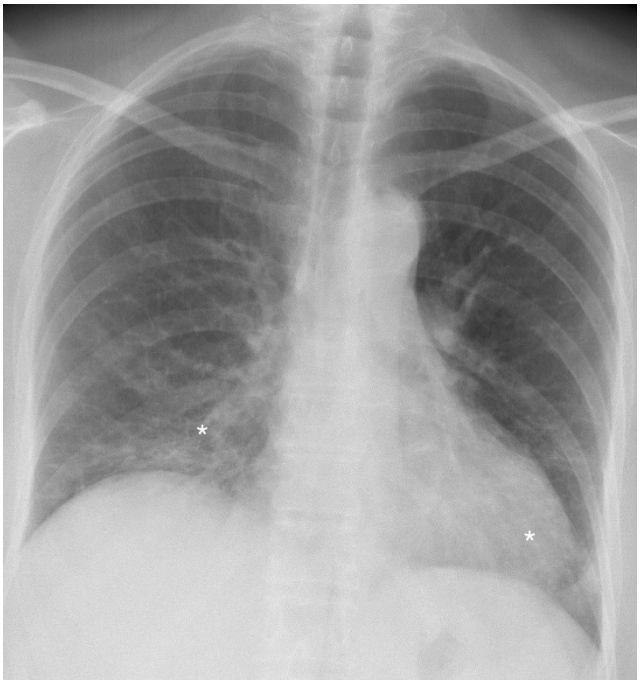

Figure 4. Chest X-ray showed minor positive dynamics mostly in the basal segments, although signs of interstitial disease remain.

SpO_2 was 96% at rest (without supplemental oxygen) and 92% during physical activity (with supplemental oxygen) were measured. Pulmonary function analysis in contrast with previous test showed minor positive dynamics, although restriction and gas diffusion impairment remain (FVC 80%, FEV_1 80%, FEV_1/FVC 84%, TLC 59%, VC 81%, DLCO 67%). Due to ongoing diminishing of symptoms prednisone dose was reduced to 10 mg/day and further prescribed for a period of 3 months.

Discussions

The onset of COP is often no longer than 3 months with a subacute period of several weeks (7). The most common symptoms are non-specific and include malaise, cough, constitutional symptoms and dyspnoea (2,3,8). The latter usually being chronic, progressive, and mild; however, occasionally can be severe in a rapidly progressive form of the disease (9). Unusually, in our patient COP course was chronic (3 years) and symptoms progressed to severe dyspnoea with acute respiratory failure without any clear reason.

As in this case, the most important issue is slow positive dynamics in treating this patient with oral steroids and the need to continue such treatment. Majority of the COP patients are treated with oral glucocorticoids causing rapid relieving of symptom as well as radiologic signs improvement (4,5). However, radiologic signs in some instances can remain for up to several months or not resolved completely at all (10). In our case, radiologic and symptomatic responses to initial dose of 30 mg/day for 1 month and changing to 20 mg/day for another 2 months of prednisone were poor.

Insufficient clinical effect of glucocorticoids in COP treatment is reported to be as high as in 40% of all COP cases (11). In addition, glucocorticoids in nearly one-third of the patients could cause adverse events including gastrointestinal bleeding, arterial hypertension, bone fracture, diabetes mellitus, body weight increase and increase mortality rate (6). Successful steroids resistant COP treatment in combination with steroids or alone with rituximab (11), azathioprine (4,5), cyclophosphamide, cyclosporine A (4) and mycophenolic acid (12) are reported (13).

Furthermore, as an alternative pharmacological single-drug therapy in patients within normal ranges of pulmonary function parameters are macrolides, such as clarithromycin and azithromycin (6,13). In comparison with glucocorticoids, macrolides cause fewer side effects and are suitable for patients for whom steroids are contraindicated or the usage of those are limited (6,13). Therefore, considering alternative treatment possibilities and the fact that in mild course of COP spontaneous regression could be seen, steroids should be only administrated in cases of severely affected in daily life and having hypoxaemia (14). The latter are both present in our patient as well.

Conclusions

It must be considered that COP can present atypically with progressing symptoms, which lead to respiratory failure. Treatment of COP with corticosteroids is the most effective in most cases, although the clinical and radiological effects may not be immediate and need relatively long-term therapy.

Conflict of Interest

The authors declare no conflict of interest.

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