

Organizing Pneumonia Associated With the Use of Pegylated Interferon Alfa

Joan-Carles Trullas Vila, Demetrio-Roberto Padilla López, Vicenta Bisbe Company, Silvia Soler Simón, Pere Cortés Hausmann, and Josep Bisbe Company

Servicio de Medicina Interna, Hospital Sant Jaume, Olot, Girona, Spain

Organizing pneumonia is a well-differentiated clinical and histologic entity whose onset is usually subacute with respiratory symptoms and pulmonary infiltrates. Its origin may be unknown (cryptogenic) or it may be associated with various medical conditions, infectious diseases, or drugs. Diagnosis is confirmed by the presence of foci of organizing pneumonia in lung biopsy specimens. Our patient was a 49-year-old man infected with the hepatitis C virus who was receiving pegylated interferon alfa-2b. He presented with dry cough, fever, dyspnea, and ground glass pulmonary infiltrates. After an open lung biopsy, he was diagnosed with organizing pneumonia. When pegylated interferon was discontinued and corticosteroids started, the symptoms and pulmonary infiltrates disappeared. To our knowledge, this is the second report of organizing pneumonia related to pegylated interferon alfa-2b.

Key words: *Organizing pneumonia. Interferon alfa-2b. Hepatitis C.*

Introduction

Organizing pneumonia is an interstitial pulmonary disease that has been well described for more than 20 years.¹ Its origin may be unknown (cryptogenic) or it may be associated with various diseases or drugs. We report the case of a patient infected by the hepatitis C virus (HCV) who, after 6 months of therapy with pegylated interferon alfa-2b, presented with subacute dry cough, fever, and dyspnea on exertion. After open lung biopsy, he was diagnosed with organizing pneumonia. We carried out a thorough MEDLINE search (1976-2006) with the key words *interferon alpha-2b*, *bronchiolitis obliterans organizing pneumonia*, and *hepatitis C*. A search of the Pneumotox² web page revealed that, to date, there has only been 1 case of organizing pneumonia associated with the treatment of hepatitis C using pegylated interferon alfa-2b.³

Correspondence: Dr J.C. Trullas Vila
Servei de Medicina Interna, Hospital Sant Jaume
Mulleras, 15
17800 Olot, Girona, Spain
E-mail: jctrullas@hospiolot.com

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Neumonía organizada asociada a tratamiento con peginterferón alfa

La neumonía organizada es una entidad clínico-histológica bien diferenciada, que suele presentarse de forma subaguda con síntomas respiratorios e infiltrados pulmonares. Puede ser de causa desconocida (criptogenética) o estar asociada a distintas enfermedades, infecciones o fármacos. El diagnóstico de seguridad requiere la demostración de focos de neumonía organizada en muestras de biopsia pulmonar. Presentamos el caso de un paciente de 49 años con infección por el virus de la hepatitis C en tratamiento con peginterferón α -2b que desarrolló un cuadro de tos seca, fiebre, disnea e infiltrados pulmonares en vidrio deslustrado, y a quien se diagnosticó por biopsia pulmonar abierta de neumonía organizada. Con la retirada del peginterferón y tratamiento con corticoides desaparecieron los síntomas y los infiltrados pulmonares. En nuestro conocimiento, éste es el segundo caso comunicado de neumonía organizada en relación con peginterferón α -2b.

Palabras clave: *Neumonía organizada. Interferón α -2b. Hepatitis C.*

Case Description

Our patient was a 49-year-old man, ex-smoker with no known allergies, who was diagnosed with chronic HCV infection (genotype 1b) as the result of an analysis made before blood donation when he was 35 years old. Because of his persistently high transaminase levels (aspartate aminotransferase and alanine aminotransferase between 50 U/L and 100 U/L) and plasma viral load (number of copies of HCV RNA), the patient began treatment with subcutaneous pegylated interferon alfa-2b (1.5 μ g/kg/week) and oral ribavirin (1000 mg/d) 6 months before admission. The patient showed good initial tolerance and adherence and it was not necessary to reduce the dose, as there were no adverse effects. The patient consulted with a 2-week history of persistent dry cough, fever, and progressive dyspnea that appeared even after minimal effort. The vital signs on admission were as follows: blood pressure 91/65 mm Hg, respiratory rate of 32 breaths/min, heart rate of 87 beats/min, and axillary temperature of 36°C. The most remarkable findings of the physical examination were coarse crackles at the bases of both lungs; the remainder of the examination was normal. The findings of arterial gas analysis (inspired oxygen fraction of 0.21, pH of 7.42, PaCO₂ of 62 mm Hg, PaO₂ of 34 mm Hg, HCO₃ of 22 mmol/L) and a chest radiograph (Figure) led us to recommend admission for further study and treatment. A standard workup during admission revealed the following values: erythrocyte sedimentation rate 24 mm/h, normal complete blood count, general biochemical parameters



Figure. Chest radiograph at admission showing predominant bibasilar interstitial infiltrates

(glucose, urea, creatinine, sodium, potassium, calcium, aspartate aminotransferase, alanine aminotransferase, γ -glutamyl transpeptidase, alkaline phosphatase, lactate dehydrogenase, creatinine kinase, total cholesterol, triglycerides, total proteins, albumen, and thyrotropic hormone) within the normal range, negative serology studies (enzyme-linked immunosorbent assay for the human immunodeficiency virus and immunoglobulins G and M for *Mycoplasma pneumoniae*, *Coxiella burnetii*, and *Chlamydia pneumoniae*), negative anticytoplasmic and antinuclear neutrophil antibodies, and normal angiotensin-converting enzyme values. Testing for the *Legionella* urine antigen was negative. Computed tomography of the thorax revealed diffuse patchy ground glass infiltrates, mainly in both lung bases. Bronchoscopy with bronchoalveolar lavage revealed the following cellular profile: 55% macrophages, 40% lymphocytes, and 5% eosinophils. Cultures for bacteria, mycobacteria, and fungi were negative. The patient finally underwent open lung biopsy that revealed foci of organizing pneumonia. On admission, the patient had interrupted his HCV treatment and started empiric antibiotic treatment (intravenous ceftriaxone at 2 g/24 h and oral clarithromycin at 500 mg/12 h), although his symptoms did not improve. Once infectious causes were reasonably ruled out by culture and serology testing and the biopsy result was available, the antibiotic was withdrawn and the patient started on intravenous methylprednisolone at 1 mg/kg/d. His symptoms improved quickly and he was discharged with oral prednisone (1 mg/kg for 1 month after which the dose was tapered until treatment was withdrawn after 6 months). After 9 months of follow-up, the patient is asymptomatic and the pulmonary infiltrates have completely resolved.

Discussion

Organizing pneumonia (previously known as bronchiolitis obliterans organizing pneumonia) has been a clearly defined clinical-histologic entity for the last 20 years.^{1,4} Its clinical manifestations—subacute cough, dyspnea, and fever—are accompanied by alveolar and/or interstitial infiltrates (sometimes migratory and even recurrent) and abnormalities in bronchoalveolar lavage (marked lymphocytosis, often associated with neutrophilia and/or eosinophilia) that may help to establish a diagnosis. A firm diagnosis is based on demonstration of foci of

organizing pneumonia in samples obtained by transbronchial or surgical biopsy. The condition may arise from any of a number of conditions, including infection, aspiration pneumonia, inhalation of toxic substances, drug toxicity (caused by agents such as bleomycin, ergot derivatives, nitrofurantoin, phenytoin, amiodarone, carbamazepine, cyclophosphamide),^{2,5} radiotherapy, collagen diseases, vasculitis, or intestinal inflammatory diseases. When no associated disorder can be identified, this disease is known as cryptogenic organizing pneumonia.^{1,4} Pegylated interferon alfa-2b is a treatment that is being applied ever more broadly. It is used not only against HCV infection but also in such other diseases as multiple sclerosis. Physicians should therefore be aware of its side effects, the most frequent of which include psychiatric, hematologic, and flu-like symptoms.⁶ Less common is pulmonary toxicity, which has usually occurred in cases of sarcoidosis⁷ and interstitial pneumonitis.⁸ There have been exceptional reports of eosinophilic pneumonia, asthma, and pleural effusion.² Our patient had a 2-month history of dry cough, dyspnea, and fever. Chest auscultation revealed dry crackles and predominantly interstitial pulmonary infiltrates mainly at the bases of the lungs. The negative results of microbiology, the lack of response to antibiotic therapy, and the rapid response to corticosteroids led to a diagnosis of organizing pneumonia, which was confirmed by lung biopsy. When pegylated interferon alfa-2b was withdrawn and treatment with corticosteroids started, both symptoms and pulmonary infiltrates disappeared. This and the absence of another medical condition or other drugs that could be associated with organizing pneumonia led us to conclude that pegylated interferon alfa-2b can cause this disorder, although no cause-effect relationship has been demonstrated. To our knowledge, after the literature search mentioned above, this is the second case report of organizing pneumonia associated with pegylated interferon alfa-2b.

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