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Case Report

A Case Report of Pegylated Interferon and Bronchiolitis Oblitrans with Organizing Pneumonia

Ahmad Khosravi[1], Mohammad Towhidi[2], Hassan Vosoughinia[3], Kamran Ghaffarzadehgan[3], Shahrzad M Lari[4], Tahmineh Tavakkoli[5]

[1]Associate Professor , Department of Gastroenterology and Hepatology, Ghaem Hospital, Mashhad University of Medical Sciences (MUMS) , Mashhad, Iran
[2]Professor, Lung Disease and Tuberculosis Research Center (LTRC), Ghaem Hospital, Mashhad University of Medical Sciences(MUMS), Mashhad, Iran
[3]Assistant Professor, Department of Gastroenterology and Hepatology, Ghaem Hospital, Mashhad University of Medical Sciences (MUMS) , Mashhad, Iran.
[4]Pathologist, Department of Gastroenterology and Hepatology, Ghaem Hospital, Mashhad University of Medical Sciences (MUMS) , Mashhad, Iran
[4]Assistant Professor, Lung Disease and Tuberculosis Research Center (LTRC), Ghaem Hospital, Mashhad University of Medical Sciences(MUMS), Mashhad, Iran
[5]Assistant Professor of Internal Medicine, Birjand University of Medical Sciences, Birjand, Iran

ABSTRACT

A 46-year-old woman presented with progressive dyspnea and cough. She was a known case of chronic hepatitis C (HCV) treated with pegylated (PEG)-interferon. Complete pulmonary studies and biopsy were compatible with bronchiolitis oblitrans with organizing pneumonia (BOOP) secondary to PEG-interferon. She discontinued PEG-interferon and was given a short course of steroids, after which the condition completely resolved. This report has shown that particular attention to possible side effects of PEG-interferon is necessary in the clinical practice.

Keywords :Bronchiolitis oblitrans with organizing pneumonia (BOOP); pegylated (PEG)-interferon; Hepatitis C virus (HCV); Iran.

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Corresponding author:
Shahrzad M Lari, MD
2199 Asrare Gharbi, Kouye doctora,
91836-33811,Mashhad,Iran
Tel: +985118452146
Fax: +985118431252
E-mail: Larish@mums.ac.ir
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INTRODUCTION

Chronic hepatitis C (HCV) infection is a major cause of hepatic dysfunction worldwide. The mainstay of treatment is a regimen that consists of pegylated (PEG)-interferon and ribavirin for 24-48 weeks (1). Drug-induced pulmonary complications may occur after treatment with interferons. We present a patient with HCV that had progressive dyspnea and hypoxemia following interferon therapy, with a final diagnosis of bronchiolitis oblitrans with organizing pneumonia (BOOP). Despite the existence of previ-

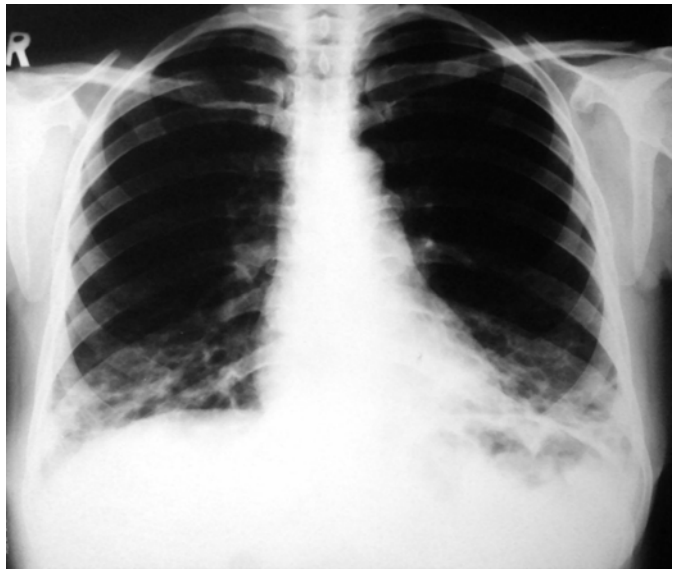

Figure 1: **Bilateral lower lung fields show patchy infiltrates seen on chest X-ray.**

ous reports about PEG-interferon related BOOP(2-4), to our knowledge this is the first reported case in Iran.

CASE REPORT

A 46-year-old woman was admitted to the hospital with progressive dyspnea and non-productive cough. Eight months before admission, she was diagnosed with HCV following serologic tests for blood donation. Diagnosis was confirmed by HCV RNA assessment with a viral load of 1,910,000 copies/ml and genotype 1a. A liver biopsy confirmed chronic active hepatitis with a hepatic activity index of grade 7, stage 1. Serum aminotransferases were within normal ranges. The patient received a treatment regimen of PEG-interferon α-2b (Interon; 100 mcq/week) and ribavirin (1000 mg/day) for 28 weeks. Subsequently, she developed progressive dyspnea and non-productive cough, and was admitted to the hospital. Ribavirin and PEG-interferon were discontinued. Apart from a history of blood transfusion during a hysterectomy eight years prior, her past medical history was unremarkable.

On physical examination, she was alert and cooperative with an oral temperature of 37.2ºC and respiratory rate of 24/min. Except for bilateral diffuse fine inspiratory crackles, the rest of her exam was normal.

Laboratory tests included complete blood count (CBC), blood chemistry, liver function tests, anti-nuclear antibody, anti-double-stranded antibody, rheumatic factor, and anti-neutrophilic cytoplasmic antibody; all within normal limits. PaO_2 was 60 mmHg upon arterial blood gas analysis. Pulmonary function tests revealed reduced forced vital capacity (FVC) and DLCO with normal forced expiratory volume in one second (FEV1), and an increased FEV1/FVC. There were bilateral patchy infiltrates in the lower zones seen on chest radiography (Fig. 1). High resolution CT (HRCT) scan of the chest showed bilateral peripheral consolidations. Fiberoptic bronchoscopy was normal. The findings of the bronchoalveolar lavage were not significant. A transbronchial lung biopsy was performed which showed granulation tissue plugs within the lumens of the small airways that extended into the alveolar ducts and the alveoli, compatible with BOOP (Fig. 2). Treatment with prednisolone (30 mg/day) was started for two months and slowly tapered over six weeks. The clinical symptoms, radiographic findings, and pulmonary function tests improved after cessation of interferon and administration of corticosteroid. At follow up evaluation, she was in good condition; the last viral load was 1,120,000 copies/ml.

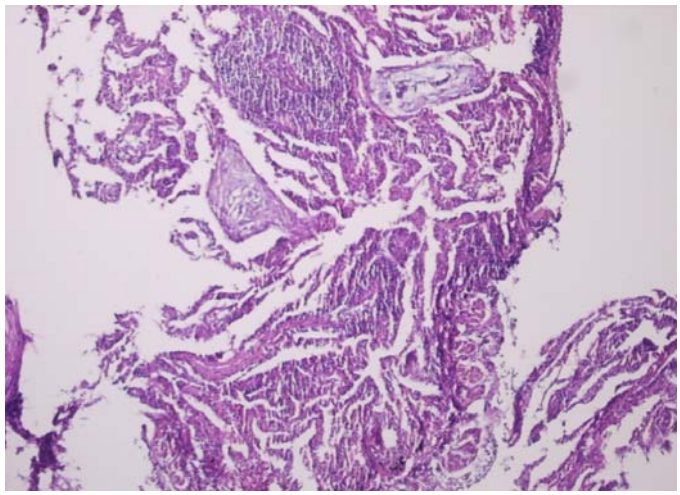

Figure 2: **Granulation tissue plugs within the lumens of the small airways extending into the alveolar ducts and the alveoli.**

DISCUSSION

Interferons have been used for treatment of various conditions such as malignancies, infections, and inflammations(5). Interferon inhibits viral replication and improves liver histopathology in chronic viral hepatitis. To extend the serum half-life of interferon, polyethylene glycol is conjugated to the interferon molecule(6). PEG-interferon in combination with ribavirin has become the therapy of choice for HCV infection(1). Interferons, like other drugs, can cause various pulmonary complications that include severe exacerbation of bronchospasms in asthmatic patients(7), sarcoidosis-like reaction(8), interstitial pneumonitis(9),and BOOP(10).

BOOP is a known clinical entity due to excessive proliferation of granulation tissue within the small airways and chronic inflammation in surrounding alveoli(11). It may be idiopathic (cryptogenic organizing pneumonia) or associated with infections, collagen vascular diseases, post-transplantation states, radiation therapy, and drugs(4).

A number of important drugs responsible for producing BOOP are acebutolol, amiodarone, bleomycin, cocaine, gold, cyclophosphamide, penicillamine, and interferon(2 ,4).

The most common signs and symptoms at presentation are dyspnea, nonproductive cough, and fine crackles. Usually, there are bilateral, diffuse alveolar opacities seen in chest radiography and air space consolidation, small nodular opacities in the periphery of the lower lung zones on chest CT scan. Mostly, pulmonary function tests show a restrictive pattern, reduced DLCO, and hypoxemia. Diagnosis is based on lung biopsy and pathologic findings(12).

Our patient had dyspnea, cough, and hypoxemia with a restrictive pattern on her pulmonary function tests. In addition, there were peripheral consolidations on the chest radiography and CT scan, all of which suggested BOOP. The patient underwent a lung biopsy, which the histopathology confirmed the diagnosis. Of note, chronic HCV infection can cause various pulmonary complications such as interstitial lung disease (mainly pulmonary fibrosis)(13). Because she was on interferon treatment, which after discontinuation of interferon and beginning steroid treatment, the patient's symptoms and imaging findings resolved. Thus, it was concluded that interferon might be the causative factor after having ruled out other possible causes of BOOP.

BOOP is a rare pulmonary complication of PEG-interferon. It should be considered in patients with hepatitis and pulmonary complaints who undergo treatment with PEG-interferon.

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