CASE REPORT

Desquamative Interstitial Pneumonitis (DIP) occurring during treatment with pegylated interferon and ribavirin

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Abbreviations: DIP, Desquamative Interstitial Pneumonitis; HCV, Hepatitis C Virus; IFN, Interferon; ASAT, Aspartate-Amino-Transferase; ALAT, Alanine-Amino-Transferase; TLC, Total Lung Capacity; HRCT, High Resolution Computed Tomography; BAL, Bronchoalveolar Lavage; BOOP, Bronchiolitis Obliterans Organizing Pneumonia.

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KEYWORDS
Pegylated interferon; Ribavirin; Desquamative Interstitial Pneumonitis

Summary
We present a case of Desquamative Interstitial Pneumonitis occurring during treatment with pegylated Interferon and Ribavirin in a man with HCV infection. © 2008 Elsevier Ltd. All rights reserved.

Introduction

Interferon is the mainstay of hepatitis C virus (HCV) treatment.\textsuperscript{1,2} Although numerous side effects have been reported during treatments with interferon in chronic hepatitis C infection: fatigue, flu-like symptoms, headache, anorexia and myalgias. Rare and serious adverse effects include permanent hearing loss, cardiac arrhythmias, cardiomyopathy, renal toxicity, bone marrow suppression and pancreatitis. Pulmonary complications of IFN are unusual, and include interstitial pneumonitis, pulmonary granulomas or a mimic of pulmonary and extra pulmonary sarcoidosis, pleural effusion and exacerbation of bronchial asthma and chronic cough.\textsuperscript{3–5} There is only one case of desquamative interstitial pneumonia (DIP) and few cases of sarcoidosis associated with interferon in literature.

Ribavirin enhances the anti-HCV activity of interferon leading to a higher and sustained virologic response. Ribavirin alone has never been reported as the cause for interstitial lung diseases. However, cough, bronchospasm and dyspnoea can occur during treatments with ribavirin. We wish to report a case of man with hepatitis C virus...
infection, who developed interstitial lung diseases during combined treatment with interferon and ribavirin.

**Case report**

A 50-year old man with chronic hepatitis C infection of unknown origin was referred for cough, dyspnoea and fever. He had recently quit smoke and denied any recent alcohol or drug consumption. He had no known pulmonary diseases and no history of respiratory infections.

In 1999, a diagnosis of HCV infection was established, based on routine analysis.

In 2003 the patient was paled on a combination therapy of pegylated interferon alpha once weekly and ribavirin 800 mg, for persistent inflammatory activity and HCV infection. After nine months into treatment initiation patient was referred for cough, dyspnoea and fever. The antiviral therapy was stopped.

At admission to the hospital in March 2004 a diffuse reticule-nodular shadow and bilateral interstitial infiltrates were present on the chest radiograph. Laboratory parameters at initial evaluation included: ASAT 118 U/L, ALAT 72 U/L. Pulmonary function tests showed a reduction in total lung capacity (TLC) and diffusion capacity to 4.67 l and 57 ml/mmHg/min. On High Resolution Computed Tomography (HRCT) there was bilateral patchy ground-glass shadowing, and an increase in density mainly involving the lower lobes was present. The HRCT also showed reticular inter and intralobular opacities. No honey-combing was present (Fig. 1). Fiberoptic bronchoscopy, bronchoalveolar lavage (BAL) and transbronchial biopsy were performed. BAL fluid showed numerous acute inflammatory cells and macrophages (Table 1). The transbronchial lung biopsy in the left lower lobe showed a desquamative interstitial pneumonia, and this confirmed by a video-assisted lung biopsy from the right lower lobe (Figs. 2 and 3). There was no evidence for interstitial fibrosis or granulomas.

The patient was started on prednisone 50 mg daily and the steroid dose was gradually tapered over 6 weeks until the last follow-up. After treatment with corticosteroid, chest HRCT findings and pulmonary function tests improved remarkably.

**Discussion**

Recently, several randomized controlled studies have shown that combination of ribavirin and IFN in chronic hepatitis C treatment is associated with significantly improved biochemical and virological response rates compared with IFN alone. Common side effects of interferon therapy include fatigue, flu-like symptoms, gastrointestinal disturbances, and neuropsychiatric symptoms, such as impaired memory, inability to concentrate, and confusion. Other less commonly described side effects are reversible alopecia, skin rashes, and thyroid dysfunction. Most of these side effects are associated with higher doses. The major side effects of ribavirin are dose-dependent haemolytic anaemia, cough, dyspnoea, rash, depression, and dyspepsia. No cases of interstitial pneumonitis caused by this drug have yet been described. Combination therapy augments the non-specific immune response. However, whether ribavirin was a synergistic cause of the development of interstitial pneumonitis in this patient remains theoretical. Published case reports of interferon and ribavirin related pulmonary toxicity during therapy for chronic hepatitis C are of interstitial pneumonitis, Bronchiolitis Obliterans Organizing Pneumonia (BOOP), pulmonary sarcoidosis, pleural effusion and exacerbation of asthma.3–5

Our case represent one of the first cases of DIP reported in the literature with combinated therapy. The toxicity occur within the first several weeks of therapy and the cases reported in literature were reversible in many instances simply by discontinuation of therapy.

It is possible that pulmonary toxicity after interferon and ribavirin therapy is more present than previously reported. A prompt investigation and interruption of therapy, if any

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**Table 1** Total cell count.

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<td>Eosinophils</td>
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**Figure 1** High-resolution CT scan of the upper lobes demonstrates ground-glass attenuation area.

**Figure 2** High-resolution CT scan demonstrates a mosaic pattern of lung attenuation; the abnormal regions are manifested as ground-glass attenuation (arrows).
sign of significant pulmonary involvement develop, are recommend.

**Conclusion**

In summary, the present case suggests that this diagnosis should be considered in patients on combination therapy who develop respiratory complaints. Until the mechanism for this effect is better understood and the roles of IFN-α and ribavirin determined, at present the most prudent course of action under these circumstances may be to stop both therapies.

**Conflict of interest statement**

The authors declare no financial and personal relationships with other people or organisations that could inappropriately influence this work.

**References**