

## Case Report

# A case of chronic hepatitis C patient of myocardial ischemia accompanied with interstitial pneumonia induced by pegylated interferon alpha-2a

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**Abstract:** After 3 months of combination treatment using interferon  $\alpha$ -2a and Ribavirin, a case of 59-year-old female patient with chronic viral hepatitis C demonstrated symptoms such as headache, dizziness accompanied by nausea, vomiting, dry cough, breathing difficulty, and shortness of breath. Dynamic electrocardiogram showed occasional atrial premature beats, paroxysmal tachycardia, and abnormal ST-T (T wave inversion and prolongation of the QT interval). Ambulatory blood pressure indicated that mean blood pressure was elevated than before. Myocardial radio-nuclide scan showed focal myocardial ischemia in left ventricular inferior wall. Pulmonary function tests showed that pulmonary diffusion function was decreased, indicating the possibility of interstitial pneumonia. The patient had no history of coronary heart disease or chest X-ray abnormalities before medication, but had hypertensive medical history for 8 years with good blood pressure control. After withdrawal of antiviral drugs, symptoms such as dry cough, breathing difficulty and T wave inversion were gradually relieved. This case indicated that myocardial ischemia and pulmonary lesions were associated with the application of pegylated interferon  $\alpha$ -2a.

**Keywords:** Pegylated interferon  $\alpha$ -2a, adverse drug reaction, myocardial ischemia, interstitial pneumonia, hepatitis C, chronic, toxic effect

### Introduction

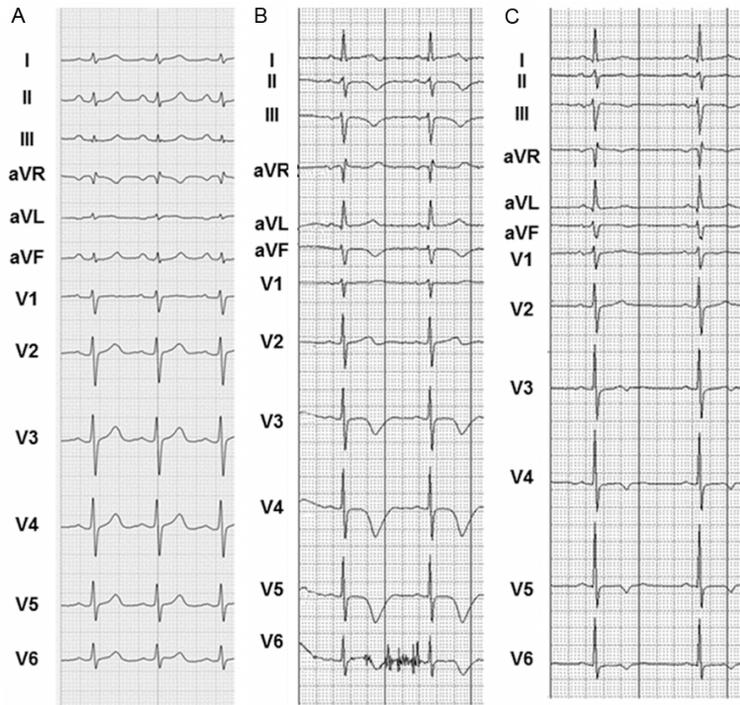
The combination of pegylated interferon with Ribavirin is the main treatment method for chronic hepatitis C, but it can cause serious adverse reactions, including retinopathy, neutropenia, anemia, abnormal thyroid function, thrombocytopenia, cardiac toxicity, pulmonary toxicity and psychiatric abnormalities [1-10]. However, serious adverse reactions that involve more than 2 organs are extremely rare. This article reports a case of chronic hepatitis C patient of myocardial ischemia associated with interstitial pneumonia, which was induced by the treatment with pegylated interferon  $\alpha$ -2a in combination with Ribavirin for 3 months.

### Case report

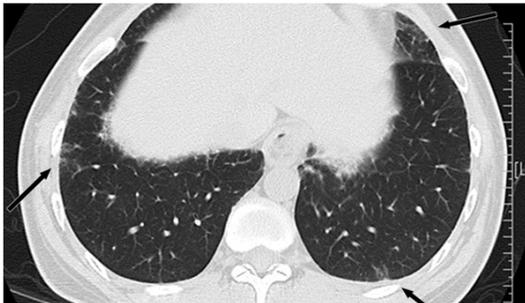
A 59-year-old female patient was hospitalized for the first time on 15 July 2013 because of chronic hepatitis C with high viral load and

recurrent liver function abnormalities. After admission, quantitative RNA examination showed that hepatitis C virus RNA ration was  $1.02 \times 10^7$  IU/mL. No abnormalities were found in total bilirubin, albumin, blood coagulation function, thyroid function, C-peptide and insulin secretion, and autoimmune hepatitis. The patient had no history of chronic diseases such as diabetes and coronary heart disease, or infectious diseases such as tuberculosis and typhoid. Since 20 July 2013, the patient started using pegylated interferon  $\alpha$ -2a (135  $\mu$ g qw, product name: Pegasys, Roche Pharmaceutical Ltd., Shanghai, China) plus ribavirin (0.3 g tid) antiviral therapy. After the first treatment, the patient felt a little muscle soreness but with stable medical condition. When interferon was injected for the fifth time, mild bone marrow suppression appeared, but did not affect the treatment. After the eleventh time of interferon injection, the patient developed headache, dizziness, nausea, and vomiting. On the next day,

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**Figure 1.** Electrocardiograms. A. Normal electrocardiogram obtained 1 month before interferon treatment. B. Electrocardiogram obtained after receiving 3 months of interferon treatment, showing marked T wave inversion in II, III, aVF and V<sub>3</sub>-V<sub>6</sub> leads. C. Electrocardiogram obtained 5 months after the withdrawal of interferon treatment, showing gradual improvement of T wave inversion in II, III, aVF and V<sub>3</sub>-V<sub>6</sub> leads.



**Figure 2.** Computed tomography of the chest on a patient with interferon-induced cardiovascular disease. The image was taken on day 7 after the withdrawal of interferon treatment. Arrows indicate peripheral predominant ground-glass opacity with mild reticulation in inferior lingular segment of upper lobe of left lung and the basal segments of lower lobes.

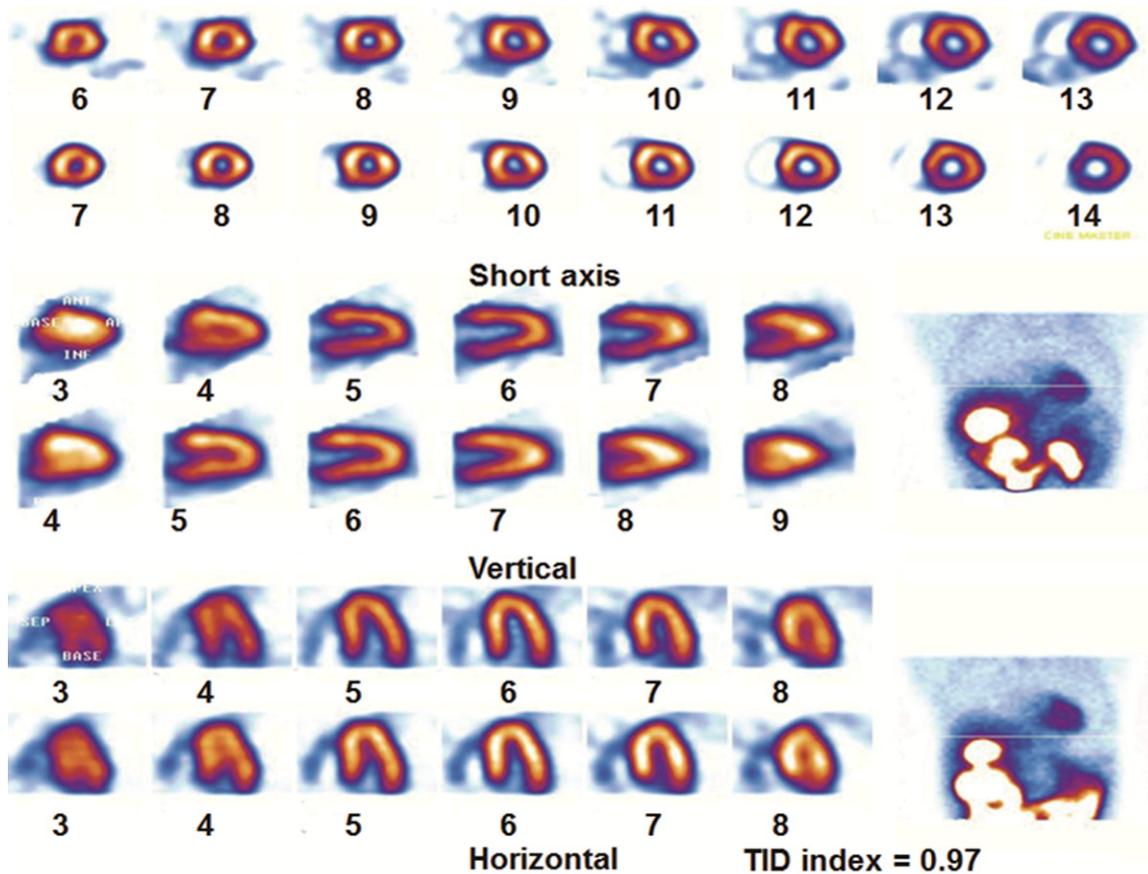
the blood pressure reached 150/100 mmHg. After adjusting medications, the blood pressure was controlled within 135-140/80-90 mmHg. After the fourteenth time of injection, the patient developed fluctuations in blood pressure, accompanied by polypnea, dyspnea,

occasional irritating cough, mild chest tightness and chest pain. Dynamic electrocardiogram showed sinus heart rate, sporadic atrial premature beat accompanied with paroxysmal tachycardia, and abnormal ST-T (T wave inversion and prolongation of QT interval) (**Figure 1**). The results indicated that the average blood pressure during 24 hours was increased to 134/87 mmHg and the mean blood pressures in the day and night were increased, which was possibly due to interferon-induced cardiovascular disease. Combined with the results of chest computed tomography (**Figure 2**), the patient was diagnosed as interstitial pneumonia.

Subsequently, pegylated interferon was temporarily suspended and the antihypertensive drug was changed into Irbesartan and Hydrochlorothiazide tablets (162.5 mg,

qd, po; product name: Yilunping). In addition, the patient was further treated with ketotifen (1 mg, bid, po), N-acetylcysteine (0.6 g, bid, po), and compound methoxyphenamine capsules (2 capsules, bid). Eight days later, quantitative RNA examination showed that hepatitis C virus RNA ration was  $3.8 \times 10^4$  IU/mL. Echocardiography showed moderate aortic calcification and regurgitation, as well as left ventricular diastolic dysfunction. Myocardial radionuclide scan showed mild focal myocardial ischemia on left ventricular inferior wall (**Figure 3**). These results suggested that pegylated interferon  $\alpha$ -2a induced cardiovascular diseases such as myocardial ischemia and increased blood pressure, as well as interstitial pneumonia. Twenty days after the discontinuation of interferon in the patient, the symptoms were relieved and T wave inversion was gradually improved. Meanwhile, the patient's condition tended to be stable. Six weeks after leaving the hospital, electrocardiogram examination showed improved T wave inversion before discharge. In addition, telephone follow-up confirmed that

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**Figure 3.** Myocardial radionuclide scanning image. Myocardial perfusion radionuclide scanning was performed 2 weeks after suspension of antiviral treatment regimen, showing mild focal myocardial ischemia on left ventricular inferior wall. The numbers represent frame numbers. “Short axis” images represent portions of the anterior, lateral, inferior, and septal walls; “Vertical” images are displayed from left to right, and from the septal edge to the lateral wall, representing the anterior wall, apex, and inferior wall; “Horizontal” images are displayed from left to right, and from inferior to superior, representing the septum, apex, and lateral walls. TID, transient ischemic dilation.

chest tightness did not appear and the blood pressure was under control for the patient.

### Discussion

Cardiac toxicity and pulmonary toxicity of interferon are rare. Literatures reported atrioventricular block and interstitial pneumonia [7-9], but the mechanism is not clear. Cardiac toxicity may be related to endothelial cell damage, immune complex overexpression and the interaction between tumor necrosis factor and interleukin [11]. Interstitial pneumonia can appear at any stage in the process of combined therapy of interferon and ribavirin for chronic hepatitis C. The mechanism may be related to interferon-induced lung-specific immune responses, increased endothelin-1 expression in pulmonary vascular smooth muscle, and enhanced

cellular expression of major histocompatibility antigens. This article reported that myocardial ischemia and pulmonary lesions were associated with the application of pegylated interferon  $\alpha$ -2a. Furthermore, the symptoms associated with interstitial pneumonia were gradually eased after withdrawal of the interferon and ribavirin combination therapy. However, due to the high mortality and poor prognosis, hormone therapy may be a more positive treatment method for severe patients [9].

Although interferon-induced myocardial ischemia and interstitial pneumonia are rare, they are still likely to develop into fatal dangers, if not diagnosed and treated in a timely and quick fashion. Therefore, before using interferon treatment, routine checks on blood routine, liver function and biochemistry, thyroid func-

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tion, abdominal ultrasound, electrocardiogram, chest X-ray, and mental status should be performed. In addition, echocardiography and cardiac function, and cardiovascular diseases such as hypertension and coronary heart disease should also be checked and screened. Importantly, regular electrocardiogram, heart function, and chest X-ray should be examined during the treatment, in order to assess changes in blood pressure, heart function and lung function according to the clinical symptoms.

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### Disclosure of conflict of interest

None.

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