Pericarditis due to interferon-α therapy during treatment for chronic hepatitis C

B. Gressens, P. Gohy

Service de médecine interne, Département de gastro-entérologie, Clinique Notre-Dame de Grâce, Gosselies.

Abstract

Pericarditis due to interferon alpha therapy during treatment for chronic hepatitis C. We report a patient with pericarditis during therapy with interferon alpha 2b for chronic hepatitis C viral infection. We review interferon alpha therapy and hepatitis C virus side-effects on the cardiovascular system. (Acta gastroenterol. belg., **2004**, 67, **301-302**).

Key words : Hepatitis C, interferon-α, pericarditis.

Introduction

For many years now, interferon-α therapy has been used in the treatment of hepatitis C. Acute pericarditis complicating interferon therapy has previously been described, either within the context of a lupus-like syndrome (1), or subsequent to the administration of a high dosage of interferon for the treatment of chronic myeloid leukaemia (2). We report a case of acute pericarditis, without clinical or biological signs of a lupus-like syndrome, during the treatment of hepatitis C infection, in which standard dosage levels of interferon-α 2b were used.

Case report

In 1983, a 28-year-old woman benefited from a blood transfusion following detachment of the placenta. In 1985, she was diagnosed with hepatitis C on the basis of a blood sample examination prior to a blood donation.

The patient was first seen in our institution in September 1998. The blood sample examination revealed aspartate-aminotransferases (ASAT) at three times the normal level, and alanine-aminotransferases (ALAT) at five times the normal level. The serology for the hepatitis C virus was found to be positive. In december 1998, the diagnosis of chronic hepatitis with portal activity (A2F1 according to the METAVIR scoring system) was histologically established following a transcutaneous hepatic biopsy. Other causes of chronic hepatopathy and HIV infection were excluded. A treatment on the basis of interferon alpha 2b (3 million units 3 times a week) and ribavirine (1200 mg per day) was started in February 1999. In March 1999, transaminase level had normalised.

In April 1999, a normo-chromic normocytic anaemia and neutropenia necessitated the ribavirine dosage level to be reduced by fifty percent before the administration of this drug was ceased due to aggravation of the anemia.

In May 1999 the patient consulted us exhibiting paraesthesia, lack of strength in the lower limbs, oedema in the lower limbs, grade II dyspnea, a dry cough and a weight increase of 4 kg.

The pulse was 96/min, the temperature was 36.2°C and respiratory rate was 16/min. The blood pressure was 100/70 mm Hg. Apart from the tachycardia, the cardiopulmonary examination was normal and the abdominal examination showed no abnormalities. Oedema was observed in the lower limbs reaching up as far as the middle of the thighs. A neurological examination revealed sensory difficulties of the lower limbs, osteotendinous reflexes were weak and symetrical.

An electrocardiogram showed aspecific repolarisation problems. Cardiac ultrasonography revealed a pericardial effusion without tamponade. An electromyography showed signs of po1yneuropathy.

The blood sample examination showed a minor inflammatory syndrome (CRP = 1.2 mg/dl, normal value 0-0.5 mg/dl)). The hepatic enzymology was normal but the HCV RNA (PCR) was still positive. Viral serologies (influenza, parainfluenza, EBV, CMV, coxsackie, adenovirus, rickettsia, borrelia, legionella), ASLO's and HIV read-outs proved negative. The anti-nuclear factor (ANF), the anti-DNAs, anti-histonic bodies and type II cryoglobulinemia proved negative. The remote viral serology checks remained unchanged at one and three month.

After discontinuation of interferon and acetylsalicylic acid had been initiated, the symptomatology disappeared and the pericardial effusion resolved within a matter of 15 days. In the same way, neurological improvement was achieved through the administration of vitamin B.

Discussion

We report the case of a 40-year-old female who developed acute pericardial effusion without tamponade during the remission stage of a course of treatment with interferon alpha 2b for chronic active hepatitis C viral infection.

Patrick Gohy, Clinique Notre-Dame de Grâce, Service de Médecine Interne, Chaussée de Nivelles 212, 6041 Gosselies.

The treatment with interferon alpha is associated with a well known range of secondary effects (3). The most common of these effects include influenza-like symptoms, headache, fatigue, fever, rigors, myalgia, thrombocytopenia and the induction of autoantibodies which are reported in over 30% of cases.

Reported with rarer frequency are polyneuropathy, paranoia and suicidal thoughts, diabetes mellitus, retinopathy, optical neuritis, diminution of hearing, seizures, loss of libido and cardiotoxicity (3). These complications are described both during the treatment of malignant illnesses as well as for the treatment of hepatitis C virus infection (1).

The cardiac toxicity of interferon alpha is also well known. With the dosage levels used in the treatment of hepatitis C, the secondary effects described include arrythmia (atrial fibrillation, sinus bradycardia, atrioventricular block), ischaemic cardiopathy and cardiomyopathy (4). In oncology, where the dosage levels are higher, interferon alpha has a wider cardiac toxicity and is responsible for ventricular fibrillation, myocardial infarctions, sudden death (4) and pericarditis (2).

The HCV itself is not devoid of a certain level of cardiotoxicity.Cases of hypertrophic cardiomyopathy, dilated cardiomyopathy and myocarditis can be directly attributed to the virus (5). The HCV is not known for being an aetiological agent of pericarditis (6). Nonetheless, one article reported a case of a pericarditis which occurred during the course of an infection with the hepatitis C virus. This was an infection by the hepatitis C virus associated with a type II cryoglobulinemia (7).

Chronic infection with the hepatitis C virus is sometimes associated with clinical and biological manifestation of auto-immune pathologies. Type II cryoglobulinemia, glomerulonephritis and thyroiditis are classically described. The association with Sjögren's syndrome, vasculitis, dermatomyositis, polyarthritis, thrombotic thrombocytopenic purpura, neuropathies, lymphomas, disseminated lupus erythematodes and other systemic auto-immune pathologies are less clear.

Boonen et al. reported a case of pericarditis during the treatment of chronic infection with HCV. This pericarditis emerged as part of a lupus-like syndrome, with clinical and biological manifestations of auto-immune pathologies (1).

The case of pericarditis which we are reporting, emerged in the course of the fourth month of remission during treatment with interferon alpha. At this stage, any effect from the HCV itself is quite unlikely, virus activity must have been low because the transaminases had normalised. The clinical and biological markers of autoimmune pathologies were absent (ANF, anti-DNA, antihistonic bodies and cryoglobulins).

We excluded other viral causes by the fact that serological tests and subsequent remote checks showed negative. We may therefore reasonably attribute the pericarditis to interferon-α, all the more so since the case was simultaneously complicated by a polyneuropathy of the lower limbs, a complication which has been imputed to the treatment with interferon. To the best of our knowledge, this is the first case of pericarditis without tamponade outside the context of a lupus-like syndrome, described during the treatment with interferon-α in classical dosage levels of an active chronic hepatitis C infection. Cases of pericarditis under treatment with interferon, with a dosage of 9 million units per day have already been described in hematology (2), but as far as we are aware never with a dosage level of 3 million units at a frequency of three times a week for chronic infection with HCV.

It would seem sensible to be mindful of this type of complication, all the more so as current protocols recommend an increase of interferon dosage levels. In light of this case, cardiac monitoring may be well-advised when using treatments based on interferon drugs for chronic HCV infections.

References

1. BOONEN A., STOCKBRUGGER R.W., VAN DER LINDEN S.J. Pericarditis after therapy with interferon-α for chronic hepatitis C. *Clin. Rheumatol.*, 1999, **18** : 177-179.
2. FAVA S., LUONI M., STIOUI S. Pericarditis during interferon-α therapy in chronic myelogenous leukemia. *Haematologica*, 1996, **81** : 484.
3. OEORG M., WALKER B. Hepatitis C virus infection. *N. Engl. J. Med.*, 2001, **345** : 41-52.
4. TERAGAWA H., HONDO T., AMANO H., HINO F., OHBAYASHI M. Adverse effects of interferon on the cardiovascular system in patients with chronic hepatitis C. *Jpn. Heart*, 1996, **37** : 905-15.
5. MATSUMORI A. Hepatitis C virus and cardiomyopathy. *Intern. Med.*, 2001, **40**: 78-9.
6. MEWAR S.H., SHAMSI S.N., ANJUR-KAPALI N., SPODICK D.H. Acute Pericarditis. Curr. Treat ; *Options Cardiovasc. Med.*, 1999, **1** : 73-77.
7. SUAREZ A., VALLINA E., NAVASCUES C.A., RODRIGUES M., OTERO L., SOTTORIO N.O. *et al.* Mixed type II cryoglobulinemia associated with chronic hepatitis C virus infection. *Rev. Clin. Esp.*, 1993, **192** : 325-26.