Reversible cardiomyopathy in a patient with hairy cell leukaemia

Gülsan Türköz Sucak, Rauf Haznedar, Ridvan Yalçın

A 64-year-old man presented with severe congestive heart failure. He was diagnosed to have hairy cell leukaemia a year ago and was receiving recombinant interferon alpha-2b injections of 5×10^6 million units, three times a week. He had responded with a partial improvement in his haematological condition with an improvement in his pancytopenia and 50% decrease in bone marrow infiltration with the hairy cells. After nine months of interferon treatment he was re-admitted to hospital due to severe congestive heart failure. He had suffered from mild hypertension for three years which was treated with amlodipine and a splenectomy had been performed just before interferon treatment commenced. He did not consume alcohol and did not take any other cardiodepressant agent. He denied a family history of cardiac disease and a viral prodrome. He had no existing cardiac complaints when he was evaluated before interferon treatment, his electrocardiogram (ECG) showed systolic strain pattern, telecardiogram was normal, the echocardiogram was also normal except for the sclerotic aortic valve, which did not cause a gradient across the valve.

He tolerated the interferon treatment very well with only a partial response, until he developed congestive heart failure after nine months. There was no electrolyte disturbance nor any dietary deficiency. Serially monitored cardiac enzymes were normal, myocarditis was excluded, both clinically and by negative viral studies. His physical examination revealed a pulse rate of 120 beats/min, bibasilar rales and a summation gallop. His chest X-ray, which had been normal, had an enlarged and globular cardiac silhouette and pulmonary congestion with bilateral pleural effusion, shown to be transudate. The ECG was unchanged except for sinus tachycardia. Although there were neither clinical nor laboratory signs suggesting ischaemia, a coronary angiogram was performed which revealed normal coronary arteries. Echocardiography demonstrated severe global hypokinesia with second degree mitral and aortic valve insufficiency and an ejection fraction of 24%. Interferon was discontinued and the patient received furosemide, digoxin and spironolactone for two weeks. He responded with a rapid improvement in his clinical condition. When he was re-evaluated echocardiographically a month later, two weeks after all his cardiac treatments were stopped, his global hypokinesia was significantly improved with no mitral and tricuspid insufficiency, near normal atrial and ventricular dimensions and an ejection fraction of 46%.

Question

What was the cause of the cardiac failure?

**Gazi University
Medical School,
Ankara, Turkey
Department of
Hematology**
G T Sucak
R Haznedar
**Department of
Cardiology**
R Yalçın

Correspondence to Dr GT
Sucak, Kader sok 4/5 06700
Gaziosmanpasa, Ankara,
Turkey

Accepted 24 October 1997

Answer

The patient was diagnosed to have interferon-related cardiomyopathy which resolved rapidly after interferon was stopped. He was switched to 2-chlorodeoxyadenosine (2-CDA) treatment for his hairy cell leukaemia, which he tolerated very well. Three months after commencing 2-CDA treatment, he was found to be in complete haematological remission. His physical examination was completely normal with an ejection fraction of 65% on his echocardiogram.

Discussion

Interferon alpha is still a useful treatment for hairy cell leukaemia. The side-effects of interferon, most commonly flu-like syndrome, fatigue, bone marrow suppression, elevated liver enzymes, gastrointestinal discomfort and neurologic symptoms, are usually mild and dose-dependent. Cardiovascular toxicity, although not frequent, has been reported in clinical trials and was the reason for the interruption of the French interferon trial¹; it has been reported in 1–3% of patients.^{2,3} Supraventricular tachyarrhythmias, hypotension, manifestations of ischaemic heart disease, and cardiomyopathy are the main cardiovascular complications of interferon. The first patient reported to develop cardiomyopathy after one week of interferon treatment and confirmed at autopsy was reported in 1988 by Cohen *et al.*⁴ Another patient with hairy cell leukaemia developed interferon-induced cardiomyopathy after six months of treatment, and improved rapidly after cessation of treatment.⁵

The patient presented here was carefully evaluated with respect to other possible causes of depressed cardiac function such as concurrent use of cardiodepressant agents, infection, myocardial ischaemia, and other heart disease, and all were excluded. Interferon seemed to be the most likely aetiological factor and was withdrawn immediately. Fortunately, similar to

reports in the literature, his condition was reversible after the cessation of interferon treatment and his cardiac condition improved dramatically, even after digitalis and diuretics were discontinued.

In a review of 44 patients with interferon cardiotoxicity, five of the 44 patients were reported to have interferon-induced cardiomyopathy.³ It is reported that cardiac effects were not related to daily dose, cumulative total dose, or duration of therapy. Previous coronary heart disease and previous cardiotoxic drug treatment were reported to be risk factors for development of other cardiac toxicities, such as ischaemia and arrhythmia. However it is interesting that none of the five patients who developed cardiomyopathy had known previous heart disease. Fortunately, in almost all reported cases of interferon-induced cardiomyopathy, the condition was reversible with the cessation of interferon treatment.³ Interferon-related cardiotoxicity is reported to be more prominent in patients with AIDS and with co-treatment with IL-2.^{6,7}

The cause and mechanism of interferon-induced cardiomyopathy is still obscure. Autoimmune mechanisms, inflammatory reaction and impaired myocyte metabolism are claimed to be the aetiological factors.⁴ Since interferons are still widely used in the treatment of hairy cell leukaemia, which is a late adulthood disease, the potential cardiotoxic effects of this drug should be kept in mind. The cardiologic condition of patients receiving interferon should be carefully monitored. 2-Chlorodeoxyadenosine may be a preferable treatment for hairy cell leukaemia patients with previous cardiac conditions.

Final diagnosis

Interferon-induced cardiomyopathy in a patient with hairy cell leukaemia.

Keywords: interferon-induced cardiomyopathy; hairy cell leukaemia

1 Dickson D. Death halts interferon trials in France. *Am J Med* 1988;85:549–50.

2 Jones GJ, Itri LM. Safety and tolerance of recombinant interferon alfa-2a in cancer patients. *Cancer* 1986;57:1709–15.

3 Sonnenblick M, Rosin A. Cardiotoxicity of interferon. A review of 44 cases. *Chest* 1991;99:557–61.

4 Cohen MC, Huberman MS, Nesto RW. Recombinant alpha-2 interferon related cardiomyopathy. *Am J Med* 1988;85:549–51.

5 Sonnenblick M, Roosenmann D, Rosin A. Reversible cardiomyopathy induced by interferon. *BMJ* 1990;300:1174–5.

6 Kruit WH, Punt KJ, Goey H, *et al.* Cardiotoxicity as a dose limiting factor in a schedule of high dose bolus therapy with interleukin-2 and alpha interferon. *Cancer* 1994;74:2850–6.

7 Deyton LR, Walker RE, Kovacs JA, *et al.* Reversible cardiac dysfunction associated with interferon alfa therapy in AIDS patients with Kaposi's sarcoma. *N Engl J Med* 1989;321:1246–9.