Case Report

Severe muscle weakness during treatment with pegylated interferon alfa for chronic hepatitis C virus infection; A rare complication

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Abstract

Background: *Interferons (IFNs) are common therapeutics for several diseases such as viral hepatitis, multiple sclerosis and malignancy. A variety of autoimmune related side effects have been observed during IFN therapy. Rare cases of myopathy, polymyositis or dermatomyositis have been reported during therapy with high doses of IFNα.*

Case Presentation: *In this report, we describe a case with severe muscle weakness but near normal muscles' enzymes during treatment of chronic hepatic C infection with pegylated IFN α 2a in a patient with major beta thalassemia*

Conclusion: *This report suggests that severe weakness with normal muscles' enzymes may occur during IFN therapy.*

Key words: *Interferon, Muscle Weakness, Pegylated Interferon, Myopathy..*

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Interferons (IFNs) are a family of proteins secreted from cells in response to various stimuli such as viral infection, double-stranded RNA, antigens and other low molecular weight agents(1). It has been more than 50 years since the discovery of IFN as an endogenously produced substance with potent antiviral properties (2). The first IFN used in clinical medicine was IFNα, introduced in 1986 for treatment of hairy cell leukemia. Today, IFNs are used for viral hepatitis B and C, Kaposi sarcoma, Behcet disease, chronic myelogenous leukemia, multiple myeloma, multiple sclerosis, and carcinoid syndrome (3).

With the increased use of IFN, many autoimmune side effects have been reported (4). Hypothyroidism, thyrotoxicosis and systemic lupus erythematosus (SLE) are examples of autoimmune disorders associated with IFNα treatment (5). Myalgia is a common side effect during the treatment for chronic hepatitis C with IFNα or pegylated IFNα, alone or combined with ribavirin, and occurs in 35–55% of cases. It is generally considered to be mild, does not induce and rise in Creatinin Kinase, (CK) and does not usually require dose modification (6). However, the rare cases of myositis, polymyositis or dermatomyositis have been reported during therapy with high doses of IFNα that usually after the discontinuation of interferon, the muscular weakness gradually is recovered with or without immunosuppressive treatment (1, 4 -15). We describe here an unusual occurrence of myopathy during treatment with pegylated IFNα in a patient with hepatitis C infection.

Case history

A 20 year old thalassemic patient was admitted to our department due to progressive muscle weakness for a month. She was diagnosed of hepatitis C virus infection (genotype 3a, viral loud of 104000 copies/ml) due to blood transfusion and thus, pegylated interferon 2a with a dosage of 180 µg once a week was administered. Three months later, HCV RNA was undetectable and the drug continued until the muscle weakness developed.

Muscle weakness was severe and progressive in proximal of her upper and lower extremities and neck. She could not walk unaided, rise from a chair and abducte from arms against gravity. She did not have any ophthalmic problem or dysphagia and did not experience any muscle weakness or pain prior to the IFN therapy. She was a single child of an unsanginous couple. There was not any similar problem in her family.

The physical examination did not show any rash, icter or lymphadenopathy, neurological deficit in cranial nerves or sensation, but the patient was pale and the proximal muscles strength were 2-3/5. Distal forces were normal.

Laboratory findings included:

Hemoglobin=9.8 mg/dl, ESR=50 mm/h,

AST=39 IU/l, ALT=64 IU/l

CK=39U/l, LDH=223U/l, Aldolase=0.7

ANA=1/80, Anti ds DNA=14.4

Anti Jo-1=5U/ml

At that time thyroid function tests were normal, and HIV antibody, HBc Ab, HBs Ag, HCV RT-PCR all were negative. HCV Ab was positive. Electromyography showed spontaneous high frequency discharges with increased insertional activity in proximal muscles of upper and lower limbs. Biopsy from quadriceps muscle was done and there was not any dystrophic lesion. A diagnosis of myopathy secondary to PEG-IFN was made but two weeks after drug discontinuation, she still suffered from severe weakness. Thus, treatment with corticosteroid (prednisolone 1 mg/ kg) was started and one week later she had an improvement in subjective symptoms and after two weeks the patient could walk without any problems. One month later, we started the tapering of prednisolone and she remained well after the steroid discontinuation.

Discussion

In this report, we describe a patient with HCV infection treated with pegylated IFNα- 2b who developed severe myopathy. An association between autoimmune disorders and IFN has been reported. The mechanism by which interferon triggers autoimmunity is probably related to the over expression of MHC class 1, 2 molecules, production of pathogenic antibodies, and over expression of bcl-2 oncoprotein (12). There are some reports about HCV-associated myopathy in the medical literature, that some of them myopathy developed after initiation of IFN therapy for chronic HCV hepatitis (16-17).

In this article, we describe a patient with HCV infection treated with pegylated IFNα-2b (180μg) intramuscularly once a week who developed severe myopathy. The interval between the onset of IFNα therapy and the occurrence of myopathy was 11 months. This is to keep with the variable onset of myopathy described in the literature in patients receiving IFN therapy ranging from weeks to years (Table 1).

Although HCV itself might cause myopathy, it is unlikely that this patient's myopathy was virus related, because she had no muscular symptoms in the initial phase of viral infection and myopathy developed after starting IFN treatment at the time when HCV RNA was undetectable and this has been demonstrated that HCV RNA is undetectable 6 months after treatment with IFNα-2b up to 98% (18). Furthermore, when IFN had been withdrawn and prednisolone instituted, there was a rapid improvement of subjective symptoms and muscle strength.

Our patient was different from the other reported cases because of near normal muscle enzymes except for a little increase in AST and ALT, but EMG showed typical changes due to myopathy. Elevated ALT and AST may be due to IFN induced myopathy in treated patients when HCV was undetectable (19). This report suggests that severe weakness with normal muscles′ enzymes may occur during IFN therapy.

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Table 1. Examples of IFN related myopathy

Author,year and reference No.	Age and sex of patients	Disease	Type of IFN	Dose of IFN	Duration of treatment	Type of myopathy/ myositis	Management	Response
Matsuya, et al, 1994. (4)	54 M	Renal cell carcinoma, HCV infection	IFNγ, IFNα	4×10^6 $3/15\times10^6$ IU/w	12 weeks	Polymyositis	IFN discontinuation only	improvement
Arai, et al, 1995. *(8)		HCV infection	IFNα			Myopathy		
Iguchi, 1996. (7)	62 F	HCV infection	IFNβ	$2/52\times10^8$ IU/w	2 months	Polymyositis	prednisolone	Improvement after 2 months
Falcone, et al,1998.(9)	26 M	Chronic myeloid leukemia	IFNα	9×10^6 Iu, daily	23 months	Polymyositis	Methyl prednisolone and plasma exchange	Improvement after 12 months
Kalkner, et al, 1998. (5)	69 F	Multiple endocrine neoplasia	IFNα	3×10^6 IU/w	6 months	Polymyositis	Prednisolone and cyclophosphamid	Improvement after 2 years
Cirigliano, et al, 1999. (10)	48 F	Malignant melanoma	IFNα	3×10^6 IU/w	8 months	Polymyositis	Methyl prednisolone	Improvement after 1 month
Schleinitz, et al, 1999. (11)	65 M	B cell lymphoma	IFNα	3×10^6 IU/w	2 years	Polymyositis	prednisolone	Rapidly improved
Dietrich, et al, 2000. (1)	57 F	Melanoma	IFNα	16×10^6 Iu 3 times a week	6.5 weeks	Dermatomyositis	Dexamethasone and Methotraxate	Improvement after 12 months
Won lee, 2002. (12)	33 M	HBV infection	IFNα	5×10^6 Iu 3 times a week	6 weeks	Polymyositis and cardiomyopathy	Prednisolone and IVIG	Improvement after 10 months
Golestein,et al ,2004.(6)	33 M	HCV infection	Pegylated IFNα	12 kilo Dalton weekly	14 weeks	myopathy	Reduce dose of IFN	Improvement after 2 months
Venezia, et al, 2005. (13)	51 M	HCV infection	Pegylated IFNα	80 µg/week	8 months	Polymyositis	Prednisolone	Improvement after 3 months
Anil john, et al ,2007. (14)	50 F	HCV infection	Pegylated IFNα	180 µg/w	2 months	Polymyositis	Prednisolone	Improvement after 2 weeks
Somani, et al, 2008. (15)	57 M	Multiple sclerosis	IFNβ	6×10^6 IU/w	5 years	Dermatomyositis	Prednisolone , IVIG and methotraxate	Improvement after 1 month

* Other datas is not available.