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

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 IFNa.

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...


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 IFNa, 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 IFNa treatment (5). Myalgia is a common side effect during the treatment for chronic hepatitis C with IFNa or pegylated IFNs, 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 IFNa 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 IFNa 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 load 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 abduct 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 unsanguinous 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 no 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 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.

**References**


### Table 1. Examples of IFN related myopathy

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

* Other data is not available.