

A Case of Polymyositis with Dilated Cardiomyopathy Associated with Interferon α Treatment for Hepatitis B

Polymyositis is a rare complication of interferon α treatment as a result of immunomodulating role of the drug itself. In this case, interferon α induced polymyositis and cardiomyopathy is diagnosed in a 33-yr-old male patient with history of chronic hepatitis B. To treat hepatitis B, interferon α was administered until the proximal muscle weakness developed. Thereafter, sixteen cycles of immunoglobulin treatment (400 mg/kg) along with corticosteroids were instituted and led to an improvement in subjective symptoms with decreases in level of CPK and LDH. However, dilated cardiomyopathy has not improved in spite of the cessation of interferon treatment. Unlike the persistently elevated serum HBV DNA level, the serum ALT and AST levels have gradually decreased. Our case shows that clinical symptoms of polymyositis improved with steroid and immunoglobulin treatment without deterioration of the hepatitis B. To our knowledge, this is the first case of polymyositis associated with dilated cardiomyopathy after the administration of interferon in a patient with hepatitis B.

Key Words : Polymyositis; Cardiomyopathy, Congestive; Interferon- α ; Hepatitis B

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INTRODUCTION

Polymyositis is an inflammatory muscle disease characterized clinically by proximal muscle weakness and histologically by chronic inflammation of the affected muscles. It has already been well documented that interferon α due to its ability to modulate immunity, can induce or exacerbate autoimmune disease (1). We report a case of a 33-yr-old male patient with chronic hepatitis B who developed polymyositis and dilated cardiomyopathy associated with interferon α therapy.

CASE

This 33 yr-old male patient visited our department due to proximal muscle weakness. He has been complaining of easy fatigability and was diagnosed of hepatitis B at other hospital before visiting our department. His mother and 5 siblings were all positive for hepatitis B virus. To treat hepatitis B, interferon α with a dosage of 5×10^6 units was commenced three times per week for six weeks until the proximal muscle weakness developed. He did not experience any muscle weakness or pain prior to the interferon α treatment. Laboratory studies revealed initial CPK and LDH levels of 11,620 U/L and 647 U/L, respectively. Initial serum ALT and AST levels were 180 IU/mL and 79 IU/mL, respectively. Autoantibodies such as anti-DNA (Crithidia luciliae immun-

ofluorescence test), anti-nRNP, and anti-Jo-1 were all negative. Viral markers were as follows, hepatitis Bs Ag/Ab (+/-), hepatitis Be Ag/Ab (+/-), hepatitis Bc Ab (-), HBV-DNA (positive: 7,300 pg/mL), which collectively suggested hep-

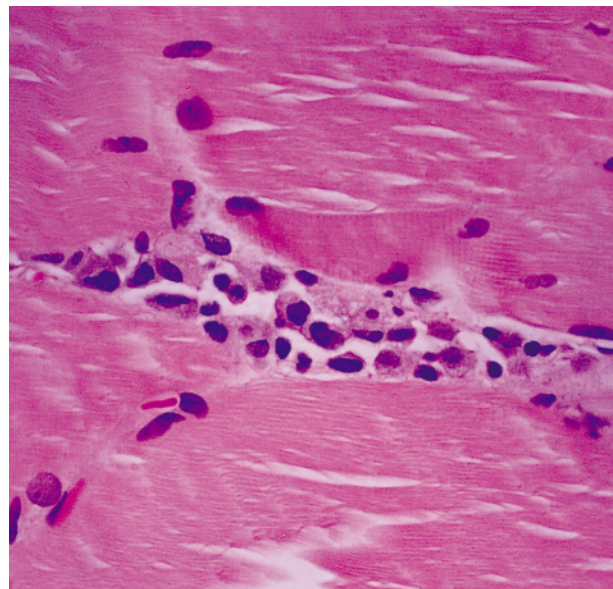


Fig. 1. Intrafascicular (endomyosial) infiltration of mononuclear inflammatory cells is shown, which is a characteristic finding of inflammatory myopathy (H&E, \times 400).

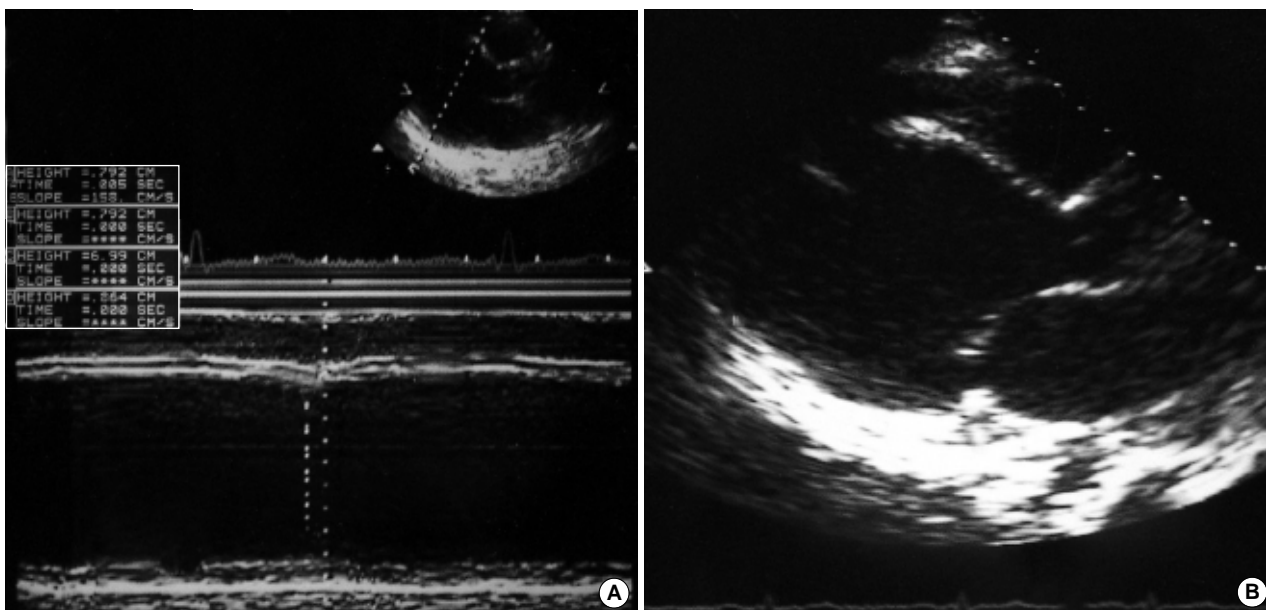


Fig. 2. A: M-mode echocardiography showing dilated left ventricular wall with decreased left ventricular wall motion. B: Parasternal long axis view showing dilated left ventricle, which corresponds to M mode findings.

atitis B in active replicative state. The muscle biopsy was done and revealed scattered degeneration of muscle fibers and regenerating basophilic fibers at stage of regeneration. In addition, there was focal intrafascicular infiltration of mononuclear inflammatory cells (Fig. 1). These histopathologic findings were compatible with those of idiopathic inflammatory myopathy. Unlike the earlier chest radiography, which were normal, cardiomegaly was noted on the following chest radiography. Echocardiography was performed and showed decreased left ventricular systolic function with an ejection fraction of 37%, as well as dilated left ventricle with decreased wall motion of entire left ventricle (Fig. 2). He received multiple administrations of interferon α treatment before polymyositis has developed, and despite well-documented report that corticosteroid is the mainstay for treating polymyositis, 6 cycles of monthly-based immunoglobulin treatment (400 mg/kg) were tried, without effect. Azathioprine (100 mg) and cyclosporin (300 mg), which were administered for four months after the cessation of immunoglobulin treatment, resulted in no improvement. Thereafter, additional 10 cycles of monthly-based immunoglobulin treatment (400 mg/kg) with prednisolone (1 mg/kg) were instituted which made CPK and LDH gradually decreased to 1,412 U/L and 373 U/L, respectively. These responses seemed to be temporary rather than permanent. At present, the serum CPK and LDH levels have further decreased but still high despite the continued treatment and the gradual improvement of muscular weakness. Regarding the hepatitis B, serum ALT and AST have decreased to 78 IU/mL and 38 IU/mL, respectively. However, HBV DNA level is 11,300 pg/mL, indicating active replication of Hepatitis B virus. In addition, the dilated

cardiomyopathy with decreased cardiac output has slowly worsened since the first blow-out of the disease.

DISCUSSION

Interferons are proteins produced by the cells as a defensive response to virus and are important modulators of the immune response. They are well-documented to be effective in treating HBV infection by improving viral titers and liver enzyme elevations. However, interferons can cause wide range of side effects from the very common flu-like symptoms to more severe psychiatric, hematologic and pulmonary effects that limit the tolerable dose, and appear to be closely involved in many aspects of the pathogenesis of autoimmunity (1-5) such as overexpression of MHC class I, II molecules, production of pathogenic antibodies, and overexpression of bcl-2 oncoprotein. However, the exact mechanisms whereby interferon contributes to the development of autoimmune disease are at the moment unclear (6, 7). A few cases of polymyositis associated with interferon therapy have been described in the literature, and showed that after the discontinuation of interferon, the muscular weakness gradually recovered with or without immunosuppressive treatment (8, 9). In addition, cardiotoxicity of interferon has been well-documented including cardiac arrhythmia, dilated cardiomyopathy, and ischemic heart disease as common presentations. Usually, these cardiac manifestations were reversible following the cessation of the interferon therapy (10).

Although hepatitis B virus itself can cause polymyositis (11-13), it is unlikely that the polymyositis in this patient

was virus-related in terms of time-sequence: the patient himself had been free of any muscle-related symptoms despite long history of hepatitis B and the polymyositis developed after the use of interferon α .

The patient did not recover from polymyositis after the withdrawal of the interferon α . In addition, the immunoglobulin treatment alone failed to bring improvement in the polymyositis, which responded only to the high dose of steroid along with the immunoglobulin. Although steroid is the treatment of choice for polymyositis, immunoglobulin was chosen for initial treatment due to the concerns that the steroid might adversely affect the replicative activity of hepatitis B virus (14). In this patient, steroid as well as azathioprine and cyclosporin was administered. Although potential for symptomatic and virologic improvement was needed to be balanced with that for the adverse effects on proliferation of the virus, the immunosuppressive treatment was inevitable since multiple cycles of sole immunoglobulin had failed. As the patient worried about changes in appearance, azathioprine and cyclosporin were chosen instead of corticosteroids, which is the treatment of choice for polymyositis. After the administration of steroid, active replication of hepatitis B virus was noticed but did not lead to any sign of further hepatic damage. Unlike usual cases, dilated cardiomyopathy gradually aggravated in spite of the cessation of interferon treatment. Given that cardiomyopathy developed after the interferon α treatment, it is highly probable that the cardiomyopathy in this patient was due to the interferon-induced polymyositis cardiotoxicity rather than the virus itself. In addition, weight gain, which is assumed to be partly due to the steroid, might have had potential detrimental influence on the cardiac function.

To our knowledge, this is the first case of polymyositis associated with dilated cardiomyopathy after the administration of interferon in a patient with hepatitis B.

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