Proximal Myopathy in Interferon Based Therapy

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ABSTRACT

Interferon based antiviral therapy is known to have many side effects, the commonest being myalgia, fever and psychiatric problems, while the rare ones include myositis and visual changes. We report a case of a patient with chronic hepatitis C who was started on pegylated interferon and ribavirin. After four months of antiviral therapy, treatment was stopped because the patient developed proximal myopathy that lead to severe functional disability. All possible causes of proximal myopathy were excluded. After three months of stopping the treatment, a gradual improvement was noted.

Keywords: Proximal Myopathy; Interferon Therapy; Hepatitis C

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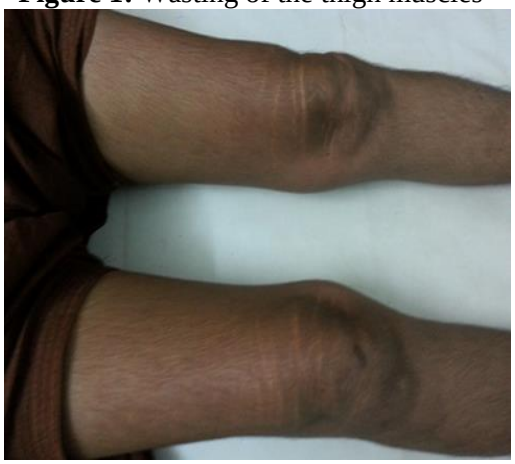
INTRODUCTION

Interferon introduction in the second last decade of previous century started a new chapter in the treatment of chronic hepatitis C [1], though there was still a question of poor sustained viral response (SVR) and a long list of side effects. With the addition of ribavirin, response rate got better from 5 to 50% [2-4], but there was further addition of some more side effects. With pegylated interferon based therapy, SVR further improved but without shortening of the list. Protease inhibitors oral antiviral drugs i.e. teleprevir and boseprevir increased the SVR in genotype 1 up to 70%, but there was problem of pruritus and rash. There was still a dire need of a therapy that was more effective with fewer side effects. Sofosbuvir recently has revolutionized the hepatitis C treatment. Out of the many interferon related side effects like fever, flu-like symptoms, myalgia, and depression, very few cases of proximal myopathy have been reported before, especially when there is no interferon induced associated conditions like thyroid dysfunction. This case drew special attention with development of severe proximal myopathy within few weeks without any clue of concrete diagnosis.

CASE REPORT

A young lady in her thirties came with inability to stand from sitting position and holding things over her head for the last one week. She was absolutely fine a year back when she developed aches and pains. There was no history of morning stiffness in the limb girdle or neck, weight loss, proximal pain at rest or during movement and tenderness of the muscles. She was not on any medication like steroids or drugs known to cause proximal myopathy. Clinical examination was unremarkable. Investigation carried out revealed normal blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein, serum albumin, prothrombin time, international normalized ratio (INR), renal functions, blood sugar levels, urine examination and chest X-ray. Liver functions showed ALT 65u/L but bilirubin and alkaline phosphatase were normal. On hepatology viral screening, she had positive anti-hepatitis C viral (HCV) antibodies. Hepatitis B surface Ag (HBsAg) and hepatitis D viral antibodies were negative. HCV ribonucleic acid by polymerase chain reaction (PCR) showed high grade viremia. Abdominal ultrasound was normal. She was counseled about the treatment plan and the possible side effects. She was put on pegylated interferon and weight based ribavirin. Her treatment was going smoothly and she achieved a rapid viral response (RVR). After three months of treatment, she developed weakness of proximal muscles of limbs that aggravated further in couple of weeks and she was unable to get up without support. On examination she had wasted thigh muscles (Figure 1) and severe functionally disability to stand without support. There was no rash over the face or any part of the body. Because of rapid deterioration, her anti-viral therapy had to be stopped at the end of 4 months. She was investigated further. Her thyroid profile, connective tissues screening like anti-nuclear antibodies (ANA), rheumatoid arthritis

Figure 1: Wasting of the thigh muscles



factor (RA factor), muscle enzymes including creatinine kinase, aldolase were normal. Urine for myoglobinuria was negative. Nerve conduction studies were normal. Electromyographic (EMG) studies showed early recruitment pattern along with enhanced interference pattern. It also showed low amplitude short duration, polyphasic motor unit action potential, suggestive of myopathy. She refused to have muscle biopsy. She was given a trial of steroids for four weeks but she did not show any improvement so it was stopped. However, it was noted that after three months of discontinuing antiviral therapy and physiotherapy, she started improving. Now she manages to get up with some difficulty.

DISCUSSION

Interferon has immune modulatory effect. Most of the side effects are autoimmune mediated, the commonest being fatigue, headache, myalgia, fever, arthralgia, nausea, anorexia, diarrhea, depression, insomnia, irritability, pruritus, rash and alopecia. Less common side effects include neutropenia, thrombocytopenia and anemia [2-4]. Ribavirin causes hemolytic anemia and has teratogenicity. Polymyositis is a condition in which patient develops proximal muscle weakness in the limb, neck and trunk muscles. A very few cases have been reported regarding patients who developed polymyositis during interferon therapy [5, 6]. In a case report, inclusion body myositis was diagnosed on muscle biopsy and the patient had markedly raised muscle enzymes. He improved with a course of steroids but relapsed after one year [7]. In another condition, interferon leading to hypothyroid myopathy was highlighted [8]. Osteomalacia can lead to proximal myopathy in her BMI was 21 and adequate sunlight exposure as per history. Her serum calcium, albumin and magnesium levels were normal and there were no pseudofractures on long bone X-rays. She had normal muscle enzymes i.e., serum creatinine kinase and aldolase levels and thyroid profile. She was negative for anti-thyroid antibodies, ANA and RA factor. She was given a trial of steroids with no response, pointing to some different type of drug-induced myopathy. Limitation in this case was the inability to perform muscle biopsy because the patient did not agree for it. However, clinically she had weakness and obvious wasting of the proximal muscles of the limbs. Severe functional disability due to proximal muscles weakness, and EMG pattern clearly pointed to myopathy. She gradually improved after discontinuation of the antiviral therapy, which indicates this to be a reversible side effect of the interferon based therapy. This type of reversibility has been reported before in a case report [10]. In another patient of chronic hepatitis C genotype 1 who was treated with pegylated interferon developed severe polymyositis and dermatomyositis. Treatment had to stop and the patient was treated with glucocorticoid along with intravenous immunoglobulin and tacrolimus without hepatitis C viral reactivation [11]. Interferon induced myositis was also reported by John A et al [12]. Interferon, both conventional and pegylated, are still in wide use world-wide and more cases are expected in the next few years. However, the introduction of oral antiviral therapy i.e. sofosbuvir that has pan-genotypic effect, turned the direction of treatment of hepatitis C with high SVR in naïve, relapsed and in non-responders [13-15] without side effects associated with interferon.

CONCLUSION

Interferon based therapy is very effective but there are a lot of reservations due to its side effects. A lot of these effects have already been reported, while uncommon side effects like proximal myopathy and myositis are still emerging. While treating the patients, physicians must be aware of these types of rare side effects.

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