A case of vacuolar myopathy during the course of chronic hepatitis C

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Summary

Several cases of inflammatory myopathy have been reported during the chronic course of hepatitis C (HC) in recent years. It has been suggested that this muscular inflammatory involvement in HC is related to an immune-mediated mechanism caused by the hepatitis C virus (HCV), as HCV RNA has been detected in the muscle of patients with concomitant inflammatory myopathy and chronic HC.

Herein, we report on a patient with a history of chronic HC, who developed a slowly progressive proximal muscle weakness; muscle biopsy revealed a vacuolar myopathy. Histological, immunohistochemical and biochemical study did not disclose any known cause of vacuolar myopathy.

To our knowledge, this is the first report of a vacuolar myopathy during the course of HC. We suggest that it may be opportune to include HC among the possible aetiologies of vacuolar myopathy, should other reports confirm this association.

KEY WORDS: chronic hepatitis, hepatitis C virus, vacuolar myopathy.

Introduction

Hepatitis C (HC) virus infection is one of the most common, and also under-diagnosed, bloodborne illnesses. Up to 3% of the world’s population is infected with the HC virus (HCV) and of those exposed to HCV, 80% become chronically infected and at least 30% of carriers develop chronic liver disease, including cirrhosis and hepatocellular carcinoma (1,2).

Extrahepatic manifestations of HCV infection are usually both organ-specific (thyroiditis, diabetes) and systemic autoimmune diseases, and haematological processes (such as cytopenias and lymphoproliferative disorders) (3).

The association between HCV infection and myopathy is, however, uncommon. In recent years, several cases of inflammatory myopathy, such as myositis (4-9) and inclusion body myositis (11-13), have been reported during the course of chronic HC.

The most probable underlying pathogenetic mechanism is an immune-mediated reaction triggered by the HCV (9); indeed, in some infected patients with concomitant inflammatory myopathy, HCV RNA has been isolated in infiltrating cells but not in muscle fibres (9).

In the present study, we report on a patient who developed muscle weakness during the course of chronic hepatitis C (CHC). Diagnostic investigations revealed a vacuolar myopathy.

Case report

A 46-year-old man with a ten-year clinical history of CHC presented with four-limb proximal muscle weakness and hyperCKaemia (1000 U/L) that had progressively worsened over the past two years. The patient denied alcohol abuse or use of glycyrrhizin-containing agents; one year before his admission to our department he had started interferon (IFN) α2A (3,000,000 U, 3 times daily) and ribavirine treatment.

Neurological examination revealed muscle weakness [4/5 on the Medical Research Council (MRC) rating scale] and wasting of both shoulder and pelvic girdles; deep tendon reflexes were normal. Coordination and all sensory modalities were preserved.

Serum creatine kinase concentration was mildly raised (570 U/L; normal value: <190). Other laboratory investigations were normal.

The electromyography revealed a myopathic pattern of the four limbs. Motor and sensory conduction studies were normal.

A muscle biopsy of the right deltoid showed an increased size variability, fibre splitting, and the presence of internal nuclei; several fibres (8%) contained...
Vacuoles (Fig. 1). Vacuoles were mostly observed in type I fibres and were unreactive for acid phosphatase; some of them showed glycogen storage. In addition, histochemical stains using Oil red O excluded lipid storage.

Biochemical analysis on muscle homogenate revealed normal enzymatic activities of glucose 6-phosphate dehydrogenase, phosphoglucoisomerase, phosphoglucomutase, phosphofructokinase, aldolase, phosphoglyceromutase, enolase, pyruvate kinase, lactate dehydrogenase, myophosphorylase, phosphorylase B kinase, phosphoglycerate kinase, triosophosphate isomerase, branching and debranching enzymes and acid maltase. Immunohistochemistry showed normal location of Lamp-1 and 2, phosphorylated neurofilaments, dystrophin, spectrine, sarcoglycans and caveolin-3.

After IFN discontinuation, the patient’s physical conditions remained stable. We repeated a muscle biopsy of left quadriceps six months after IFN withdrawal; histological, histochemical and biochemical analysis confirmed the diagnosis of a vacuolar myopathy.

Discussion

The most interesting aspect of this study is that it concerns a case of concomitant vacuolar myopathy and chronic HC. To our knowledge such an association has not previously been reported.

Vacuolar myopathies are a clinically and pathogenetically heterogeneous group of neuromuscular disorders that share the histological feature of vacuoles in the muscle fibres. Acquired vacuolar myopathies commonly have a toxic or iatrogenic aetiology and are usually caused by alcohol abuse and by the use of some drugs, such as colchicines, corticosteroids and glycyrrhizin-containing agents (14).

On the other hand, several reports of muscular involvement during the course of chronic HCV infection have been published. In most of these cases, inflammatory changes of varying degrees were observed in the muscle tissue; however the pathological mechanisms underlying the muscular damage during CHC are still unclear.

A first pathogenetic hypothesis links muscular changes occurring during CHC to IFN therapy, as patients significantly improved (5,9,15) or even recovered (16) after IFN withdrawal; in addition, rhabdomyolysis has been observed as a dose-dependent side effect in patients treated with IFN α and β for other systemic disorders, such as melanoma (17) or multiple sclerosis (18). Following the detection of HCV RNA in the muscle biopsies of some patients with CHC and concomitant inflammatory myopathy, as well as in that of patients with inclusion body myositis, some authors hypothesized a directed pathogenetic role of the HCV (8,9,12,13). However, there are no convincing data on direct muscle fibre infection by HCV, as neither the viral antigen nor the replicative intermediate of the virus have been identified in the muscle fibres.

In a recent report, both NS3 antigen and HCV RNA were detected in infiltrating cells, but not in muscle fibres (9), suggesting that a humoral immune-mediated mechanism, triggered by the HCV, may sustain the inflammatory reaction, rather than direct infection of the muscle by the HCV.

Finally, a further suggestion is that the increased oxidative stress induced by the HCV could also contribute to the muscular damage in patients with CHC (11). Herein, we reported on a patient with chronic HCV infection treated with IFNα who developed mild proximal muscle weakness. The muscle biopsy showed myopathic changes and vacuoles in 8% of the fibres. Some of the vacuoles contained glycogen, therefore a biochemical analysis was performed to exclude a glycogenosis. Histological, immunohistochemical and biochemical studies did not disclose any known cause of vacuolar myopathy. In addition, the lack of a temporal relationship with IFN treatment and of an improvement of either the clinical or the histological features after its withdrawal suggests that the IFN treatment did not play a role in the development of this patient’s vacuolar myopathy. All these findings raise the hypothesis of a causal relationship between CHC and the vacuolar myopathy in the case here presented. However, testing for HCV RNA in the affected muscle, which could provide a useful indicator of an aetiological role of the virus, was not performed in this patient. With regard to this hypothesis, this is the main limitation of our study.

In view of the high incidence of HCV infection in the general population, it is also possible that the occurrence of a vacuolar myopathy in infected patients is merely coincidental.

To conclude, we reported on a case of vacuolar myopathy in the course of CHC. To date there is no bibliographic or biological evidence supporting an aetiological relationship between these two diseases and HCV RNA was not investigated in our patient’s muscle biopsy. Should further case reports confirm such an association, these findings will expand the clinical and histological spectrum of muscular involvement during the course of CHC and make it opportune to consider HC among the possible aetiologies of acquired vacuolar myopathy.

References

Vacular myopathy and chronic hepatitis C