P 2-63

Telbivudine induced mitochondrial myopathy in a patient with chronic hepatitis B: A Case report

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Introduction

Chronic hepatitis B virus (HBV) infection is a major global health problem. It is a leading cause of liver cirrhosis, hepatocellular carcinoma and liver failure. Recently, there have been two approved antiviral therapy for chronic HBV infection. One is interferon therapy and the other strategy is nucleotide analogues. Telbivudine is a synthetic nucleotide analogue. It is a common therapeutic option for chronic HBV infection. However, it has been related with creatine kinase (CK) elevations and on rare occasions, clinical myopathy. The actual prevalence of telbivudine induced myopathy is unknown. Reports of electromyography (EMG) and muscle biopsy studies have been rare. We report here a case of telbivudine induced mitochondrial myopathy confirmed by muscle biopsy in patient after long term administration of telbivudine for chronic HBV infection.

Case report

A 52-year-old man who had received telbivudine plus adefovir therapy for chronic hepatitis B presented with weakness of his extremities, dysphagia and weight loss over the previous 5 months. At the time of admission to the clinic, he was taking 600 mg of telbivudine and 10 mg of adefovir once daily for 40 months. His serum HBV DNA level had decreased to less than 20 IU/ml, and serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were normal. However, the patient suffered from dysphagia and generalized weakness, especially of his legs, and had difficulty in climbing stairs. He had decreased deep tendon reflexes, and atrophy was observed in the proximal muscle of upper extremity. Decreased pharyngeal contraction, large amount of pharyngeal residue and laryngeal penetration were observed on the videofluoroscopic swallowing study (VFSS). The EMG study indicated myopathy with characteristic myopathic discharges on all extremities. The patient was admitted for further evaluation of the weakness and dysphagia. Laboratory test on admission showed AST of 27 U/L (reference range: 0 to 34 U/L), ALT 17 U/L (10 to 49 U/L), and CK 206 U/L (32 to 294 U/L). Tests for serum autoimmune markers were negative. MRI findings on both thighs showed no definite abnormal signal intensity. We planned to perform a muscle biopsy for confirmation. A muscle biopsy performed on the vastus lateralis muscle showed many degenerating atrophic and multiple regenerating myofibers, variation in fiber size. Telbivudine was discontinued and the patient was switched to tenofovir. The extremity weakness and dysphagia were improved two months after discontinuation. He was able to climb stairs more easily than before. Follow up VFSS showed a slight reduction of pharyngeal residue, decreased aspiration tendency, and improved subjective swallowing.

Conclusion

Despite few cases of telbivudine induced mitochondrial myopathy were reported, physicians should take into consideration the possibility of the relationship with telbivudine to detect this reversible adverse event without delay.

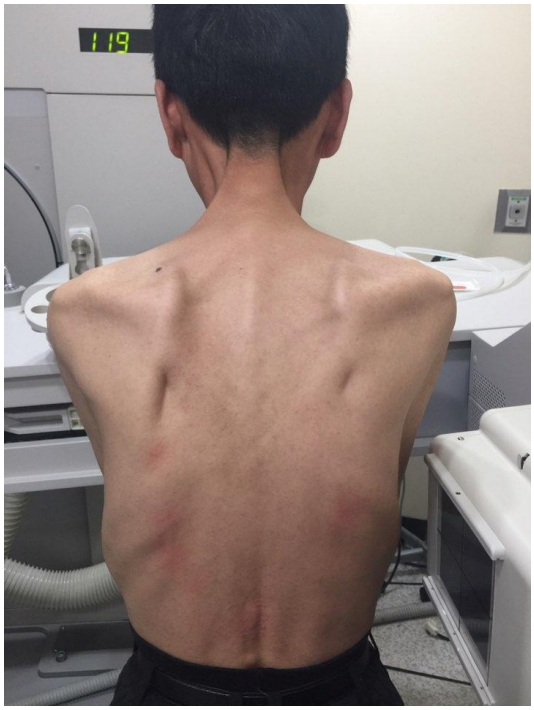

Figure 1. The patient shows proximal muscle atrophy, especially of the both infraspinatus and rhomboid muscle.

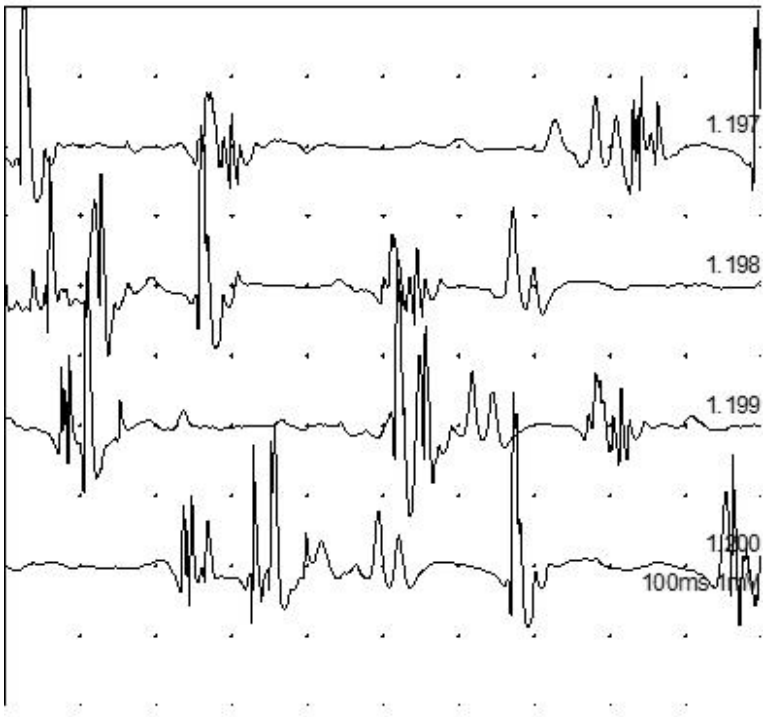

Figure 2. Electromyographic findings of the patient. Short duration and polyphasic motor unit action potentials with early recruitment patterns were recorded in the right vastus medialis muscles.

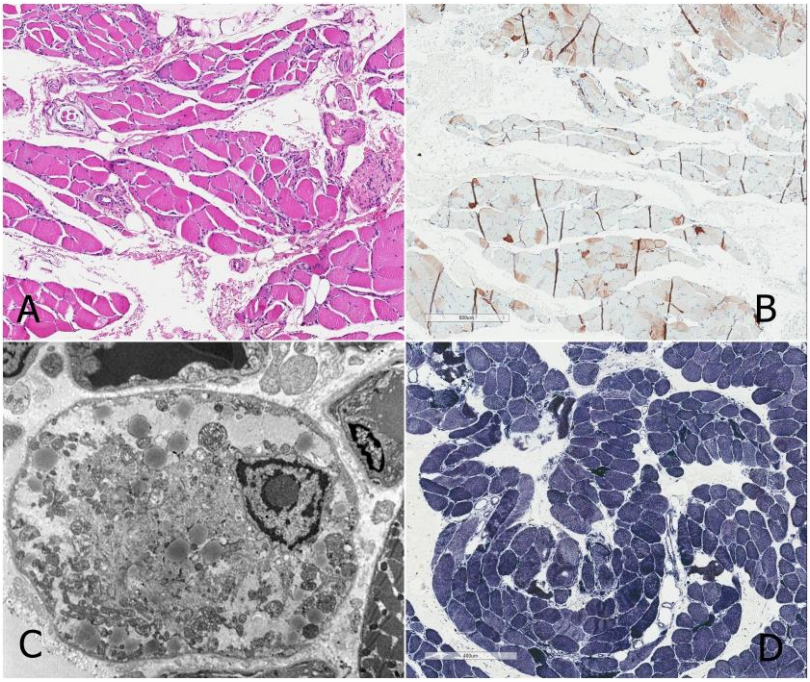

Figure 3. Muscle biopsy specimen (A) Many degenerating and regenerating myofibers and mild endomysial fibrosis and fat ingrowth (Hematoxylin and eosin stain) (B) Many degenerating myofibers (CD56 immunohistochemistry) (C) Many degenerated myofibers with moderate size variation and subsarcolemmal accumulation of swollen mitochondrias with abnormal arrrangements of cristae or vesicular cristae (Electron microscopy; magnification, 6000x) (D) Type I fiber predominance, no grouping and hyperstained and mottled myofibers (NADHase stain)