eNeurologicalSci 16 (2019) 100204

Contents lists available at ScienceDirect

eNeurologicalSci

journal homepage: www.elsevier.com/locate/ensci

Case report

Effect of intravenous immunoglobulin therapy on anti-NT5C1A antibody-positive inclusion body myositis after successful treatment of hepatitis C: A case report

Motonori Takamiya[a,*], Yoshiaki Takahashi[a], Mizuki Morimoto[a], Nobutoshi Morimoto[a], Satoshi Yamashita[b], Koji Abe[c]

[a] Department of Neurology, Kagawa Prefectural Central Hospital, 1-2-1 Asahimachi, Takamatsu City, Kagawa 760-8557, Japan
[b] Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan
[c] Department of Neurology, Graduate School of Medicine, Dentistry and Pharmaceutical Science, Okayama University, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan

ARTICLE INFO

Keywords:
Inclusion body myositis
Anti-skeletal muscle protein 5′-nucleotidase 1A antibody
Chronic hepatitis C
Dysphagia
Intravenous immunoglobulin therapy

ABSTRACT

Inclusion body myositis (IBM) is the commonest idiopathic inflammatory myopathy of older persons. Pathophysiological mechanism of IBM remains unknown; however, an association of IBM with chronic hepatitis C virus (HCV) infection and serum autoantibodies against skeletal muscle protein 5′-nucleotidase 1A (NT5C1A) has recently been reported. No effective treatment for IBM has yet been developed. We here present a 70-year-old man who was anti-NT5C1A antibody-positive in association with IBM and chronic hepatitis C. The initial treatment of ombitasvir/paritaprevir/ritonavir for his chronic hepatitis C was successful; however, his symptoms of IBM did not improve. On the contrary, his quadriplegic paralysis became more severe and he developed dysphagia. Next, steroid pulse therapy was initiated for IBM and, although his hyper-creatine phosphokinase-emia improved, his symptoms did not; indeed, they worsened. Subsequent intravenous immunoglobulin therapy (IVIg) resulted in obvious improvement in his dysphagia. Thereafter IVIg therapy was repeated at approximately 2-monthly intervals. His dysphagia remained improved for more than 1 year; however, his quadriplegia continued to progress slowly. Although IBM can reportedly be associated with hepatitis C, we inferred that there was no direct relationship between these conditions in our patient because his IBM did not improve after treatment of his hepatitis C. Although his IBM-associated quadriplegia did not improve, IVIg therapy did result in improvement in his dysphagia.

1. Introduction

Inclusion body myositis (IBM), the most common idiopathic inflammatory myopathy of older persons, is characterized clinically by asymmetric finger flexor and knee extensor weakness and histologically by lymphocytic endomysial inflammation and autophagic rimmed vacuoles [1]. The pathophysiological mechanism of sporadic IBM remains unknown; however, an association between IBM and chronic hepatitis C virus (HCV) infection was recently reported [2,3]. Furthermore, serum autoantibodies against skeletal muscle protein 5′-nucleotidase 1A (NT5C1A) is reportedly a relatively specific diagnostic marker for IBM [4,5].

2. Case report

A 70-year-old man had difficulty climbing stairs because of weakness of both lower limbs and did not improve despite undergoing rehabilitation. These symptoms slowly worsened over a 1-year period, during which he had difficulty walking and the grip strength of both hands weakened, prompting admission to our hospital. He presented with predominantly left-sided proximal leg, particularly quadriceps muscle, weakness, finger flexor muscle weakness, and atrophy. Serum creatine phosphokinase (CPK) concentration was slightly increased (650 IU/L). The histopathological findings on a biopsy of the rectus femoris muscle performed two months after first visit to our hospital were consistent with IBM in that he had marked endomysial fibrosis with lymphocyte infiltration partially surrounding non-necrotic muscle

* Corresponding author.
E-mail address: m-takamiya@chp-kagawa.jp (M. Takamiya).

https://doi.org/10.1016/j.ensci.2019.100204
Received 10 June 2019; Received in revised form 11 August 2019; Accepted 19 August 2019
Available online 22 August 2019

fibers and muscle fibers with rimmed vacuoles. Furthermore, anti-NT5C1A antibodies were detected in the patient's serum by cell-based assay [5], and he had mild liver dysfunction caused by chronic hepatitis C (virus genotype 1b, serum HCV RNA concentration 5.9 logIU/mL). He was initially treated with ombitasvir/paritaprevir/ritonavir for hepatitis C for 3 months, which resulted in improvement in his liver function and negative conversion of HCV-RNA. However, his hyper-CPKemia persisted, accompanied by progression of limb muscle weakness and he began to develop dysphagia. In order to confirm the response to steroid hormones, steroid pulse therapy (methylprednisolone 500 mg/day for 3 consecutive days) was administered about 2 months after HCV treatment because an autoimmune mechanism was suspected due to anti-NT5C1A antibody positivity, in addition to the histopathological findings of myositis with no significant clinical improvement other than an improvement in his hyper-CPKemia. Subsequent intravenous immunoglobulin (IVIg) (400 mg/kg/day for 5 consecutive days) was administered 1.5 months after steroid administration, which improved his dysphagia (Video 1, 2). Thereafter, IVIg treatment was continued at 2-month intervals. His dysphagia remained improved over a year; however, his quadriplegic paralysis continued to become more severe, resulting in difficulty standing and walking.

3. Discussion

There are currently no effective treatments for IBM. Adrenocortical hormone preparations are often administered as for polymyositis/dermatomyositis; however, many patients are refractory to this treatment, evidencing slowly progressive muscle weakness even though serum CPK concentrations decline [1]. A relationship between IBM and HCV infection has been reported [2,3], necessitating monitoring for HCV reactivation associated with treatment with steroid hormones or immunosuppressants; however, there are no reports of IBM improving with treatment of HCV. Consistent with this, our patient's symptoms did not improve after successful treatment of HCV. Even after resolution of hepatitis, hyper-CPKemia continued and his limb strength was also reduced. Thus, although HCV may be associated with the onset of IBM, it is not considered to be directly associated with the progression of the pathological condition.

It has been proposed that seropositivity for NT5C1A antibody is associated with severity of dysphagia [6]. A double-blind comparative study has not yielded a significant difference between IVIg therapy and placebo to date [1]. However, IVIg therapy is reportedly effective for dysphagia and thus may be worth trying, especially when the dysphagia is relatively mild [7]. Our patient's symptoms did not improve with administration of steroid hormones; his quadriplegic paralysis progressed, as did his dysphagia. Subsequent IVIg therapy was associated with obvious improvement in his dysphagia. Thereafter IVIg therapy at 2-month intervals stabilized his swallowing for more than 1 year; however, his quadriplegia and muscle atrophy progressed. Although no effective treatment has yet been developed for quadriplegia associated with IBM, it is worth trying IVIg therapy for IBM-associated dysphagia.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ensci.2019.100204.

Acknowledgments

We would like to express our gratitude to Dr. Satoshi Yamashita, Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, for analyzing anti-NT5C1A antibody in this case. We are also thankful to Dr. Ichizo Nishino, Department of Neuromuscular Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, for histopathological examination in this case. Finally, we thank Dr. Trish Reynolds, MBBS, FRACP, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

References

[1] P. Machado, S. Brady, M.G. Hanna, Update in inclusion body myositis, Curr. Opin. Rheumatol. 25 (2013) 763–771.
[2] Y. Tsuruta, T. Yamada, T. Yoshimura, M. Satake, K. Ogata, T. Yamamoto, et al., Inclusion body myositis associated with hepatitis C virus infection, Fukuoka Acta Med. 92 (2001) 370–376.
[3] A. Uruha, S. Noguchi, Y.K. Hayashi, R.S. Tsuburaya, T. Yonekawa, I. Nonaka, I. Nishino, Hepatitis C virus infection in inclusion body myositis: a case-control study, Neurology 86 (2016) 211–217.
[4] T.E. Lloyd, L. Christopher-Stine, I. Pinal-Fernandez, E. Tiniakou, M. Petri, A. Baer, et al., Cytosolic 5′-nucleotidase 1A as a target of circulating autoantibodies in autoimmune diseases, Arthritis Care Res. 68 (2016) 66–71.
[5] N. Tawara, S. Yamashita, X. Zhang, M. Korogi, Z. Zhang, T. Doki, et al., Pathomechanisms of anti-cytosolic 5′-nucleotidase 1A autoantibodies in sporadic inclusion body myositis, Ann. Neurol. 81 (2017) 512–525.
[6] N.A. Goyal, T.M. Cash, U. Alam, S. Enam, P. Tiemey, N. Araujo, et al., Seropositivity for NT5c1A antibody in sporadic inclusion body myositis predicts more severe motor, bulbar and respiratory involvement, J. Neurol. Neurosurg. Psychiatry 87 (2016) 373–378.
[7] P. Cherin, S. Pelletier, A. Teixeira, P. Laforet, A. Simon, S. Herson, et al., Intravenous immunoglobulin for dysphagia of inclusion body myositis, Neurology 58 (2002) 326.