Myositis with Anti-mitochondrial Antibody Type 2 with Diplopia and Ptosis

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Abstract:
Anti-mitochondrial antibody type 2 is a diagnostic marker of primary biliary cirrhosis and complicates myositis. Myositis with anti-mitochondrial antibody type 2 is clinically characterized by slowly progressive limb, cardiac, and respiratory muscle weakness as well as serum creatinine kinase elevations. However, there has been few cases with eye symptoms. We herein report a 59-year-old woman with anti-mitochondrial antibody type 2 who presented with diplopia and ptosis. Magnetic resonance imaging revealed bilateral ocular muscle enlargement and abnormally high intensities in the lower limb muscles. Corticosteroid therapy improved these symptoms. Myositis with anti-mitochondrial antibody type 2 can present with eye symptoms.

Key words: myositis with anti-mitochondrial antibody type 2, myositis, diplopia, ptosis

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Introduction

Anti-mitochondrial antibody type 2 is an antibody against mitochondria used as a diagnostic marker of primary biliary cirrhosis (PBC) (1, 2); furthermore, patients positive for anti-mitochondrial antibody type 2 may present with myositis (3, 4). Therefore, myositis with anti-mitochondrial antibody type 2 is often characterized by muscle weakness of the four extremities, cardiac involvement, and dyspnea (5-9). Although Magrini et al. reported PBC patient with ocular myositis (10), there has been few reported cases involving ocular paresis.

We herein report the first case of myositis with anti-mitochondrial antibody type 2 that presented with ocular muscle symptoms.

Case Report

A 59-year-old Japanese woman with an unremarkable medical and family history was diagnosed with diplopia and right ptosis. On day 26, she presented with left ptosis, and her left eye was almost completely covered by her eye lid. She also showed adduction restriction of the left eye. She was admitted to our hospital on day 40.

A neurological examination revealed left slight blepharoptosis, exotropia, and restriction of the left eye movement in all directions (Fig. 1). However, there was no right ptosis at this time. Furthermore, she did not present with anisocoria, light reflex abnormalities, bulbar symptoms, or limb muscle weakness.

Laboratory tests revealed elevated serum levels of creatine kinase (CK) (935 IU/L), aspartate aminotransferase (46 IU/L), alanine aminotransferase (35 IU/L), and gamma-glutamyl transferase (42 IU/L). The thyroid function (free T3, free T4, thyroid-stimulating hormone [TSH]) and autoantibodies, including thyroid-related antibodies (anti-thyroglobulin, anti-thyroid peroxidase, and anti-TSH receptor antibodies) and anti-ribosomal RNA synthetase antibodies were normal. In addition, anti-acetylcholine receptor antibody and anti-muscle-specific kinase antibody were negative. Anti-nuclear antibody (×80) and anti-SS-B antibody (12.1 U/mL) were weakly positive; however, there was a significant elevation of anti-mitochondrial antibody type 2 (99.9 index).

Findings on repetitive nerve stimulation of orbicularis oculi muscle, the cerebrospinal fluid test, an electrocardiogram, the respiratory function test, and cardiac and abdomi-
Figure 1. On admission, we observed restriction of the left eye movement, slight blepharoptosis, and exotropia. After corticosteroid therapy, left eye abduction restriction remained; however, most of the other eye movement restrictions, blepharoptosis, and eye position had improved.

Figure 2. On admission, ocular muscle swelling was observed on T1-weighted imaging (a). Abnormal high intensities were observed in the bilateral gluteus maximus on the axial pelvis section (b, arrowheads) and in the right tibialis posterior and left extensor hallucis longus muscles on the axial knee section (c, arrowheads) of short-T1 inversion recovery (STIR) imaging. After corticosteroid therapy, the ocular muscle swelling had improved (d), and the abnormally high intensities had disappeared (e, f).

normal echo tests were unremarkable. There was no malignancy on contrast-enhanced computed tomography. On magnetic resonance imaging (MRI), T1-weighted images revealed swollen bilateral ocular muscles (Fig. 2a). In addition, there were high intensities in the bilateral gluteus maximus muscles, right tibialis posterior muscle, and left extensor hallucis longus muscle on short T1 inversion recovery (STIR) images of the lower limbs (Fig. 2b, c). Electromyography (EMG) of the biceps brachii revealed an early recruitment pattern and numerous lower amplitude motor unit potentials, which was compatible with the myogenic pattern. Although we did not perform a muscle biopsy, the patient was diag-
nosed with myositis with anti-mitochondrial antibody type 2 and comorbid ocular symptoms based on laboratory tests, EMG, and MRI findings.

On day 53, the patient started methylprednisolone pulse therapy (1,000 mg for 3 days) followed by oral prednisolone therapy (1 mg/kg). Although the serum CK level promptly normalized, the eye movement response was delayed. The patient underwent two additional courses of methylprednisolone pulse therapy with continued oral prednisolone therapy. On day 95, slight adduction restriction of the left eye reappeared (Fig. 2e, f) with oral steroid therapy being continued without relapse.

**Discussion**

We herein report a woman diagnosed with myositis positive for anti-mitochondrial antibody type 2 who presented with ocular symptoms. Corticosteroid therapy improved her symptoms.

In the present case, the chief complaints were ocular symptoms. Laboratory tests revealed increased serum CK levels and positivity for anti-mitochondrial antibody type 2. The EMG findings were suggestive of a myopathy pattern, while the MRI findings revealed ocular muscle swelling and abnormally high intensities of skeletal muscles. Generally, myositis with anti-mitochondrial antibodies type 2 is characterized by slow-progressive limb, cardiac, and respiratory muscle weaknesses; arrhythmia; liver dysfunction with or without primary biliary cirrhosis; and increased CK levels (5-9). Our patient did not present with muscle weakness, disturbances of the respiratory or cardiac muscles, or complications of PBC. However, the patient did present with increased serum CK levels, EMG findings, and abnormalities on leg MRI (gluteus maximus, extensor hallucis longus, and tibialis posterior muscles in the STIR sequence). Given that the pelvis and thigh muscles, including the gluteus maximus, can be affected in patients with myositis with anti-mitochondrial antibodies type 2 (11), our clinical findings, except for the ocular symptoms, are consistent with the previously reported ones.

Diplopia, ptosis, and ocular muscle swelling are suggestive of orbital myositis. Since corticosteroid therapy improved both the abnormal skeletal muscle findings and ocular symptoms, the skeletal and ocular symptoms may have shared inflammatory pathogenesis. Good responsiveness to corticosteroid therapy is consistent with previous reports on myositis with anti-mitochondrial antibody type 2 (3, 5-9). Although we did not perform an EMG study after corticosteroid treatment, the EMG findings may have been normalized by treatment. Furthermore, since ocular muscles require large energy amounts given their quick contraction, they can be affected by certain mitochondrial diseases, including chronic progressive external ophthalmoplegia (CPEO) (12). In CPEO patients, ptosis is also the common clinical feature (13, 14). Some CPEO patients present with fluctuating ptosis, which is speculated to be due to neuromuscular impairment (14). Furthermore, there is one case report of a PBC patient with ocular myositis (10). These reports may explain the mechanisms underlying the clinical features in this case.

Although our report is the second case of myositis with anti-mitochondrial antibody type 2 with ocular symptoms, it is worth reporting because we evaluated the skeletal muscle symptoms for the first time. Furthermore, we also observed good responsiveness to both skeletal muscle myositis and ocular symptoms. Given the limited number of cases and the undefined diagnostic criteria regarding myositis with anti-mitochondrial antibody type 2, there is a need for further research on myositis with anti-mitochondrial antibodies type 2.

The present case report shows that myositis with anti-mitochondrial antibody type 2 can involve ocular myositis in addition to conventional skeletal myositis; furthermore, these symptoms respond to corticosteroid therapy. Further evidence is required to clarify the detailed characteristics of myositis with anti-mitochondrial antibody type 2. It is crucial to consider myositis with anti-mitochondrial antibody type 2 when patients present with ocular symptoms in addition to serum CK elevation.

The authors state that they have no Conflict of Interest (COI).

**References**

1. Mutimer DJ, Fussey SP, Yeaman SJ, Kelly PJ, James OF, Bassendine MF. Frequency of IgG and IgM autoantibodies to four specific M2 mitochondrial autoantigens in primary biliary cirrhosis. Hepatology 10: 403-407, 1989.
2. Van de Water J, Cooper A, Surh CD, et al. Detection of autoantibodies to recombinant mitochondrial proteins in patients with primary biliary cirrhosis. N Engl J Med 320: 1377-1380, 1989.
3. Harada N, Dohmen K, Itoh H, et al. Sibling cases of primary biliary cirrhosis associated with polymyositis, vasculitis and Hashimoto’s thyroiditis. Intern Med 31: 289-293, 1992.
4. Varga J, Heiman-Patterson T, Munoz S, Love LA. Myopathy with mitochondrial alterations in patients with primary biliary cirrhosis and antimitochondrial antibodies. Arthritis Rheum 36: 1468-1475, 1993.
5. Shimizu H, Nishino I, Ueda T, Kohara N, Nishioha H. Anti-mitochondrial antibody-associated myositis with eosinophilia and dropped head. eNeurologicalSci 11: 15-16, 2018.
6. Maeda MH, Tsuji S, Shimizu J. Inflammatory myopathies associated with anti-mitochondrial antibodies. Brain 135 (Pt 6): 1767-1777, 2012.
7. Albayda J, Khan A, Casciola-Rosen L, Corse AM, Paik JJ, Christopher-Stine L. Inflammatory myopathy associated with anti-mitochondrial antibodies: A distinct phenotype with cardiac involvement. Semin Arthritis Rheum 47: 552-556, 2018.
8. Konishi H, Fukuzawa K, Mori S, et al. Anti-mitochondrial M2 Antibodies Enhance the Risk of Supraventricular Arrhythmias in Patients with Elevated Hepatobiliary Enzyme Levels. Intern Med 56: 1771-1779, 2017.
9. Tanaka K, Sato A, Kasuga K, et al. Chronic myositis with cardiomypathy and respiratory failure associated with mild form of organ-specific autoimmune diseases. Clin Rheumatol 26: 1917-1919, 2007.
10. Magrini L, Rotiroti G, Conti F, et al. Orbital myositis in a patient with primary biliary cirrhosis: successful treatment with methotrexate and corticosteroids. Isr Med Assoc J 5: 825-826, 2003.
11. Minamiyama S, Ueda S, Nakashima R, et al. Thigh muscle MRI findings in myopathy associated with anti-mitochondrial antibody. Muscle Nerve 61: 81-87, 2020.
12. Carta A, Carelli V, D’Adda T, Ross-Cisneros FN, Sadun AA. Human extraocular muscles in mitochondrial diseases: comparing chronic progressive external ophthalmoplegia with Leber’s hereditary optic neuropathy. Br J Ophthalmol 89: 825-827, 2005.
13. Caballero PE, Candela MS, Alvarez CI, Tejerina AA. Chronic progressive external ophthalmoplegia: a report of 6 cases and a review of the literature. Neurologist 13: 33-36, 2007.
14. Le Forestier N, Gherardi RK, Meyrignac C, et al. Myasthenic symptoms in patients with mitochondrial myopathies. Muscle Nerve 18: 1338-1340, 1995.

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