HyperCKemia Related to the Initial and Recurrent Attacks of Neuromyelitis Optica

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Abstract

We herein report the case of a 60-year-old man showing overexpression of creatine kinase (hyperCKemia) related to initial and recurrent attacks of neuromyelitis optica (NMO). He showed reduced vision, ataxia and dysesthesia, but no symptoms originating in the muscles. Magnetic resonance imaging (MRI) revealed lesions in the optic nerve, medulla oblongata, and spinal cord similar to typical NMO patients. However, femoral MRI and whole positron emission tomography (PET) demonstrated no abnormal findings during an episode of hyperCKemia. This case suggests that hyperCKemia is partly involved in the pathogenesis of NMO in both the central nervous system and myofiber surface, which is usually difficult to detect by clinical imaging modalities alone.

Key words: neuromyelitis optica, aquaporin 4, hyperCKemia

Introduction

Neuromyelitis optica (NMO) is a demyelinating disease typically manifesting transverse myelitis and bilateral optic neuritis. An antibody for aquaporin 4 (AQP4) was recently detected in the serum of patients with NMO (1, 2). AQP4 is a member of the AQP superfamily, which is expressed in the brain and implicated in the development of brain edema, and ion and water homeostasis at the synaptic level (3). AQP4 is also strongly expressed in the skeletal muscle, and the expression is altered by various disease conditions (4). Although hyperCKemia has previously been reported in patients with anti-AQP4 antibody positive NMO (5), their cases presented hyperCKemia only before the initial attack of NMO or at times unrelated to NMO relapse. On the other hand, we herein report the first case of NMO showing hyperCKemia during both initial and recurrent attacks.

Case Report

A 60-year-old Japanese man without any past medical history and who was not taking any medication subacutely developed frequent vomiting and a fever of 38.0°C on July, 2009. He was admitted to a nearby hospital. Blood tests showed a high creatine kinase (CK) level 7 days after the onset (17,215 IU/L; normal range 41-258 IU/L). Upper gastrointestinal endoscopy and abdominal and pelvic computer tomography (CT) revealed no abdominal lesion related to the vomiting. Although his vomiting improved without any specific treatment within 14 days, his high fever and hyperCKemia persisted for more than two weeks. He was transferred to our hospital (Okayama University Hospital) on October, 2009 for further evaluation and treatment.

General medical examinations showed no abnormal findings except for a slight fever of 37.4°C. Neurological examinations showed slight dysarthria, a deviation of the tongue to the left, gait disturbance due to truncal ataxia and numb-
ness in left fourth and fifth fingers. He complained of no spontaneous myalgia or grasping muscle pain.

Biochemical tests of the blood showed that the CK level remained elevated at 2,387 IU/L 26 days after the onset of symptoms. A cerebrospinal fluid (CSF) analysis revealed slight pleocytosis (17/mm$^3$) and an IgG index that was elevated to 0.80. A brain MRI revealed a lesion in bilateral dorsal medulla oblongata (Fig. 1A, B, arrows). A spinal MRI revealed several short lesions at the C6/7, Th4, Th5/6 and Th7 levels of the spinal cord (Fig. 1B, C, arrowheads). However, both a femoral MRI (Fig. 2A-C) and a positron emission tomography-computed tomography scan (PET-CT; Fig. 2D, E) revealed no lesion. He was administered one course of intravenous methylprednisolone (mPSL; 1,000 mg/day) for three successive days. All of his symptoms gradually improved after the first intravenous dose of mPSL, and the CK level decreased to 78 IU/L, which was within the normal limits. He was discharged from our hospital at 47 days after the onset. At that point, the administration of oral steroids after the intravenous mPSL therapy had not been started, because his diagnosis had not yet been confirmed.

However, on November, 2010, he visited our hospital again due to new dysesthesia in the left lower extremity and reduced vision in the right eye. General medical examinations showed no abnormal findings, but neurological examinations showed a severe reduction of the visual acuity (right eye; 20/666, left eye; 20/17) and dysesthesia in his left trunk below the Th 7 level and in his left leg.
A biochemical analysis showed that the CK level was again elevated to 1,407 IU/L. The CSF analysis revealed no pleocytosis (3/mm$^3$) but an elevated IgG index (to 0.67). A brain MRI revealed a lesion in the right optic nerve (Fig. 3B, C, E, F; arrows). A spinal MRI revealed new lesions at the C2-4 levels of the cervical spinal cord (Fig. 3H, I, arrowheads) and the same lesions in C6/7, Th4, Th5/6 and Th7 (H, I; arrows) as had been observed 1 month prior, which showed increased swelling with enhancement by contrast-enhanced MRI (I; arrows and arrowhead).

Electromyography was performed to evaluate the patient for hyperCKemia, and showed no apparent myogenic findings. He was administered two courses of intravenous mPSL for three successive days and underwent nine courses of plasma exchange. However, his symptoms deteriorated in his left eye (50 cm/finger counting). Although all these symptoms gradually improved after an additional three courses of lymphocyte depletion, he is still suffering from bilateral severe visual defects. His serum data on the first admission after the first course of steroid therapy. The recurrence of NMO was lower than that during the initial attack suggesting a reduction of the second muscle insult unrelated to NMO relapse. On the other hand, our case showed hyperCKemia not only before the initial attack but also at the recurrence of NMO. The present case suggests that anti-AQP4 antibodies may bind central nervous tissue and the cell surface of myofibers (4) to cause inflammatory responses. The fact that the serum CK level at the recurrence of NMO was lower than that during the initial attack of NMO suggests a reduction of the second muscle insult after the first course of steroid therapy.

Although hyperCKemia is rare in NMO, the serum CK level in this case was remarkably elevated and the patient had vomiting and a high fever. However, hyperCKemia may be asymptomatic and overlooked in many NMO cases. It has been reported that the expression of AQP4 in normal skeletal muscles is different from that in the various diseased muscles (4). The targets of anti-AQP4 antibody and the change of AQP4 in the muscle of NMO patients should therefore be examined. In addition, more attention should be paid to extra-CNS symptoms at the onset of NMO.

We herein reported a patient who presented with hyperCKemia without symptoms of clinical myopathy such as myalgia, grasping muscle pain, or muscle weakness at onset, who was eventually diagnosed to have NMO based on the subsequent symptoms of bilateral severe optic neuritis and myelitis, and positivity for anti-AQP4 antibodies.

The patient’s asymptomatic hyperCKemia did not show a focus of disturbed muscle, although muscle MRI and PET-CT are generally useful techniques for detecting muscle inflammation prior to obtaining a muscle biopsy (7, 8). This discrepancy suggests that the insult of skeletal muscles associated with NMO is not focally strong inflammation and rhabdomyolysis, but rather mild diffuse involvement.

Suzuki et al. (5) previously reported three cases of NMO with episodes of hyperCKemia only before the onset of neurological disorders, with one case who had hyperCKemia unrelated to NMO relapse. On the other hand, our case showed hyperCKemia not only before the initial attack but also at the recurrence of NMO. The present case suggests that anti-AQP4 antibodies may bind central nervous tissue and the cell surface of myofibers (4) to cause inflammatory responses. The fact that the serum CK level at the recurrence of NMO was lower than that during the initial attack of NMO suggests a reduction of the second muscle insult after the first course of steroid therapy.

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

References


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