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A Case with Acute Quadriplegic Myopathy Following Intensive Care for Idiopathic Interstitial Pneumonia

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We reported a patient who developed acute quadriplegic myopathy (AQM) following treatment with a combination of high-dose steroid and nondepolarizing blocking agent for idiopathic interstitial pneumonia (IIP). Few cases of AQM with IIP have been reported in the literature. The IIP progressed rapidly in our patient, but the high-dose steroid therapy was effective. The rehabilitative intervention comprised of passive range-of-motion exercise, functional training, and muscle strengthening. After the initial presentation with severe weakness, the AQM gradually improved and the patient regained full physical function in 8 months. The clinical course was almost identical to that of AQM patients with other lung diseases. Though unlikely to influence the improvement of muscle weakness in AQM patients, the lung diseases associated with AQM may require specific consideration in determining suitable rehabilitation programs and observing patients before and after full recovery from dysmobility.

Key words : Acute Quadriplegic Myopathy, Rehabilitation, Interstitial Pneumonia, Steroid, Nondepolarizing Blocking Agent

INTRODUCTION

Acute quatriplegic myopathy (AQM) sometimes develops in patients treated with a combination of high-dose steroid and nondepolarizing blocking agent to facilitate mechanical ventilation [1, 2, 4, 9, 11, 12]. AQM was initially noted in asthmatic patients [13], but patients treated for other lung diseases or critical illnesses may also develop the condition. Even if initially severe, the diffuse weakness generally improves.

We encountered a case with AQM following treatment for idiopathic interstitial pneumonia (IIP) that caused rapid onset of respiratory failure. Since rapidly progressive IIP has a poor prognosis with high mortality rate, little has been reported on AQM associated with this type of IIP. We, therefore, describe the clinical course of the patient and the management including rehabilitative intervention. Specific concerns to the AQM following IIP are also discussed.

A CASE REPORT

A 60-year-old housewife without a history of medical problems was hospitalized due to severe dry cough and dyspnea on December 31, 2000. On admission, arterial Po_2 and Pco_2 were 27.9 mmHg and 23.5 mmHg, respectively in room air. Chest x-ray film (Fig. 1) showed diffuse interstitial, reticular shadow compatible with IIP. The modified lung injury score developed by Murray *et al.* [14] was 3.5, indicating severe lung injury.

She was intubated and paralyzed with nondepolarizing blocking agent (continuous infusion of vecuronium bromide, 40 mg/day) to facilitate mechanical ventilation from January 1. Midazolam was also administered. After an

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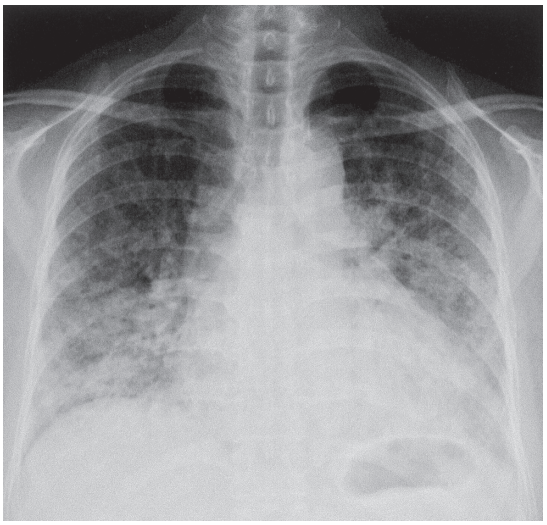

Fig. 1 Chest XP on admission (December 31, 2000).

initial 3 days of steroid pulse-treatment (1 g of intravenous methylprednisolone daily) commencing on January 3, the patient was intravenously administered 60 mg prednisolone per day. The intensive treatment described above was effective, and her respiratory condition gradually improved. However, the patient was noted to be diffusely weak when the mechanical ventilation was discontinued on January 15.

Neurological examination clarified that she was alert and fully oriented but had severe muscle weakness in the trunk and four extremities (1 or 2 in manual muscle testing). She could not sit up and not even hold herself in a sitting position. Tendon reflexes were absent, without Babinski's sign or other pathological reflexes. No sensory impairment, arthralgia, or any other type of pain was found. Cranial nerves were grossly intact. Bladder function was normal without urinary incontinence, retention, or dysuria.

Laboratory data (January 24) were as follows: WBC count, 10,500; serum CK, 278 U/L (normal, 30 to 140); sodium, 137 mEq/L; potassium, 4.1 mEq/L; calcium, 8.4 mEq/L; C-reactive protein, 1.29 mg/dL (normal, $<$ 0.3); creatinine, 0.3 mg/dL (normal, $<$ 0.8); GOT, 40 U/L (normal, $<$ 30); GPT, 81 U/L (normal, $<$ 35); LDH, 821 U/L (normal, 230 to 450). Blood culture and antinuclear antibody were negative

A nerve conduction study performed on January 25 revealed normal motor (55, 63, 53, and 48 m/s for the right median, ulnar, tibial, and peroneal nerves) and sensory (60, 63, and 58 m/s for the right median, ulnar, and left sural nerves, respectively) conduction velocities (CV). Compound muscle action potentials (CMAP) evoked by stimulation at the wrist or ankle were small (2.3, 0.9, 4.6, and 0.3 mV for the right abductor policis brevis, abductor digiti minimi, abductor hallucis, and extensor digitorum brevis, respectively) (normal, $>$ 6, $>$ 7, $>$ 10, and $>$ 2 mV). The amplitudes of sensory nerve action potential (SNAP) antidromically evoked by stimulation at the wrist or calf skin were within the reference range (21, 16, and 5.2 μV for the median, ulnar, and sural nerves). Repetitive stimulation (2, 3, and 20 Hz) was given to the ulnar nerves before and after maximum contraction (10 s) of the abductor digiti minini. No change in the CMAP amplitude was found.

In needle electromyography, motor unit potentials with short duration and low amplitude, so called myopathic units, were found diffusely in upper and lower extremities, together with positive sharp wave and fibrillation potential. The interference pattern was well preserved and showed rapid recruitment.

The patient's clinical course is shown in Fig. 2. The rehabilitative intervention commenced with passive range-of-motion exercise on January 6, while she was still sedated and ventilated. Her pulmonary function gradu-

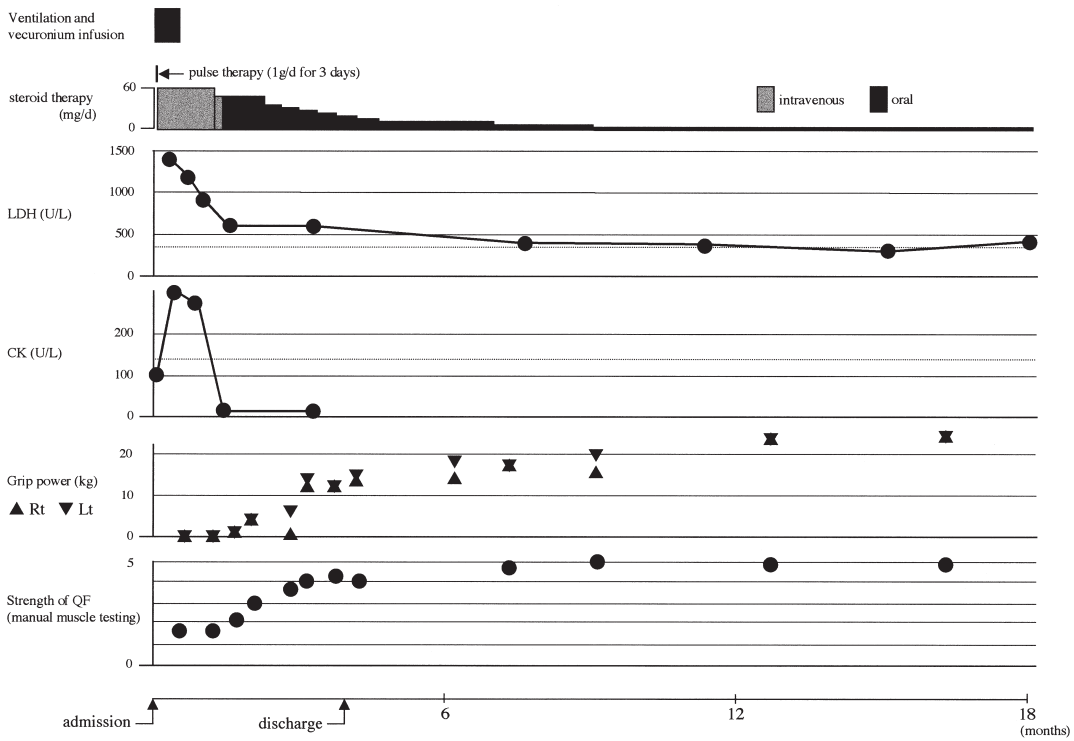

Fig. 2 The time course of the medication, laboratory data, and muscle strength of the patient. Dotted lines show the upper reference values. Since no marked discrepancy was found in the strength of the QF (quadriceps femoris) between sides, we use one black circle to present the muscle strength for both sides.

ally improved, and administration of oxygen was discontinued on January 29. The oxygen saturation level obtained by a pulse oximeter was around 93 % in room air. Her persistent muscle weakness was still so severe at that time that the ADL was fully dependent.

Functional training in basic activities steadily progressed, with gradual improvement in strength as follows: bed mobility, supine to sitting, sitting to standing, ambulation in parallel bars, ambulation with equipment as needed, and ascending and descending the stairs. The patient came to a training room in a wheelchair and started standing exercise from February 9. The oxygen saturation level (pulse oximeter) was monitored and maintained above 90 %. We regulated the exercise load to ensure that it could not cause fatigue or dyspnea. The training menu and exercise load were left unchanged while the dose of steroids was tapered. Her muscle weakness gradually improved and two months after admission she could start gait training using parallel bars. She was discharged on April 17 after regaining her gait with a cane. The %VC and FEV1.0 % in the pulmonary function test were 60.2 % and 84.5 %, respectively, indicating a mild restrictive change. Rehabilitative intervention was continued in our outpatient clinic. We had the patient perform a home program including gait and muscle strengthening training. Eight months after admission she was fully recovered and could ambulate up and down stairs without the aid of a cane or handrail. She felt no physical difficulty in her housework or other daily activities. She is still receiving low-dose oral steroid (5 mg of prednisolone), now at 19 months after discharge, and no sign of recurrent muscle weakness is observed.

DISCUSSION

This case presented persistent paralysis following treatment with high-dose-steroid together with vecuronium. Hansen-Flaschen *et al.* [8] pointed out two distinctive mechanisms leading to muscle paralysis after prolonged

administration of pancronium or vecuronium for more than 2 days. The first is short-term persistent paralysis due to persistent blockade of the neuromuscular junction. This is thought to relate to the accumulation of the drug or its metabolites in patients with renal or hepatic failure [8, 15]. The second is attributed not to delayed recovery from neuromusclular blockade, but an acute, generalized myopathy. A number of case reports suggest that combined treatment of neuromuscular blocking drug and high-dose-steroid can cause severe myopathy [1, 2, 4, 9, 11, 12].

Our patient did not show renal and hepatic failure. In a nerve conduction study, the motor and sensory CVs were normal only with decreased CMAP amplitude. Motor unit potential predominantly showed low amplitude and short duration. The interference pattern was well preserved with rapid recruitment. No evidence of a neuromuscular transmission disorder was detected. These electrophysiological findings were consistent with a primary myopathy [5, 9, 11, 12].

Douglas *et al*. investigated clinical findings in 70 patients with both diffuse interstitial lung disease and either polymyositis (PM) or dermatomyositis (DM) [6]. The lung disease may take the form of acute interstitial pneumonia with rapid progression to respiratory failure. Thirty percent of their patients initially complained of respiratory symptoms without obvious signs or symptoms of PM or DM. In our patient we did not identify scleroderma, skin rash, Raynaud's sign, or any other clinical findings associated with PM or DM. Antinuclear antibody was negative. Moreover, severe weakness was noted during the corticosteroid therapy, a course of treatment that suppresses the PM and DM. Serum CK showed only a slight elevation and rapidly returned to the reference range even though the severe quadriplegia persisted. Given these clinical findings, the patient's severe myopathy did not seem to be due to PM or DM. Douglas *et al*. pointed out that steroid therapy for lung disease sometimes delayed the diagnosis of PM or DM for weeks to years. Mindful of this point, we have carefully followed our patient for almost two years from the initial diagnosis of IIP. Still, no sign or symptom relating to PM or DM has been observed.

Critical illness polyneuropathy (CIN) is also a potential cause for acute weakness [16, 17]. CIN relates to systemic inflammatory response in sepsis. Electrophysiological findings in CIN are decreased CMAP and SNAP, and positive sharp wave and fibrillation potentials with relatively preserved CV [3, 16]. The present case did not show septic condition, and no sensory impairment was found in clinical examination or nerve conduction studies. In addition, CMAP amplitudes were relatively preserved in some muscles (around 50 % of lower limit of the reference values) in spite of the patient's clinically severe quadriplegia. The interference pattern in needle electromyography was well preserved. These findings are inconsistent with the presence of CIN.

Kupfer *et al*. [10] reported 7 patients with prolonged weakness after long-term infusion of vecuronium. Five of them had polyneuropathy. The mean total dose of vecuronium in patients with polyneuropathy (1352 mg) was significantly larger than that in patients without polyneuropathy (528 mg). Considering these values, the 560 mg of vecuronium administered to our patient was probably not the cause of her polyneuropathy. Hence, the acute weakness in our patient did not seem to be principally due to CIN or any other form of peripheral nerve dysfunction, although we were unable to rule out the coexistence of polyneuropathy.

Unlike other cases with AQM, our patient had IIP with a sudden onset of dyspnea followed in a few days by respiratory failure. Yet the clinical course of AQM was similar to that in cases with other lung disease. We monitored the CK and O_2 saturation levels during the physical exercises even after the O_2 administration was discontinued. Escalante *et al*. [7] studied the effects of resistive exercise and functional training in PM and DM patients treated with oral predonione of 50 to 100 mg/day. As their patients responded favorably to the exercises, we also prescribed functional training consisting of activities progressing stepwise with improvements in muscle strength. Considering the therapeutic effect of steroid on IIP, we took care to avoid the unwanted influence of physical overload on pulmonary function by keeping the exercise load at the same level while the drug was being tapered. Specific consideration of a suitable rehabilitation program and consecutive observation even after full recovery from dysmobility may be necessary for patients with some types of lung diseases.

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