Pseudo-Locked-In Syndrome and Apnea Due to Critical Illness Myopathy

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About the Authors

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Abstract

Critical Illness myopathy and polyneuropathy are common complications that occur in critically ill patients. Critical Illness myopathy and polyneuropathy are typically recognized in the ICU setting by the development of acquired weakness and failure to wean from ventilatory support. We report a case of a patient who developed severe critical illness myopathy that resulted in near-quadruplegia, apnea and ophthalmoplegia.

Résumé

La myopathie et les polyneuropathies associées à des maladies graves sont des complications couramment observées chez les patients dont l'état est critique. Dans les unités de soins intensifs, on les reconnaît généralement par le développement d'une faiblesse acquise et d'une incapacité à se passer d'une assistance respiratoire. Nous décrivons le cas d'un patient ayant développé une grave myopathie associée à des maladies graves et qui a entraîné une quasiquadruplégie, de l'apnée et une ophthalmoplégie.

Case Report

A previously healthy 71-year-old man presented with acute onset epigastric pain and was diagnosed with gallstone pancreatitis complicated by septic shock, acute kidney injury, and hypoxemic respiratory failure. Abdominal computed tomography (CT) scanning showed necrotizing pancreatitis. He was transferred to the intensive care unit (ICU) for mechanical ventilation, hemodynamic support, and further medical care. He did not require continuous pharmacological neuromuscular blockade or corticosteroids at any point. Due to clinical findings of abdominal compartment syndrome, the patient underwent decompressive laparotomy, followed by temporary maintenance of an open abdomen, on day 4 of admission. Laparotomy confirmed necrotizing gallstone

pancreatitis, as well as an ischemic left colon necessitating resection. Multiple surgeries were required, including complete colectomy, creation of end-ileostomy, cholecystectomy, pancreatic debridement, abscess drainage, and finally wound closure on day 14 of admission.

Despite discontinuation of sedation 1-week post admission, the patient exhibited profound generalized weakness including severe quadriparesis and ophthalmoplegia. The patient was consistently able to perform multistep tasks such as, "Tap your left index finger once, tap your right middle finger twice, and then tap with your left index finger again." The patient continued to demonstrate wakefulness through a tapping communications method developed in the ICU. Pupils were 3-4 mm with a sluggish light response. Bilateral

ptosis was present. When lids were held open, the patient was able to recognize family members as well as count fingers. Formal visual acuity testing was not performed. Extraocular movements were completely absent. The oculoccephalic reflex was absent. Muscles of facial expression were intact but were profoundly weak, with only flickers of movement seen.

Peripherally, there was grade 0/5 proximal muscle strength. Grade 1-2/5 muscle strength was noted for his hands and feet. Reflexes were absent. Sensation via light touch and pain was preserved.

In addition to his near “locked in” neurologic state, the patient displayed complete apnea. Ventilator sensitivity for a flow-triggered breath was maximized, but there was absence of any flow indicating spontaneous breathing despite the development of a marked respiratory acidosis.

Given that such profound cranial nerve involvement and apnea is atypical our workup was extended to exclude less common causes of ICU-acquired weakness. An MRI scan of the brain was unremarkable. The cerebrospinal fluid white blood cell count, protein and glucose concentration were within normal limits. Polymerase chain reaction testing for CSF viruses and extensive testing for autoimmune neurological diseases and GBS variants such as: GM1, GM2, GM3, GD1a, GD1b, GQ1b, GT1b, NMDA-NR1 antibodies as well as a comprehensive autoimmune paraneoplastic disease profile (see <http://mitogen.ca/diagnostic.html> for a full list) was negative.

An ice test and neostigmine trial failed to provide any improvement. IVIG was administered on a provisional basis given the severity of the disease, while pending the above workup for GBS and associated variants. It had no effect.

An electromyogram and nerve conduction studies were performed twice during this patient’s admission, after 3 weeks and 5 weeks in hospital. Both showed similar results. There was minor evidence of an underlying polyneuropathy (absent right median sensory response) and mildly-to-markedly reduced amplitude of compound muscle action potentials, consistent with a primary myopathic process. No evidence of neuromuscular junction dysfunction was found.

Following the above results, a left deltoid muscle was performed. It showed a loss of myosin thick filaments and type 2 atrophy. Electron microscopy demonstrated small angulated fibers and the ultrastructural loss of myosin thick filaments; these features are consistent with critical illness myopathy.

After a total of 8 weeks in the ICU, the patient’s condition as well as level of consciousness deteriorated, in part due to an infected sacral pressure ulcer. Due to this decline in clinical status the patient’s family requested that he be made palliative. An autopsy was preformed. The muscle procured

at the time of autopsy showed extensive artifact and did not add any additional diagnostic information. No histological abnormality was identified upon examination of brain, spinal cord and phrenic nerve tissue by a neuropathologist.

Discussion

Acquired weakness in the ICU setting is common and can be the result of several disease processes. Critical illness myopathy is known to result in quadriplegia in severe cases. Facial weakness and ophthalmoplegia are rare, but well documented manifestations of severe critical illness myopathy.^{1,2} To our knowledge, there have been no published cases where the complete absence of respiratory effort was observed.

Involvement of the diaphragm in addition to skeletal muscle has been demonstrated before in patients with critical illness myopathy. It is known that patients with critical illness myopathy often require a longer duration of mechanical ventilation.¹

Supporting this is a recent electrophysiological study preformed on septic patients with greater than 14 days of mechanical ventilation and evidence of peripheral critical illness myopathy and/or polyneuropathy. In 89% of these patients there was coexisting evidence of critical illness myopathy and/or polyneuropathy found during electrophysiological study of the diaphragm.³

Given the above studies and our investigations, we were left to conclude that not only was critical illness myopathy the cause of this patient’s quadriparesis and ophthalmoplegia but respiratory muscle paralysis as well. The observed lack right median nerve response on the nerve conduction study may represent a neuropraxia caused by the patient’s prolonged and severe immobility.

In severe cases characterized by quadriparesis or quadriplegia and prolonged ventilation there is cause for guarded optimism in regards to recovery. Recovery is slow and on the order of weeks to months, with some patients failing to fully recover. Those who survive their hospitalization appear to have a moderate chance of full or partial recovery. A literature review identified a total of 263 patients who had a diagnosis of critical illness myopathy and/or polyneuropathy and some form of outpatient follow-up. The mean duration of follow-up was 3-6 months. At the time of follow-up, 68% (180 patients) regained the ability to walk and breathe independently, while 28% (74 patients) were unable to do both.²

The distinction between isolated critical illness myopathy, polyneuropathy or a combination of both may also influence prognosis. Follow-up studies of small numbers of patients have elucidated differences between these diseases. Critical illness

myopathy patients tended to recover quicker (3–6 months) while those patients with critical illness polyneuropathy or both recovered over a longer time period (6–12 months). Similarly, these patients were more likely to have persistent deficits at one year.^{4,5}

Conclusion

Critical illness myopathy is common in the critically ill and is a common cause of weakness and prolonged ventilator dependence in the ICU setting. This case is the first described in which the findings of ophthalmoplegia, severe quadriparesis and apnea were all attributable to severe critical illness myopathy. Even in severe cases, there is potential for recovery after a period of several months.

References

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Figure 1- Nerve Conduction Studies

Left: Compound muscle action potential (CMAP) obtained for the right abductor pollicis brevis muscle at the level of wrist and elbow (left). Amplitudes of the action potentials are markedly decreased at 0.3mV and 0.1mV respectively.

Right: CMAP obtained for the abductor hallucis brevis muscle at the levels of ankle, and knee. Again, amplitudes of the action potentials are markedly decreased at 0.2mV and 0.1mV respectively.

O = onset of CMAP, P = peak of CMAP

Figure 2 - Deltoid Muscle Biopsy

Hematoxylin-eosin (A) and neuron specific enolase (B) staining showing acute neurogenic features, including frequent small angulated myofibers (black arrows), positive neuron specific enolase histochemistry (darkly staining fibers marked by asterisks) as well as myopathic features including split fibers (white arrows) and type 2 myofiber atrophy (not shown). Trichrome stains (C) demonstrated that several myofibers contain fine sarcomeric repeats (black arrows), while others have lost these repeating units (white arrows). Electron microscopy (D - F) shows a nearly normal myofiber (D) with its Z bands, M lines, and both I and A bands, a moderately affected area (E) having a paucity of thick filaments in the A band, and a more severely affected area (F) showing only remaining Z-bands with a marked paucity of thick myosin filaments. The small, angulated fibers and the ultrastructural loss of myosin thick filaments are characteristic features of critical illness myopathy.