

Critical Illness Neuropathy and Myopathy

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Severe weakness with respiratory failure is a serious and common complication of critically ill patients in the intensive care unit setting. Recent studies have elucidated 2 entities characterized by severe weakness that occur as a result of these circumstances: critical illness neuropathy and critical illness myopathy. Both are the result of a serious illness, in contrast to weakness arising from a primary neurological disorder that results in admission to an intensive care unit (eg, myasthenic crisis, Guillain-Barré syndrome, rhabdomyolysis, or botulism).¹ Critical illness neuropathy and myopathy are difficult to distinguish from each other on purely clinical grounds, although certain clues may make one more likely. Nerve conduction studies, needle electromyography, and muscle biopsy are often necessary to make a firm diagnosis.

CRITICAL ILLNESS NEUROPATHY

As initially described by Bolton et al² in 1984, critical illness neuropathy is a sensorimotor polyneuropathy that is often a complication of sepsis and multiorgan failure, occurring in 70% of such patients. The severity of the underlying illness, the frequently associated encephalopathy, and the use of nondepolarizing neuromuscular blocking agents and ventilator support make recognition of the onset of the neuropathy difficult. It usually becomes apparent when the patient cannot be weaned from the ventilator. Flaccid weakness of the extremities, often severe, and loss of tendon reflexes are associated findings.³

Critical illness polyneuropathy is primarily a distal axonopathy in which distal degeneration of both motor and sensory axons, without inflammation, occurs. The underlying cause of the axonal degeneration may relate to a lack of vascular autoregulation and increased microvascular permeability resulting in endoneurial edema and capillary occlusion.^{2,3} Electrophysiological studies show reduction or absence of both compound muscle and sensory nerve action potentials, fibrillations, and loss of motor unit potentials with a maximal effort. Significant slowing of nerve

conduction or nerve conduction blocks are not expected findings and, if present, would implicate other diagnostic possibilities, eg, Guillain-Barré syndrome. Reduction of diaphragmatic compound muscle action potentials and the presence of fibrillations of chest wall muscles reflect the weaning difficulties.^{2,3}

The differential diagnosis includes Guillain-Barré syndrome, acute porphyria, botulism, myasthenic crisis, prolonged effect of nondepolarizing neuromuscular blocking agents, and critical illness myopathy. Multiorgan failure, sepsis, and critical illness polyneuropathy have a mortality rate of 50%. The neuropathy shows spontaneous improvement, with resolution of the underlying illness, but recovery may be limited or absent when the neuropathy is severe. Physical therapy is the only effective rehabilitation therapy available.³

CRITICAL ILLNESS MYOPATHY

Critical illness myopathy is underrecognized because it has a clinical appearance that is similar to critical illness polyneuropathy. It has been referred to by a number of different terms in the literature, including *acute myopathy*,⁴ *acute quadriplegic myopathy*,⁵ *critical care myopathy*,⁶ *acute necrotizing myopathy*,⁷ and *acute myopathy with selective loss of myosin filaments*.⁸ Muscle bi-

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opsy is usually necessary to firmly establish the diagnosis. The most common predisposing condition is an acute respiratory disorder, such as acute respiratory distress syndrome,⁸⁻¹⁰ pneumonia,⁸⁻¹⁰ or severe asthma in conjunction with the use of high-dose intravenous steroids, nondepolarizing blocking agents, and aminoglycosides.^{4,5,9-11} Other predisposing conditions include liver¹² and lung transplantation,^{13,14} hepatic failure,¹⁰ and acidosis.^{8,13}

The pathological features of critical illness myopathy are somewhat complex. Light microscopy commonly shows angulated atrophic myofibers that are predominantly type 2, with basophilic cytoplasm on hematoxylin-eosin stain.^{5,9,11,13,15} Associated vesicular nuclei and positive staining with alkaline phosphatase suggest that regeneration is occurring.⁹ Decreased or absent myosin adenosine triphosphatase staining of atrophic fibers may be localized or maximal in the center of myofibers.^{4,5,8,11-14} Myofiber necrosis is usually mild but is occasionally severe.¹⁰ Electron microscopy may show widespread loss of all filaments^{4,13} but often reveals selective loss of myosin filaments with relative sparing of actin filaments and Z discs.^{5,6,8,11-15} The electron microscopic findings seem to correlate with the altered staining of atrophic fibers with adenosine triphosphatase staining.

Selective myosin filament loss can be produced in the denervated soleus muscle of rats receiving simultaneous high-dose corticosteroids.¹⁶ The combination of a superimposed polyneuropathy (occurring in a number of the patients) or the use of nondepolarizing neuromuscular blocking agents in conjunction with high-dose intravenous corticosteroid therapy may simulate the rat experimental model and result in the selective myosin filament loss.⁶ The expression of steroid receptors is enhanced in denervated muscle, making myofibers potentially more vulnerable to corticosteroid injury.¹⁷

The clinical diagnosis of critical illness myopathy is challenging, and there are few distinctive features, other than muscle biopsy, that help to distinguish it from critical illness polyneuropathy. The clinical features are similar. The fact that both entities may occur concurrently increases the difficulty.^{4,5,6,9,10,12}

The presence of normal sensory nerve action potentials in the face of small compound muscle action potentials suggests that critical illness myopathy is present,^{5,10,12-14} but small or absent sensory nerve action potentials,^{4,5,6,9,12,15} indicative of the neuropathy, do not exclude the latter diagnosis. Slowed nerve conduction or conduction blocks are not consistent with either critical illness neuropathy or myopathy. Small, brief, polyphasic motor unit potentials with a good interference pattern despite muscle weakness are an indication that a myopathic process is present.^{4,5,9-11,13-15} These motor unit potential changes might also occur with delayed neuromuscular junction blockade from the use of nondepolarizing blocking agents and require routine 2-Hz nerve stimulation studies as part of the electrophysiological evaluation. Inexcitability of muscle to direct electrical stimulation has recently been suggested as an additional criterion.¹⁴ Fibrillations on needle electromyography may be absent or plentiful, and creatine kinase levels are often normal, making these features of little value in differentiating the myopathy from the neuropathy. Muscle biopsy remains the ultimate diagnostic study.

The prognosis of critical illness myopathy depends on the severity of the underlying illness and age of the patient. Young patients with status asthmaticus may have complete recovery in 2 to 3 months.^{4,11}

CONCLUSIONS

Critical illness neuropathy and critical illness myopathy, either singly or in combination, are a common complication of critical illnesses. Both disorders may lead to severe weakness and require mechanical ventilation. Multiorgan failure and sepsis predispose to the neuropathy, while a variety of serious problems (eg, pneumonia, severe asthma, and liver or lung transplantation) and the concomitant use of high-dose intravenous corticosteroids and nondepolarizing neuromuscular blocking agents predispose to the myopathy. Minimizing the use of corticosteroids and nondepolarizing neuromuscular blocking agents in the critical illness setting may prove helpful in preventing the occurrence of these disorders. The prognosis is directly related to the age of the patient and the seriousness of the underlying illness.

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