Bangladesh Crit Care J March 2013; 1: 45-48

Review Article

Electrodiagnostic Test: An Important Tools in the Evaluation of Critical Illness Neuromuscular Complications

Aminur Rahman[1], Rumana Habib[2], Nirmalendu Bikash Bhowmik[3], Amirul Haque[4]

Introduction:

Critical illness neuromuscular disorders are more common than might first think. The literature is full of cases of individuals who have survived being critically ill only to emerge with profound neuromuscular dysfunction, developing in e"25 percent of patients who are in the intensive care unit (ICU) and ventilated for at least 7 days[1].

Weakness is partly a consequence of improved survival in patients with multiorgan failure and sepsis, but is also a consequence of treatments administered in the ICU.

Spitzer et al reported that 62% of patients with prolonged weaning from ventilation had an unsuspected neuromuscular disorder[2]. However, patients who become critically ill and survive their ICU stay often go on to have significant impairment directly related to a critical illness neuromuscular disorder. DeJonghe [3] reported on 95 patients who were ventilated for greater than 7 days and went on to awaken and improve. Familiarity with critical illness disorders assists the intensive care specialist in designing and implementing ventilatory weaning strategies. Sir William Osler described a syndrome of muscular wasting in an individual who had survived sepsis[4]. In the 1960s and 1970s unexplained neuropathies were described in patients who had been in a coma or who had been seriously burned or septic [5, 6, 7]. In 1977 Bischoff and Rich described a polyneuropathy associated with gentamicin toxicity[8]. The term critical illness polyneuropathy was not coined until the early 1970s and 1980s[9, 10].In 1998 Coakley et al[11] performed Electrodiagnostic(EDX) studies on 44 patients who were critically ill and required an ICU stay greater than 7 days. These EDX studies revealed that only 9% of patients were normal; 43% of these patients had mixed sensory and motor nerve dysfunction.

1. Dr. Aminur Rahman, Assistant Professor,
2. Dr. Rumana Habib, Registrar
3. Dr. Nirmalendu Bikash Bhowmik, Associate Professor
4. Prof. Amirul Haque, Professor

All the authors are working in the department of Neurology, BIRDEM General Hospital, 122 Kazi Nazrul Islam Avenue, Shahbag, Dhaka.

Corresponding Author : Dr. Aminur Rahman, Assistant Professor, Department of Neurology, BIRDEM General Hospital, 122 Kazi Nazrul Islam Avenue, Shahbag, Dhaka-100, Email: aminurdr@gmail.com. Cell Phone: +8801715327378

Diagnostic Considerations

The patient with a critical illness neuromuscular disorder typically presents when the health care team determines that there is difficulty weaning from the ventilator[12]. Unfortunately, even in cases with significant weakness or sensory abnormality, the critical illness neuromuscular disorder can remain undiagnosed[13].

When seeing the patient who is critically ill and weak for an EDX medicine consultation, the clinician should recall the broad differential diagnosis for individuals with weakness. The articles by Wijdicks et al[14, 15] provide a nice mnemonic of the word muscle to support remembering the different diagnostic entities that should be considered when evaluating a patient with weakness (Table-I).

Table-I

Mnemonic for remembering differential diagnosis of weakness in the critically ill patients.

M edications (IV contocosteroids, panucuronium, vacuronium, metronidazole
U ndiagnosed neuromuscular disorders (PM DM GBS ALS MG LEMS)
S pinal cord damage
C ritical illness neuromuscular disorders
L oss of muscle mass
E lectrolytes disorders
S ystemic illness

PM-Polymyositis, DM-Dermatomyositis, GBS-Gullaine-Bare syndrome, ALS-Amyotrophic lateral sclerosis, MG-Myasthenia Gravis, LEMS- Lambert –Eton-Myasthenic syndrome

The unexpected failure of ventilatory weaning, accelerated peripheral muscle atrophy, or an inability to hold the head or a limb off the bed should be clues to the health care team that a critical illness neuromuscular disorder is present. It was also found to be independently predicted by the development of a critical illness neuromuscular disorder[16].

Etiologic Considerations

The cause of critical illness neuromuscular disorders is not clear, and it is likely multifactorial. One thing that has

become quite clear is that the systemic inflammatory response syndrome (SIRS) plays a significant role[17]. The term SIRS• was coined in 1992 during a consensus conference between the Society of Critical Care Medicine and the American College of Chest Physicians (ACCP) [18]. Bolton[17] has highlighted the significant role that the SIRS has in the development of critical illness neuromuscular disorders. This is extremely important as the different critical illness neuromuscular disorders can have very different functional outcomes[19].

It is also clear that critical illness neuromuscular disorders develop in the pediatric population. The spectrum of critical illness disorders mimics those found in adults[20].

Critical illness Myopathy

The most common form of ICU-acquired myopathy is critical illness myopathy (CIM). This disorder is also known by other names, including acute quadriplegic myopathy and thick filament myopathy

Epidemiology and risk factors

In prospective studies, approximately one-third of patients with status asthmaticus or chronic obstructive pulmonary disease and 7 percent who receive a liver transplant develop CIM[21,22].

The strongest risk factor for CIM is the use of IV glucocorticoids in the ICU setting, and there is some correlation between the likelihood of occurrence and severity of disease with glucocorticoid dose[21,23,24-26]. The length of chemical paralysis, when used in conjunction with corticosteroids, has been associated with the development of thick filament Myopathy[27, 28]. Douglass et al [29] have shown that the serum CK level is elevated in 76% of patients with severe asthma exacerbations who require ventilation. They also found that 36% of these individuals go on to develop a symptomatic myopathy. Based on the work of Dubois and Almon[30], there has been some association made with the development of thick filament myopathy in patients who receive corticosteroids.

Clinical features of CIM

Critical illness myopathy usually begins several days after IV glucocorticoid treatment is initiated. The most common presenting features of CIM are[31, 32, 33, 34-36] flaccid quadriparesis that may affect proximal more than distal muscles, Failure to wean from mechanical ventilation.

EDX findings in CIM

The EDX study of CIM are normal to low motor amplitudes with occasional broadening of the compound muscle action potential[36,37]. Phrenic motor amplitudes may also be low. Sensory responses are normal or only mildly reduced, Depending upon the degree of weakness, observation of the recruitment of motor unit potentials (MUPs) may be difficult. MUPs are short in duration, low in amplitude, and sometimes polyphasic[38]. Some muscles exhibit electrical inexcitability to direct muscle stimulation [39,40] .

Diagnosis of CIM

The diagnosis of CIM is suspected in patients who have particularly flaccid muscle weakness and ventilatory failure, in the setting of critical illness. Exposure to intravenous glucocorticoids is an important clue. An elevation in serum creatine kinase is usually present but, among patients treated with intravenous glucocorticoids, can occur in the absence of CIM[29].The diagnosis of CIM can sometimes be confirmed by EDX testing (Table-II) with nerve conduction studies (NCS) and EMG. Muscle biopsy can provide additional diagnostic information.

Table-II

Suggested diagnostic criteria for Critical illness Myopathy

The major diagnostic features of CIM are

- Sensory nerve amplitudes >80 percent of the lower limit of normal in two or more nerves on NCS
- Needle EMG with short-duration, low-amplitude MUPs with early or normal full recruitment, with or without fibrillation potentials
- Absence of a decremental response on repetitive nerve stimulation
- Muscle histopathologic findings of myopathy with myosin loss

Supportive diagnostic features of CIM are

- Motor amplitudes <80 percent of the lower limit of normal in two or more nerves without conduction block on NCS
- Elevated serum CK (best assessed in the first week of illness)
- Muscle inexcitability on direct muscle stimulation

Critical Illness Polyneuropathy

CIP is an acute, diffuse, mainly motor peripheral neuropathy due to axonal dysfunction, clinically presented as sensory-motor polyneuropathy with relative preservation of cranials nerves function. The predominance of motor involvement in CIP was best described by Hund et al[41] in a study of 28 patients with moderate to severe CIP. CIP typically occurs in patients who have sepsis or multiorgan system dysfunction. The incidence has been reported to be 50% to 75% in individuals who meet these criteria[17,42,43]. Cerebrospinal fluid studies during this period have been reported as normal except for very mild elevations in protein[19, 43, 44].

In 1987 Zochodne et al[45] reported on 19 patients with CIP. They found moderate to severe weakness in 47% of patients, sensory disturbance in 47% of patients, and reduced or absent reflexes in 68% of patients. Consistent with current studies, they found a mortality rate of 58% in their cohort[45]. Hyperglycemia and hypoalbuminemia have both been associated with the development of CIP[42, 45]. There has been an association made with individuals who are receiving parenteral nutrition and the development of CIP and multiorgan system dysfunction[46].

EDX findings in CIP

The EDX findings in CIPN are typical of an axonal sensory and motor peripheral neuropathy. Phrenic motor amplitudes are commonly reduced.Spitzer et al[2] have proposed a way to categorize the EDX findings in CIPN as a measure of severity (Table-III). These categories of severity are expected to reflect the prognosis for recovery from the neuropathy.

Table-III

Classification of findings in CIP

Severe
SNAP absent, Fibrillation potential in all muscles groups & multiple CMAP amplitude less than 1mV
Moderate
SNAP amplitude <5microV, Multiples CMAP amplitude between 1mV- 3mV, Fibrillation and positive sharp waves present
Mild
SNAP amplitude >5microV, CMAP amplitude > 3mV

Muscle biopsy typically shows grouped fiber atrophy, especially when the neuropathy has been present for a significant period of time[47].

Diagnosis of CIP

It is often difficult to distinguish CIP from CIM or from combined CIM and CIP on the basis of clinical features and neurologic examination findings alone. The diagnostic criteria are shown in Table-IV.

Table-IV

Diagnostic criteria for CIP

Major features of CIP are
• Setting of critical illness, particularly if complicated by sepsis, multiorgan failure, and the systemic inflammatory response syndrome
• Difficulty weaning from ventilator that is not related to cardiopulmonary causes
• Possible limb weakness
• EDX evidence of axonal motor and sensory polyneuropathy
Features favoring the diagnosis
• Sensory and motor nerve amplitudes <80 percent of the lower limit of normal in two or more nerves on nerve conduction studies
• Absence of conduction block or prolongation of F-waves
• Needle EMG with reduced recruitment of normal motor unit potentials (MUPs) (early) followed by fibrillation potentials and reduced recruitment of long-duration, high-amplitude MUPs (after weeks)
• Absence of a decremental response on repetitive nerve stimulation
Supportive features
• Normal cerebrospinal fluid protein
• Normal serum creatine kinase

Management

There is no current effective treatment for critical illness neuromuscular disorders. Prompt identification and management of underlying conditions such as sepsis or multiorgan system dysfunction will likely result in a decreased incidence of these syndromes. Early studies suggested that the use of intravenous immunoglobulin (IVIG) may help to protect against the development of severe CIP[48]. There is evidence that intensive insulin therapy (target blood glucose 80 to 110 mg/dL [4.4 to 6.1 mmol/L]) may lower the incidence of CIM and CIP among critically ill patients who remain in the intensive care unit for seven or more days[49,50] .

Outcome

The mortality rate in critical illness neuromuscular disorders ultimately depends on the underlying conditions, and the development of neuromuscular pathology does not worsen it. Typically many patients who develop these syndromes die from the multiorgan system dysfunction or sepsis. Throughout the recovery process, the quality of life is often impaired, and in some cases the severe neuromuscular weakness can contribute to later deaths.

References

1. De Jonghe B, Sharshar T, Lefaucheur JP, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA 2002; 288:2859.
2. Spitzer AR, Giancarlo T, Maher L, et al. Neuromuscular causes of prolonged ventilator dependency. Muscle Nerve 1992;15:682-686.
3. DeJonghe B, Sharshar T, Lefaucheur JP, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA 2002;288: 2859-2867.
4. Beck TP. The expanding spectrum of critical illness polyneuropathy. Crit Care Med 1996;24: 1282-1283.
5. Mertens HG. Disseminated neuropathy following coma. Nervenarzt 1961;32:71-79.
6. Henderson B, Koepke GH, Feller I. Peripheral polyneuropathy among patients with burns. Arch Phys Med Rehabil 1971;52:149-151.
7. Olsen CW. Lesions of peripheral nerves developing during coma. JAMA 1956;160:39-41.
8. Bischoff A, Meier C, Roth F. Gentamicin neurotoxicity. Schweiz Med Wochenschr 1977;107:3-8.
9. Bolton CF, Gilbert JJ, Hahn AF, Sibbald WJ. Polyneuropathy in critically ill patients. J Neurol Neurosurg Psychiatry 1984; 47:1223.
10. Roelofs, R, Cerra, F, Bilka, N, et al. Prolonged respiratory insufficiency due to acute motor neuropathy: A new syndrome?. Neurology 1983; 33:s240.
11. Coakley JH, Yarwood GD, Hinds CJ, et al. Patterns of neurophysiological abnormality in prolonged critical illness. Intensive Care Med 1998;24:267-271.

12. Leijten FSS, DeWeerd AW, Poortvliet DCJ, et al. Critical illness polyneuropathy in multiple organ dysfunction syndrome and weaning from the ventilator. Intensive Care Med 1996;22:856-861.

13. Jarrett SR, Mogelof JS. Critical illness neuropathy: diagnosis and management. Arch Phys Med Rehabil 1995;76:688-691.

14. Wijdicks EF, Litchy WJ, Harrison BA, et al. The clinical spectrum of critical illness polyneuropathy. Mayo Clin Proc 1994;69:955-959.

15. Wijdicks EF, ed. Neurologic complications of critical illness, 2nd ed. New York: Oxford University Press, 002:69.

16. De Jonghe B, Bastuji-Garin S, Sharshar T, et al. Does ICU-acquired paresis lengthen weaning from mechanical ventilation? Intensive Care Med 2004; 30:1117-1121.

17. Bolton CF. Sepsis and the systemic inflammatory response syndrome: Neuromuscular manifestations. Crit Care Med 1996, 24:1408-1416.

18. Members of the American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992;20:864-874.

19. Bolton CF. Neuromuscular manifestations of critical illness. Muscle Nerve 2005; 32:140-163.

20. Tabarki B, Coffinieres A, Van den Bergh P, et al. Critical illness neuromuscular disease: clinical, electrophysiological, and prognostic aspects. Arch Dis Child 2002;86:103-107.

21. Amaya-Villar R, Garnacho-Montero J, García-Garmendía JL, et al. Steroid-induced myopathy in patients intubated due to exacerbation of chronic obstructive pulmonary disease. Intensive Care Med 2005; 31:157.

22. Campellone JV, Lacomis D, Kramer DJ, et al. Acute myopathy after liver transplantation. Neurology 1998; 50:46.

23. Douglass JA, Tuxen DV, Horne M, et al. Myopathy in severe asthma. Am Rev Respir Dis 1992; 146:517.

24. Shee CD. Risk factors for hydrocortisone myopathy in acute severe asthma. Respir Med 1990; 84:229.

25. Lacomis D, Giuliani MJ, Van Cott A, Kramer DJ. Acute myopathy of intensive care: clinical, electromyographic, and pathological aspects. Ann Neurol 1996; 40:645.

26. Panegyres PK, Squier M, Mills KR, Newsom-Davis J. Acute myopathy associated with large parenteral dose of corticosteroid in myasthenia gravis. J Neurol Neurosurg Psychiatry 1993; 56:702.

27. Danon MJ, Carpenter S. Myopathy with thick filament (myosin) loss following prolonged paralysis with vecuronium during steroid treatment. Muscle Nerve 1991;14:1131-1139.

28. Al-Lozi MT, Pestronk A, Yee WC, et al. Rapidly evolving myopathy with myosin-deficient muscle fibers. Ann Neurol 1994;35:273-279.

29. Douglass JA, Tuxen DV, Horne M, et al. Myopathy in severe asthma. Am Rev Respir Dis 1992;146:517.

30. Dubois DC, Almon RA. A possible role for glucocorticoids in denervation atrophy. Muscle Nerve 1981;4:370-373.

31. Campellone JV, Lacomis D, Kramer DJ, et al. Acute myopathy after liver transplantation. Neurology 1998; 50:46.

32. Lacomis D, Giuliani MJ, Van Cott A, Kramer DJ. Acute myopathy of intensive care: clinical, electromyographic, and pathological aspects. Ann Neurol 1996; 40:645.

33. Showalter CJ, Engel AG. Acute quadriplegic myopathy: analysis of myosin isoforms and evidence for calpain-mediated proteolysis. Muscle Nerve 1997; 20:316.

34. Bolton CF, Young GB, Zochodne DW. The neurological complications of sepsis. Ann Neurol 1993; 33:94.

35. Hanson P, Dive A, Brucher JM, et al. Acute corticosteroid myopathy in intensive care patients. Muscle Nerve 1997; 20:1371.

36. Zochodne DW, Ramsay DA, Saly V, et al. Acute necrotizing myopathy of intensive care: electrophysiological studies. Muscle Nerve 1994; 17:285.

37. Goodman BP, Harper CM, Boon AJ. Prolonged compound muscle action potential duration in critical illness myopathy. Muscle Nerve 2009; 40:1040

38. Road J, Mackie G, Jiang TX, et al. Reversible paralysis with status asthmaticus, steroids, and pancuronium: clinical electrophysiological correlates. Muscle Nerve 1997; 20:1587.

39. Rich MM, Bird SJ, Raps EC, et al. Direct muscle stimulation in acute quadriplegic myopathy. Muscle Nerve 1997; 20:665.

40. Allen DC, Arunachalam R, Mills KR. Critical illness myopathy: further evidence from muscle-fiber excitability studies of an acquired channelopathy. Muscle Nerve 2008; 37:14.

41. Hund E, Genzwurker H, Bohrer H, et al. Predominant involvement of motor fibers in patients with critical illness polyneuropathy. Br J Anaesth 1997;78:274-278.

42. Witt NJ, Zochodne DW, Bolton CF, et al. Peripheral nerve function in sepsis and multiple organ failure. Chest 1991;99:176-184.

43. Nates JL, Cooper DJ, Day B, et al. Acute weakness syndromes in critically ill patients: a reappraisal. Anaesth Intens Care 1997;25:502-513.

44. Hund E, Fogel W, Krieger D, et al. Critical illness polyneuropathy: clinical findings and outcomes of a frequent cause of neuromuscular weaning failure. Crit Care Med 1996;24:1328-1333.

45. Zochodne DW, Bolton CF, Wells GA, et al. Critical illness polyneuropathy: a complication of sepsis and multiple organ failure. Brain 1987;110:819-842.

46. Waldhausen E, Mingers B, Lippers P, et al. Critical illness polyneuropathy due to parenteral nutrition. Intensive Care Med 1997;23:922-923.P.375

47. Kerbaul F, Brousse M, Collart F, et al. Combination of histopathological and electromyographic patterns can help to evaluate functional outcome of critical ill patients with neuromuscular weakness syndromes. Critical Care 2004;8:358-365.

48. Mohr M, Englisch L, Roth A, et al. Effects of early treatment with immunoglobulin on critical illness polyneuropathy following multiple organ failure and gram-negative sepsis. Intensive Care Med 1997;23:1144-1149.

49. Van den Berghe G, Schoonheydt K, Becx P, et al. Insulin therapy protects the central and peripheral nervous system of intensive care patients. Neurology 2005; 64:1348.

50. Hermans G, Wilmer A, Meersseman W, et al. Impact of intensive insulin therapy on neuromuscular complications and ventilator dependency in the medical intensive care unit. Am J Respir Crit Care Med 2007; 175:480.