Novel management of critically induced polyneuropathy in intensive care patients: A case report of two patients

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Abstract
There has been tremendous growth in patients requiring critical care with severe infections. During a prolonged stay in the intensive care unit (ICU), patients develop critical illness polyneuropathy (CIP). The early identification of neurological involvement requires special attention during ICU care. We describe two cases who developed complete motor weakness after a prolonged stay in ICU. Patients were successfully managed with pyridostigmine and testosterone hormonal therapy initially and later with pyridostigmine only. The present case series highlights the need for early recognition, assessment, and novel management of CIP in ICU patients. However, the role of nutrition, physiotherapy, and supportive care is equally essential for the successful outcome in these patients.

Keywords: Critical illness polyneuropathy, intensive care unit, pyridostigmine, testosterone

Introduction
There has been tremendous growth in patients requiring critical care with severe infections. These patients during prolonged intensive care unit (ICU) stay develop critical illness polyneuropathy (CIP). The incidence of CIP is 70% in individuals with sepsis or systemic inflammatory response syndrome and 100% in multiple organ failure patients. It is noted that 25% of the ICU patients developed weakness and 49-84% electrophysiological abnormalities. We describe two cases who developed complete motor weakness after a prolonged stay in ICU and were successfully managed with pyridostigmine and testosterone hormonal therapy initially and later with pyridostigmine only. The present case series highlights the need for assessment and early management of CIP in ICU patients.

Case History

Case 1
A 45-year-old female with uncontrolled diabetes mellitus, high-grade fever, and severe abdominal pain presented to the emergency department of our hospital. The septic shock with severe metabolic acidosis was managed with broad-spectrum antibiotics, fluids, inotropes, and sodium bicarbonate correction. During an emergency, laparotomy pus was drained from the pelvis and peritoneal drain was placed. Postoperatively, the patient was shifted to ICU for the continuation of resuscitative measures. Lungs were ventilated with synchronized intermittent ventilation (SIMV), midazolam, and morphine infusion for sedation and analgesia; variable rate insulin infusion, blood and blood products were started. Initial investigations revealed deranged renal function test (RFT) (blood urea: 131 mg/dl, serum creatinine 3.9 mg/dl), hypoalbuminemia (2 gm/dl), and...
hypocalcemia (7.7 mg/dl). A chest X-ray revealed right side lung pleural effusion. During two months, the patient received antibiotics according to culture and sensitivity (ceftriaxone, imipenem, metronidazole), high inotropic support and several attempts to wean from the ventilator. No neuromuscular drugs were administered. During this course of ICU stay, the patient developed motor weakness in all four limbs. The power in lower limbs was 2/5 and 3/5 in the upper limbs. Nerve conduction velocity (NCV) study suggested severe sensorimotor neuropathy. On neurology consultation, oral pyridostigmine 30 mg thrice daily and intramuscular (IM) testosterone analogue 250 mg (Inj. SUSTANON®, Aspen, Dublin) once in every five days was started. There was a gradual improvement in patient’s motor power over a few weeks and the patient was discharged with a tracheostomy tube in situ. However, the patient had sudden aspiration at home and died after two months of discharge from the hospital.

Case 2

An 18-year-old male with no known comorbidities was admitted to a private hospital with shortness of breath. Initially, he was managed on high flow nasal cannula and non-invasive ventilation. He was diagnosed with scrub typhus IgM positive before presenting to the present hospital. The high resolution computed tomography of the chest showed areas of consolidation and ground-glass opacities in bilateral lungs with lower lobe predominance. The echocardiography was normal. The patient developed acute respiratory distress syndrome (ARDS) and septic shock. As per records of referring hospital, the patient had a witnessed cardiac arrest and return of spontaneous circulation was achieved in a few minutes. Magnetic resonance imaging (MRI) of the brain was done with the findings suggestive of acute disseminated encephalomyelitis (ADEM) and hypoxic encephalopathy. Electroencephalogram (EEG) showed low voltage β activity. After one month, the patient was shifted to ICU of the present tertiary care hospital. The patient was hemodynamically stable with a tracheostomy tube in situ. However, the patient had sudden aspiration at home and died after two months of discharge from the hospital.

Discussion

Prolonged ICU stay and ventilator dependence are seen due to respiratory muscle and limb weakness. Early prevention and intervention in the initial 48-72 hours of the disease may be more effective to prevent the development of the CIP. Females are more vulnerable than men because of less muscle mass. The most common risk factors for CIP are malnutrition, sepsis, multi-organ failure, prolonged mechanical ventilation, use of neuromuscular blocking drugs, hyperglycemia, and insulin resistance. Mechanical ventilation carries a complex risk factor, because of ventilator-induced diaphragmatic weakness and injury.[7] In case 1, the risk factors involved in CIP were sepsis, hyperglycemia, deranged renal function test, prolonged ventilation, and prolonged use of inotropes. In case 2, the risk factors for CIP were prolonged mechanical ventilation, muscle immobilization, muscle atrophy, and cardiac arrest. An improvement was observed in our patients following hormonal testosterone derivatives and pyridostigmine therapy.

Testosterone, an anabolic steroid has been shown to increase weight, reduce morbidity, and increase inspiratory muscle strength helping in early weaning off from the ventilator.[8] Researchers have reported a superior role of oral nutritional support with anabolic steroids in malnourished patients with alcoholic hepatitis, burn patients, and chronic obstructive pulmonary disease as compared to only nutritional support. It has been observed that despite similar weight gain in both the groups, patients receiving both nutritional support and anabolic steroids had larger improvement in respiratory muscle strength and improved functional capacity of the patient.[8,9] Anabolic steroids increase muscle protein synthesis and stimulate the growth hormone and insulin-like growth factors.[9]

Another important point is the time of administering testosterone (i.e., anabolic steroids), which should be in the recovery phase of illness in ICU patients. It implies that the patient should not have any ongoing organ support, inotropes or vasopressors administration, and no increasing inflammatory markers. Lowering of testosterone levels in critically ill patients is an energy conservation mechanism since the body is under
stress. The addition of anabolic steroids in the recovery phase after critical illness patients, assist them to regain their muscle strength with the addition of early mobility programs.\[10\]

Pyridostigmine is a carbamate inhibitor of acetylcholinesterase and is mainly used to treat myasthenia gravis. Pyridostigmine indirectly increases the concentration of acetylcholine at the neuromuscular junction and promotes increased cholinergic nicotinic receptor activation. The increase in acetylcholine levels in neuromuscular junctions improves motor tone. Ozyurek H et al. used pyridoxine and pyridostigmine for the treatment of vincristine-induced cranial and peripheral neuropathies in a 4-year-old boy who was diagnosed with B precursor acute lymphoblastic leukemia (ALL). During the treatment, the patient developed severe weakness in lower extremities, bilateral foot drop, and reduced deep tendon reflexes. The addition of pyridostigmine in the treatment resulted in clinical improvement of neuropathic signs of the patient more rapidly than those managed only by the elimination of vincristine.\[11\]

In addition, nutritional and supportive treatment reduced the patient’s ICU stay and improved the prognosis. In prolonged critical illness, there is an imbalance between catabolic and anabolic hormones that leads to the loss of lean body mass. CIP has medical, economical, and psychosocial adverse outcomes for the patient and community. There are limited medical interventions available now for the treatment.\[10\]

To conclude, patients with CIP were successfully managed with pyridostigmine and hormonal therapy initially and later with pyridostigmine only. The role of nutrition, physiotherapy, and supportive care is important for a successful outcome.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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