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Critical Illness Polyneuropathy Complicating Weil's Disease

KEYWORDS: Weil's disease, encephalopathy, flaccid quadriparesis, Critical illness Polyneuropathy.

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ABSTRACT *Weil's disease is characterized by variable combination of Jaundice, Acute kidney injury, hypotension and hemorrhage – most commonly involving the lungs. Critical illness Polyneuropathy comprises the neuromuscular syndrome of acute limb and respiratory weakness that commonly accompanies patients with multi organ failure and Sepsis. It is a major cause of difficulty in weaning off the patient from the Ventilator. It is usually an Axonal motor and sensory Polyneuropathy. Multi organ failure, Encephalopathy/coma, elevated serum glucose and reduced serum albumin are risk factors for development of Critical illness polyneuropathy. We report the case of 45 year old woman having Weil's disease with hepatic encephalopathy with respiratory failure who developed flaccid quadriparesis during stay in the hospital and posed great difficulty in weaning from Ventilator. Nerve conduction study confirmed diagnosis of critical illness neuropathy.*

INTRODUCTION :

Weil's disease is the most severe form of Leptospirosis characterized by Jaundice, acute kidney injury, hypotension, hemorrhage in the lungs, gastrointestinal tract, retroperitoneum, pericardium and brain.[1]

Critical illness Polyneuropathy refers to the most common PNS (Peripheral Nervous System) complication related to critical illness. It is seen in the setting of prolonged critical illness, Sepsis and multisystem organ failure. Neurologic findings include diffuse weakness, decrease of reflexes and distal sensory loss. Electrophysiological studies demonstrate a diffuse, Symmetric, distal axonal sensorimotor Polyneuropathy. The precise mechanism of Critical illness Polyneuropathy remains unclear. Cytokines, which are associated with Sepsis and SIRS are thought to play a role.[2] We report a case of Critical illness Polyneuropathy complicating Weil's disease with multi organ failure.

CASE REPORTS :

A 45 year old female patient referred from private hospital as a case of Leptospirosis with hepatic encephalopathy with respiratory failure. Patient had endotracheal tube in situ and was on ambu bag ventilation. She had history of fever with chills and rigors of 15 days duration, yellowness of eyes and urine of 6 days duration, breathlessness and altered Sensorium of 4 days duration. Clinical examination revealed a seriously ill patient with pulse rate- 130/min, Bp-100/70mmhg, Patient had pallar, icterus with bilateral pedal edema. Patient had poor spontaneous respiratory efforts and required Ventilatory support. She was disoriented to time, place and person, was moving all four limbs. The deep tendon reflexes were present and both plantars were flexor . There was no clinical sign of meningeal irritation. For further management patient was transferred to intensive care unit.

The lab investigations are shown in table 1. Other investigations include serum Lactate dehydrogenese 130u/l. INR – 1.97, corrected serum calcium 8.2 mg/dl, phosphorus 4.5 mg/dl. Serum immunoglobulin M (IGM) antibodies for leptospira were done, detected by enzyme linked immunoassay, paired samples were found to be positive in rising titers. Her HIV, HBsAg, Rapid malarial test (RMT), peripheral smear for malarial parasite and widal test were negative. Ultrasonography of the abdomen showed hepatosplenomegaly with mild ascites with bilateral mild pleural effusion, The kidneys were normal. Chest radiograph showed bilateral lower zone haziness with slight blunting of CP angle on right side. Ectrocardiogram showed sinus tachycardia.

Patient was started with Injection ceftriaxone, injection vitamin K, Syp lactulose, multi vitamin infusion and high bowel wash. 4 units of fresh frozen plasma to correct the coagulation defect. Considering her poor spontaneous respiratory efforts, she was put on VCV mode of ventilator. ABG was found to be normal. Few hours after admission in ICU, her condition deteriorated and she became unconscious, was responding to deep painful stimulation. Mechanical ventilation and treatment of hepatic encephalopathy continued. Sensing need of prolonged mechanical ventilation, planned tracheostomy was done on 2nd day of admission. Patient's consciousness improved on 4th day, Started obeying commands and recognized her son on day 5. On day 6 patient was fully alert, was shifted to SIMV mode of ventilator. During routine examination it was noticed that patient was not able to move her limbs since regaining consciousness. On motor system examination, patient did not have muscle wasting, had hypotonia and grade zero power in all four limbs with poor neck holding. DTR (deep tendon reflexes) were absent, plantar reflex was also absent bilaterally. Sensory system examination was normal. Clinical diagnosis was kept as pure motor flaccid quadriplegia. As patient already had folley's catheter in situ and was on intravenous fluids, it was not possible to comment on bowel-bladder involvement. Serum potassium, magnesium, calcium were found to be within normal limits. Meanwhile patient was shifted to CPAP and PSV mode of ventilation on trial basis, but could not sustain, become tachypneic and required shifting back to SIMV mode. The general condition started improving with stabilization of vital parameters and improvement in liver function and coagulation profile by 10th day of admission, but she remained

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quadriplegic and ventilator dependent. Repeated SBT (Spontaneous breath trials) failed and patient remained on SIMV mode of ventilator for another 10 days. Her creatinine phosphokinase levels were normal. EMG was normal. Nerve conduction study showed axonal degeneration with normal conduction velocities, suggesting critical illness polyneuropathy. By this time her Renal and liver functions improved but she remained ventilator dependent. On day 24 patient developed ventilator associated pneumonia with total Leukocyte count rising to 28000/cu mm. Culture showed Pseudomonas – sensitive to Meropenem, treated accordingly. Patient was able to maintain on CPAP and PSV mode (PSV-18) and over next three days, we could slowly decrease the Pressure support. On day 34, patient was kept on spontaneous respiration and managed to maintain her oxygen saturation. On day 36 the tracheostomy tube was removed and patient was shifted to general ward. MRI of cervical spine was done to rule out myelopathy, turned out to be normal. On day 38 the patient was discharged from the hospital. At the time of discharge she had improvement in weakness with Grade 2 power in limbs. 6 weeks after discharge when patient came to OPD for follow up, she was walking with support, had Grade 4 power in limbs and was doing well.

DISCUSSION :

Common presentations of Neuroleptospirosis include aseptic meningitis and meningo encephelitis. The less common neurological manifestations include myeloradiculopathy, myelopathy, guillain-barre syndrome like presentation, intracerebral bleed and cerebellar dysfunction.[1]

In the study on 'Primary neuroleptospirosis' by Panicker et al three patients had Guillain Barre syndrome like presentation.[3] Clinical report by Mumford et al on 'Leptospirosis presenting as a flaccid paraplegia' also had weakness of legs and retention of urine as primary presentation.[4] The patient in present case report developed quadriplegia during her stay in the hospital. The time lag between onset of illness and development of quadriplegia was 21 days. Hence the quadriplegia does not seem to be a manifestation of neuroleptospirosis.

Critical illness polyneuropathy is a complication of clinical disorders that are associated with progressive and uncontrolled systemic inflammation. These conditions include the systemic inflammatory response syndrome (SIRS), severe sepsis and multi-organ failure. Although common, these neuromuscular complications often go undetected because they are over shadowed by the more prominent clinical manifestations of the inciting conditions.[5] Although there may severe limb and trunkal involvement, the weakness usually becomes apparent only after the underlying illness begins to resolve. Similarly in the present case the weakness of limbs was discovered only after the patient recovered from hepatic encephalopathy. In many cases, the weakness is first discovered when a patient is unable to wean from mechanical ventilation. Distal muscle weakness and loss of deep tendon reflexes are usually found. Pain and paraesthesias are usually absent, critical illness polyneuropathy is often preceded by septic encephalopathy. [6] Elevated serum glucose levels and reduced serum albumin levels are risk factors for nerve dysfunction as is prolonged stay in intensive care unit. The onset of Polyneuropathy is variable occurring from 2 days to a few weeks after the onset of the inciting illness.[7]

The pathogenesis of critical illness polyneuropathy is not known. A prospective study by Witt and colleagues showed that the development of critical illness neuropathy was associated with hyperglycaemia and inversely related to hypoalbuminaemia.[8] Bolton has proposed a disturbance in the microvascular function in peripheral nerves to be responsible for the neuropathy. The primary axonal damage may be due to the involvement of axonal transport system; this fact may explain the predominantly distal nerve segment involvement. Moreover it is known that the blood nerve barrier shows increased permeability to histamine and serotonin. Several mediators of the septic syndrome are known to have histamine-like action. Circulating toxins could potentially gain access to the endoneural space and directly damage the axon. Additional theories include : (1) axonal degeneration due to glucose-induced phosphate depletion from parenteral nutrition with subsequent depletion of high energy phosphate compounds; (2) damage of neural microvasculature due to oxidative effects of parenterally administered lipids; (3) impaired transport of axonal proteins. [9]

Critical illness polyneuropathy must also be differentiated from other acute polyneuropathies, including Guillian Barre syndrome, neuropathies of metabolic origin (e.g., vitamin deficiency, hypophosphatemia, porphyria)and toxic effects of antibiotics (metranidazole, aminoglycosides or penicillin).

Electrophysiologic findings are those of a pure axonal degeneration, affecting motor than sensory fibers. Conduction velocities and distal latencies are relatively intact, but there is a reduction in the compound muscle and the sensory nerve action potentials.[8]

Nerve biopsy reveals axonal degeneration without evidence of demyelination or inflammation. Treatment is supportive, initially consisting of aggressive pulmonary hygiene and prevention of secondary complications of immobility such as skin breakdown and deep venous thrombosis. Hypoalbuminemia and hyperglycaemia should be corrected.

CONCLUSION :

Critical illness polyneuropathy should be suspected in all critically ill patients who develop limb & trunk weakness during their stay in hospital especially when the weaning from mechanical ventilation is difficult despite recovering from primary illness.

Table Showing Lab Investigations

Sr.No.	Parameter	Day 1	Day 5	Day 10	Day 15
1	Hemoglobin (g/dL)	8.3	7.8	9.1	9.3
2	Total Leukocyte count (cells/cubic mm)	10,300	18,400	13,800	11,000
3	Platelet count (cubic mm)	265000	280000	284000	280000
4	Blood urea mg/dL)	90	86	39	29
5	Serum Creatinine (mg/dL)	1.2	0.9	1.3	1.0
6	Total serum Bilirubin (mg/dL)	12.4	10.2	6.7	1.6
7	ALT u/L	102	86	36	31
8	AST u/L	84	93	52	36
9	Alkaline Phosphate u/L	238	192	227	124
10	Na+ (meq/L)	147	145	150	135
11	K+ (meq/L)	4.5	5.0	5.2	4.2
13	Serum Albumin (g/dL)	2.3	1.9	1.7	2.8

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