Hypophosphataemic neuropathy in a patient who received intravenous hyperalimentation

A malnourished patient that received intravenous hyperalimentation (IVH) without inorganic phosphate (IP) developed hypophosphataemia and acute sensorimotor neuropathy. F waves in the peripheral nerve trunk were absent or diminished, while nerve conduction velocities were nearly normal. The sural nerve biopsy revealed the presence of some subperineurial oedema and mild axonal atrophy. Prompt IP administration reversed the patients' neurological symptoms and normalised F waves. Our data suggest that hypophosphataemia plays a role in the pathogenesis of neuropathy that develops in patients following IVH without IP.

Intravenous glucose administration is the most common cause of hypophosphataemia in hospitalised patients.¹ While most of these cases are asymptomatic, severe hypophosphataemia, when combined with phosphorus depletion, can cause acute neuropathy that mimics Guillain-Barré syndrome. However, prompt IP administration can reverse this clinical condition. While there have been several reports of acute neuropathies caused by hypophosphataemia, most are anecdotal and no report has described an associated peripheral nerve pathology. Thus the clinical and pathological features of acute neuropathy that develops as a result of hypophosphataemia have not been well characterised.

Case report

A 60-year-old Japanese man who had suffered from diabetes for 5 years and a prior myocardial infarction was admitted to our hospital with melaena and diarrhoea. Colonoscopy confirmed a diagnosis of ulcerative colitis. Despite treatment with mesalamine and low dose prednisolone, the diarrhoea did not abate. On hospital day 30, the patient was started on IVH containing IP as his severe diarrhoea persisted and he became malnourished. On day 59, his serum

total protein was 4.5 mg/dl and his albumin was 1.6 mg/dl. To better facilitate the reversal of his malnourished state, his IVH formula was changed to one containing more calories (750 g glucose, 50 mEq sodium, 6 mEq magnesium, 6 mEq calcium, 98 mEq chloride, 20 mEq Zinc, amino acid and multivitamin preparations) but no IP. On day 66, he began to experience dysarthria and a tingling sensation in all four of his limbs and in the perioral region. He went on to develop muscle weakness and ataxia in all four limbs, which significantly impaired his ability to walk. Neurological examination revealed normal cognitive function, but moderate bilateral facial palsy, and severe dysarthria and dysphagia were present. Muscle strengths assessed by the Medical Research Council (MRC) score were 4/5 in the proximal portion of the upper extremities and 3/5 in the distal portion of the upper extremities. Glove and stocking type sensory impairment was severe. Severe sensory ataxia was present in all limbs, and position and vibration senses were remarkably reduced predominantly in the distal limbs. Pain and temperature sensations were also diminished distally but dysaesthesia was not seen. Deep tendon reflexes were generally absent; no pathological reflexes were demonstrable. Serum glucose, vitamins B1 and B12, sodium, potassium and calcium levels were all normal, but serum phosphorus was 0.2 mg/dl (normal 2.2–4.4).

IP was administered intravenously (40 mEq/day), 3 days after the onset of neurological symptoms. Total protein level in CSF was 40 mg/dl and the cell count was normal. MRI of the cervical spine and brain revealed no remarkable abnormalities. Motor conduction velocity, distal latency and amplitude of compound muscle action potential in the median nerve were 53 m/s, 4.3 ms and 6.4 mV, respectively; those in the tibial nerve were 34 m/s, 5.1 ms and 13.2 mV, respectively. Sensory conduction velocities and sensory nerve action potential in the median nerve were 47 m/s and 12 μ V, respectively; those in the sural nerve were 39 m/s and 25 μ V, respectively. Temporal dispersion and

conduction block were not seen. F waves were absent in the median and ulnar nerves, and were diminished in the tibial nerve. The latencies of the median nerve N13 and N20 somatosensory evoked potentials were prolonged but their interpeak latency was normal (latency of N13/N20 17.6/23.0 ms).

A test for the presence of antiganglioside antibodies (anti-GM1, GM1b, GM2, GD1a, GalNAc-GD1a, GD1b, GD2, GT1a, GT1b, GQ1b) was negative. Following initiation of IP treatment, the patient's neurological symptoms gradually improved. Sural nerve biopsy performed on day 82 showed well preserved myelinated fibre density with mild axonal atrophy and moderate subperineurial oedema (fig 1); pathological demyelination and axonal degeneration were not seen. Nearly complete reversal of neurological impairment was attained 2 months following the initiation of IP treatment, which was accompanied by normalisation of F waves.

Discussion

Our patient showed severe acute sensorimotor neuropathy after receiving IVH with a formulation that lacked IP. Guillain-Barré syndrome and critical illness polyneuropathy were considered in the differential diagnosis, but the neurological symptoms appeared soon after hypophosphataemia developed and was reversed following IP administration. Therefore, hypophosphataemia was considered the cause of this patient's neuropathy.

While hypophosphataemia is not rare in hospitalised patients, it is usually asymptomatic. Severe hypophosphataemia, when combined with phosphorus depletion, has been known to cause a number of clinical conditions, including haematological impairment, metabolic acidosis, osteomalacia, central nervous system dysfunction, myocardial dysfunction, rhabdomyolysis and peripheral neuropathy.¹ Anecdotal reports of the development of neuropathy in patients with hypophosphataemia have been published.^{2–4} Most of those patients were malnourished and received IVH without IP. In the absence of IP administration, unconsciousness and respiratory failure developed, which were rapidly reversed by IP administration.

The pathogenic mechanisms that lead to the development of neuropathy in hypophosphataemic individuals are unclear. Marked reductions in the concentrations of 2,3-diphosphoglycerate and adenosine triphosphate (ATP) in red blood cells and increased haemoglobin-oxygen affinity were reported to occur in a patient with hypophosphataemia.⁵ Diminished nerve oxygen levels resulting from increased red blood cell oxygen affinity could result in nerve dysfunction or damage. It is also possible that reduced ATP concentrations in nervous tissue directly disrupt nerve function as phosphorus is essential for carbohydrate metabolism.

In our case, although nerve conduction velocities were nearly normal, F waves were not evoked in the acute phase. Prompt IP administration normalised these F waves. Sural nerve biopsy revealed only the presence of subperineurial oedema and mild axonal atrophy, supporting the notion, along with our nerve conduction data, that hypophosphataemia can cause functional impairment, resulting from an abnormality in the proximal portion of the nerve trunk or spinal root. Further investigations, including pathological and electrophysiological studies, will be needed to more fully characterise this condition.

Figure 1 Sural nerve pathology. Transverse section of the right sural nerve of the patient (toluidine blue stain). (A) Oedematous tissue is shown in the subperineurial space (arrowheads). (B) Myelinated fibre densities were well preserved but there were signs of mild axonal atrophy.

In summary, our data suggest that hypophosphataemia plays a key role in the pathogenesis of neuropathy that develops in patients following IVH without IP, and highlights the importance of rapid phosphate replacement therapy in these patients.

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Poliomyelitis-like syndrome with matching magnetic resonance features in a case of Lyme neuroborreliosis

Lyme disease is a multisystemic disorder caused by an epizootic organism of the spirochete group, called *Borrelia burgdorferi* (Bb), which is transmitted to humans by ticks of the genus *Ixodes*.¹ Three sequential clinical stages have been described: (i) early localised; (ii) early disseminated; and (iii) late persistent disease. Lyme neuroborreliosis may occur during the early dissemination phase, most often as a painful meningo-radiculitis and very rarely as a radiculo-myelitis, whereas encephalomyelitis is observed in the late phase.² We report the case of a patient with an early

Figure 1 Magnetic resonance (MR) workup of the cervical spine at admission. (A) Post-contrast mid-sagittal T1 weighted image showing abnormal enhancement of both the anterior pia mater (ball-arrowheads) and anterior horns of central grey matter from C2 to C5 (arrows). (B) Mid-sagittal T2 weighted image (similar slice location as in (A)) showing abnormal linear hypersignal intensity in the anterior horns of central grey matter in the same C2–C5 area (arrows). (C) Post-contrast transverse T1 weighted image at the C5 level showing thickened, abnormally enhancing, anterior roots due to inflammatory blood root barrier disruption (arrows), together with enhancement within the left anterior horns (ball-arrowhead). (D) T2 weighted transverse image at a comparable level showing abnormal hypersignal intensity within the anterior horns (arrows).

subacute poliomyelitis-like syndrome closely matching the selective involvement of the anterior horns and roots of the cervical spinal cord seen on magnetic resonance (MR) imaging.

A previously healthy 21-year-old man presented in September 2006 with painless weakness in both arms that had increased over a period of 2 weeks. He had a short history of neck