Acute Motor Axonal Neuropathy with Bulbar Symptoms- Case report

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Abstract
Acute motor axonal neuropathy (AMAN), a rare variant of Guillain-Barré Syndrome (GBS) presents with rapid paralysis. A 14-year-old boy exhibited bulbar symptoms alongside limb weakness. Clinical examination revealed positive Gowers's sign and inability to walk on toes. Sensory function was normal, with intact reflexes and sphincter control. Investigations including cerebrospinal fluid, viral serology, and magnetic resonance imaging of the brain and spinal cord yielded no abnormalities. Electromyography confirmed motor axonal polyneuropathy. Treatment with intravenous immunoglobulin led to symptom regression within two weeks. AMAN, lacking sensory involvement, often follows a severe course, necessitating consideration of IVIg due to hyperreactive humoral response.

Introduction

Acute motor axonal neuropathy (AMAN) is classified among the axonal variants of Guillain-Barré syndrome (GBS) (1-3). GBS typically manifests as a rapidly progressive ascending paralysis of the lower extremities resulting in a tetraplegia and is characterized by an albumin-cytological dissociation in the cerebrospinal fluid (1, 3, 4). Clinically it is subdivided into motor, sensory, sensorimotor, autonomic involvement and Miller Fisher syndrome (4, 5). Neurophysiological study can define different GBS variants, such as an acute motor axonal neuropathy (AMAN), an acute motor sensory axonal neuropathy (AMSAN) and acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (4). AMAN is the pure motor variant without sensory or autonomic nerve involvement.

The etiopathogenesis of AMAN remains unclear. Autoimmune mechanisms leading to axonal degeneration are taught to be involved (1, 5). *Campylobacter jejuni* infection may precede muscle weakness but is only observed in a third of cases (6). Molecular mimicry is widely accepted in explaining the pathogenesis of axonal degeneration in Guillain-Barré syndrome (3). The best-known example of this mechanism is *C. jejuni*. Ganglioside-like epitopes on the lipopolysaccharide (LPS) and the lipo-oligosaccharide (LOS) of this bacteria are recognized by the innate immune system. Antigen presenting cells recognize these epitopes and activate B cell and T helper cell proliferation. B cells develop into plasma cells and produce anti-ganglioside antibodies. These antibodies attack the invader but also destroy sodium channels at the nodes of Ranvier (3, 4, 6). As anti-ganglioside IgM and IgG can be detected in patients with AMAN, this suggests the condition is an autoimmune disease of the peripheral nervous system (3). In AMAN, anti-GM1b and anti-GD1a antibodies are directed against GM1-like and GD1a-like LOS of *C. jejuni*. Electrophysiological studies reveal a reversible conduction block, reversible conduction failure (RCF) or decreased compound muscle action potential (CMAP) amplitudes with normal sensory conduction. These abnormalities become apparent mainly 3-6 weeks after the acute phase and can differentiate AIDP from AMAN. Today, there is no consensus on the electrophysiological criteria. Intravenous immunoglobulin IVIG and plasma exchange are the most commonly used therapies. IVIG inhibits macrophage activation and prevents antibody and complement binding. 1 out of 4 AMAN patients have a rapid recovery after IVIG therapy, in the paediatric population the results are more favourable (3).

Case report

A 14-year-old boy was admitted to the emergency room with reduced muscle strength mainly in lower limbs. Initially the weakness was mainly noticeable at the left side. Over the past four days, he was unable to keep up with his basketball teammates, necessitating him to pull himself toward on the banister to climb the stairs. Additionally, parents reported he choked during feedings the last few days.

Recently, he had no respiratory or gastrointestinal symptoms. Apart from allergic rhinitis, there was no significant medical history. There were no known muscle or neurologic diseases in the family, and his siblings were in good health. Born in India, he had been residing in Belgium for the past five years. On physical examination he could stand supported but couldn't walk on his toes, Gowers's sign was positive. Sensory examination was normal, tendon reflexes and sphincter control were present. There was no respiratory distress. Heart rhythm and oxygen saturation were normal.

Investigations

Laboratory tests were within the normal range for blood cell count, C reactive protein, creatine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), thyroid stimulating hormone, lead, cyanocobalamin, thiamine, pyruvate kinase and creatine kinase. The erythrocyte sedimentation rate (25 mm/hour

[N < 15 mm/hour]) was mildly elevated and albumin was high-normal (47.2 g/L [N 35,0 – 52,0 g/L]). Serological test for *Borrelia burgdorferi*, *Mycoplasma pneumoniae*, cytomegalovirus, Epstein-Barr Virus and varicella-zoster virus were negative. Unfortunately, anti-ganglioside antibody determination was not feasible in our hospital. Urine toxicology screening was also negative. Stool culture was negative for *Campylobacter jejuni*. The cerebrospinal fluid protein level was within the normal range and no cells were detected. Magnetic resonance imaging of the brain and spinal cord revealed no abnormalities. Electromyography was consistent with a motor axonal polyneuropathy affecting all four limbs. The motor nerve conduction study at the level of the 4 limbs shows reduced to borderline normal amplitudes with normal conduction velocities and borderline normal terminal latencies. The CMAP durations are borderline normal to prolonged. Needle EMG shows no signs of active denervation in the muscles examined. In the m. vastus medialis R and lateralis L, only a few motor units are recruitable. The sensory nerve conduction study at the level of the limbs is normal.

Treatment

Initial treatment regime was 400 mg/kg/day intravenous immunoglobulin for five days.

Outcome and follow-up

After five days of IVIg, he was able to stand on his toes again, although a complete recovery of strength had not yet occurred. Bulbar complaints were no longer present. A follow-up two weeks later revealed a regression of all symptoms.

Discussion

AMAN is a rare axonal variant of GBS. It is more prevalent in East Asia, Central and South America, possibly due to increased infection rates with *C. jejuni*. Other pathogens, such as *Haemophilus influenza* and *M. pneumoniae* are reported to be involved in the molecular mimicry mechanism. Despite our efforts no pathogen could be identified. Genetic susceptibility may contribute to AMAN onset and prognosis, although this remains insufficiently understood to date. Most documented cases are reported in Asia and as our patient has Indian roots genetic predisposition is plausible. Large genome-wide association studies (GWAS) on patients with axonal GBS are needed to explore this further. Bulbar palsy is more prevalent in children than in adults (2, 4). Anti-GT1a and anti-GM1b antibodies are associated with bulbar palsy. Failure to determine anti-ganglioside antibodies is a limitation in this case report. A typical finding of GBS is an albumin-cytological dissociation in cerebrospinal fluid. In this patient, the cerebrospinal fluid protein level was normal in the first week of symptoms. Albumin-cytologic dissociation is often not seen until two to three weeks after the acute onset. If found in the first week, the prognosis is often worse. Decreased CMAP amplitudes and RCFs are typical electrophysiological features of axonal GBS (3). The patients EMG confirmed our clinical diagnosis.

Children with AMAN seem to respond better to IVIG than AIDP (8). This suggests the underlying auto-antibody-mediated immune response in AMAN patients is inhibited by IVIg. Five days after the administration of IVIG, the patient could stand on his toes again, and there were no more bulbar symptoms. Two weeks later all symptoms had disappeared.

The present report describes an adolescent with acute motor axonal neuropathy, without evidence of a gastrointestinal infection. It occurred in summer, consistent with earlier reports of summer epidemics. The patient made a full recovery. Clinicians should be aware of this rare axonal variant of GBS in children, characterized by a pure motor involvement (muscle weakness) and co-occurring bulbar palsy.

Take away lessons

1. Axonal GBS is an important variant of classical GBS. AMAN is a pure motor variant without the involvement of the sensory or autonomic nerves.
2. The classic type of GBS is characterized by demyelination, while in AMAN, axonal degeneration occurs, and the myelin sheath remains intact. This is characterized by a reversible conduction block, a reversible conduction failure or decreased compound muscle action potential (CMAP) amplitudes on electrophysiological studies.
3. Further studies are necessary to unravel the etiopathogenesis, define electrophysiological criteria, establish prognostic factors and optimal treatment.

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