CONCOMITANT PEDIATRIC LONGITUDIONAL EXTENSIVE TRANSVERSE MYELITIS
(LETM) AND ACUTE MOTOR AXONAL NEUROPATHY (AMAN):
CASE REPORT AND LITERATURE REVIEW
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Abstract
Acute motor axonal neuropathy (AMAN) is a subtype of Guillain-Barre syndrome (GBS).
AMAN diagnosis is based on decreased compound muscle action potentials (CMAP) and absence of
demyelinating findings.

Case report: We present an 8-year-old boy admitted to our clinic for further evaluation and
therapy of an unknown and progressive loss of motor function of the lower extremities. The serum
pneumoslide results included: respiratory syncytial virus IgG +/- and Mycoplasma Pneumoniae IgM +/-.
Due to positive cerebrospinal fluid (CSF), magnetic resonance imaging (MRI) and electromyography
(EMG) findings, diagnosis of longitudinal extensive transverse myelitis (LETM) was established and
therapy with intravenous immunoglobulins (IVIg) and pulse corticosteroid therapy was given. After 6
months, a repeat EMG evaluation found an underlying axonal neuropathy with signs of axonal damage,
lack of peripheral demyelination, and pathologic F-wave-findings. Due to the clinical worsening and
changes in electrophysiologic findings, additional diagnosis of atypical GBS of acute motor axonal
neuropathy was established. After immunomodulatory therapy, gradual recovery of the functions occured
and the clinical picture stabilized. Maintenance immunomodulatory therapy was intiated and safely
utilized over the following year.

Pediatric patients can develop post-infectious or idiopathic occurance of concomitant LETM and
AMAN with overlapping neurological symptoms. Succsesful management of such cases should include
both vigilant diagnosis through neurological examination, EMG and MRI, as well as treatment with both
acute and maintaining immunomodulatory therapy.

Key words: acute motor axonal neuropathy, Guillain-Barre syndrome, longitudinal extensive
transverse myelitis

Introduction
Guillain-Barre syndrome(GBS) is an inflammatory,widespread degeneration of peripheral nerves,
characterized by rapidly progressive symmetrical muscle weakness and loss of deep tendon reflexes.
There are four main subtypes of GBS, according to clinical and pathological features: acute inflammatory
demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor-
sensory axonal neuropathy (AMSAN), and Miller-Fisher syndrome (MFS)[1].Diagnosis is made based on
medical history and physical examination, as well as cerebrospinal fluid (CSF) analysis, magnetic
resonance imaging (MRI), and nerve conduction studies [2]. Electrophysiological findings play
determinant role in diagnosis and classification of GBS [3].AMAN diagnosis is based on decreased
compound muscle action potentials (CMAP) and absence of demyelinating findings [4].

Case report
We present a 8-year-old boy admitted to our clinic for further evaluation and therapy of an
unknown and progressive loss of motor function of the lower extremities. He was born full-term, and the
pregnancy was monitored. Two episodes of vaginal bleeding during the first and the last trimester of
pregnancy were noted. The patient was delivered spontaneously, with body weight of 2980 g, body length
of 55 cm, and an Apgar score of 9 and 10.
The psychomotor development was normal, with regular achievements according to the developmental milestones. The medical history recorded previous several episodes of obstructive bronchitis treated with topical steroids and Varicella with a mild clinical appearance at the age of two years. Two months before the current hospitalization, the patient started to experience unstable gait with a few falls.

At the moment of admission, he had a normal somatic status, he was conscious, oriented, with good cognition and learning abilities according to his age. The cranial nerves were with normal findings. The right leg was 0.5 cm thinner than the left one. Muscle strength was lower on the right leg, and the right arm too. Deep tendon reflexes were preserved, and there was a positive Babinski sign on the right leg. General laboratory findings were within normal ranges. ANA-Hep2 (IFA), anti-dsDNA, c-ANCA, AFA and LE-cells were negative. The echocardiogram and ECG were normal.

The abdominal ultrasound was normal. The MRI of the CNS showed cerebellar hypoplasia with mega cisterna magna and transverse myelitis in the cervical region, ranging from C2 to C6. Evoked potentials demonstrated prolonged conductive properties of the somatosensory pathways. Protein profile of CSF and function of the hemato-liquor barrier analysis showed transudative IgM type of immunoglobulin of peripheral nerve with normal isoelectric focus, followed by intrathecal IgG synthesis (IgG 105 mg/L, IgG synthesis in CNS 28.5 mg/24h, IgG index 1.21 × 10^5 albumin 301 mg/L, total proteins 0.50 g/L). The serum pneumoslide results included: respiratory syncytial virus IgG +/- and Mycoplasma Pneumoniae IgM +/-.

The molecular genetic analysis for Friedreich’s ataxia did not show presence of mutation (expansion of GAA trinucleotide sequence) in the third non-translational region of the FRDA gene. Genetic analysis for deletions/duplications in genes associated with Charcot-Marie-Tooth did not show presence of duplication or mutation of GJB1, MPZ, KIF1B, chromosome 17p, PMP22 or surrounding genes. Due to the positive CSF, MRI and electromyography (EMG) findings, diagnosis of longitudinal extensive transverse myelitis was established, and therapy with intravenous immunoglobulins (IVIg) and pulse corticosteroid therapy was administered over the following month.

The initial treatment only resulted with partial response and 6 months later, the patient was re-admitted for further evaluation. At the follow-up, the patient demonstrated hyporeflexia of the the upper extremities. Repeat EMG evaluation found an underlying axonal neuropathy with signs of axonal damage, lack of peripheral demyelination, and pathologic F-waves. Due to the clinical worsening and changes in electrophysiologic findings, additional diagnosis of atypical GBS of acute motor axonal neuropathy was established. A new set of immunomodulatory therapy with pulse corticosteroid therapy (20 mg/kg BW/day) and IVIg (2 g/kg in 2 repeated cycles) was initiated. Further use of methylprednisolon pulse therapy in a weekly manner for at least 4 more cycles; immune adsorption therapy or plasmapheresis for at least 10 cycles; and single application of rituximab before the switch of the immunomodulatory treatment to plasmapheresis.

Over the next few months, gradual recovery of the functions occurred and the clinical picture stabilized with residual tendon hyperreflexia and inability to walk. Maintenance immunomodulatory therapy with mycophenolate moefetil (250 mg bid) was initiated and safely utilized over the following year.
Table 1. Case reports in literature that report both central and peripheral nervous system involvement

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Case report</th>
<th>Infectious agent</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TM and AMSAN/CIPNM</td>
<td>Two 10-year-old females</td>
<td>Unknown</td>
<td>(Chung et al., 2015) [5]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>4-year-old female</td>
<td>Unknown</td>
<td>(Tolunay et al., 2016) [6]</td>
</tr>
<tr>
<td>TM, GBS and myositis</td>
<td>14-year-old female</td>
<td>Mycoplasma pneumoniae</td>
<td>(Topcu et al., 2013) [7]</td>
</tr>
<tr>
<td>TM and CIPNM</td>
<td>8-month old male</td>
<td>Influenza virus</td>
<td>(Adamovic et al., 2009) [20]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>12-year-old male</td>
<td>Bartonella henselae</td>
<td>(Carman et al., 2013) [8]</td>
</tr>
<tr>
<td>TM and GBS/AMAN</td>
<td>14-year-old male</td>
<td>Unknown</td>
<td>(Howell et al., 2007) [9]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>10-year-old female</td>
<td>Bartonella henselae</td>
<td>(Zakhour et al., 2018) [10]</td>
</tr>
<tr>
<td>TM and AMSAN</td>
<td>7-year old female</td>
<td>Legionella pneumophila</td>
<td>(Canpolat et al., 2013) [11]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>5 pediatric cases (8-15 years old)</td>
<td>Flu-like</td>
<td>(Lin et al., 2011) [12]</td>
</tr>
<tr>
<td>ADEM and GBS</td>
<td>4 pediatric cases (5-16 years old)</td>
<td>Mycoplasma, EBV</td>
<td>(Bernard et al., 2008) [13]</td>
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Adult cases:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Case report</th>
<th>Infectious agent</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TM, GBS and encephalitis</td>
<td>Adult female (24 years old)</td>
<td>Zika virus</td>
<td>(Mancera-Paez et al., 2018) [14]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>Adult female (28 years old)</td>
<td>Mumps virus</td>
<td>(Bajaj et al., 2001) [15]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>Adult female (62 years old)</td>
<td>Bartonella henselae</td>
<td>(Rissardo and Caprara, 2019) [16]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>Adult female (34 years old)</td>
<td>Influenza virus</td>
<td>(Tripp, 2008) [17]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>Adult male (28 years old)</td>
<td>Unknown</td>
<td>(Schulze Beehorst et al., 2007) [18]</td>
</tr>
<tr>
<td>TM and GBS</td>
<td>Adult male (32 years old)</td>
<td>Varicella</td>
<td>(Chua et al., 2001) [19]</td>
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</table>


**Discussion**

In this case report, we described sequential occurrence of LETM and AMAN with undetermined etiology and good long-term response with immunomodulatory therapy.

Similar cases have been previously reported in both pediatric and adult populations. (The specific pathology, case demographics and references are summarized in Table 1). This rare concurrence of pathologies has a significant variability in the demographic and clinical presentation. It can range from an 8-month-old toddler to very rare cases of elderly patients (≥60 years old)[20]. Interestingly, even with the absence of the significant cervical spinal cord finding, previous studies of atypical GBS cases have demonstrated presence of either a significant hyperreflexia or unilateral positive Babinski sign[21].

The same paradoxical feature was also seen in our case, as well. In the terms of treatment, the literature usually reports the use of IVIg, plasmapheresis, intravenous corticosteroids and immunomodulatory therapy, such as rituximab, mycophenolate mofetil, azathioprine, and in severe cases cyclophosphamide. However, studies demonstrating long-term follow-up and drug efficacy in such cases are currently missing and necessary.

Our case report has certain limitations. Most cases of pediatric AMAN cases exhibit autoantibodies towards the ganglioside 1 (GM1), which were not investigated in our patient [22]. Furthermore, the medical history was not able to determine a specific infectious event that may have
predisposed the occurrence of both LETM and AMAN. By far, the most common pathogen associated with such consequences is Campylobacter jejuni, with a smaller proportion of Mycoplasma pneumoniae, influenza infection, cytomegalovirus (CMV), Epstein-Barr virus (EBV) and herpes virus[23]. In particular, the lipopolysaccharides isolated from Campylobacter jejuni contain a structure that highly resembles the ganglioside 1-like molecule [24]. That said, the viral examination in our patient did demonstrate postnatal recent Mycoplasma pneumoniae infection, which may have remained asymptomatic.

Case reports of Mycoplasma-associated AMAN are seen in the literature [25]. On the other hand, the EBV homology with other CNS molecules predisposes the development of ADEM, LETM and MS [26]. Lastly, awareness of a differential diagnosis with polyradiculoneuritis with myelitis is needed [27].

Conclusion
Pediatric patients can develop a post-infectious or idiopathic occurrence of concomitant LETM and AMAN with overlapping neurological symptoms. Successful management of such cases should include both vigilant diagnosis through neurological examination, EMG and MRI, and treatment with both acute and maintaining immunomodulatory therapy. Although AMAN is geographically more prevalent in Asia, reports of such cases are seen throughout the world.

References


