JMS 2020;3(1):12-16
UDC:616.74-009.54-085.37

CONCOMITANT PEDIATRIC LONGITUDIONAL EXTENSIVE TRANSVERSE MYELITIS (LETM) ANDACUTE MOTOR AXONAL NEUROPATHY (AMAN): CASE REPORT AND LITERATURE REVIEW

Bojadzieva Sonja[1], Duma F[1], Sofijanova A[1], Murtezani A[1], Tankoska M[1], Ramadani A[2] ,Jordanova O[1]
[1]PHI University Clinic for Children Diseases [2]PHI University Clinic for Gastroenterohepatology, Faculty of Medicine, University "St.Cyril&Methodius", Skopje, R.of NMacedonia

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 elecrophysiologic findings, additional diagnosis of atypical GBS of acute motor axonal neuropathy was established. After immunomodulatory therapy, gradual recovery of the funcitons occured and the clinical picture stabilzed. 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 managment 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 presentan8-year-oldboy 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 thelast trimester of pregnancy were noted. The patient was delivered spontaneously, with body weight of 2980 g, body length of 55 cm, andan Apgar score of 9 and 10.

The psychomotor development was normal, with regular achievements according to the developmental milestones.The medical history recorded previous severalepisodes of obstructive bronchitistreated 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 was0,5 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 showedtransudativegamaglobulin type of electrophrogram with normal isoelectric focus, followed byintrathecal IgG synthesis (IgG 105mg/L, IgG synthesis in CNS 28,5mg/24h, IgG index $1,21x10^{3,}$ 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 thirdnon-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 surroundinggenes. 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 therapywas 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-wave-findings.

Due to the clinicalworsening 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 (20mg/kg BW/day) and IVIg (2g/kg in 2 repeated cycles) was initiated. Further use of methylprednisolon pulse therapy in a weekly manner for at least 4 more cycles; immune adsorbtion 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 funcitons occured and the clinical picture stabilzed with residual tendon hyperreflexia amd unability to walk. Maintenance immunomodulatory therapy with mycophenolate moefetil (250mg bid) was intiated and safely utilized over the following year.

Table 1. Case reports in literature that report both central and peripheral nervous system involvement

Diagnosis	Case report	Infectious agent	Reference
TM and AMSAN/CIPNM	Two 10-year-old females	Unknown	(Chung et al., 2015) [5]
TM and GBS	4-year-old female	Unknown	(Tolunay et al., 2016) [6]
TM, GBS and myositis	14-year-old female	Mycoplasma pneumoniae	(Topcu et al., 2013) [7]
TM and CIPNM	8-month old male	Influenza virus	(Adamovic et al., 2009) [20]
TM and GBS	12-year-old male	Bartonellahenselae	(Carman et al., 2013) [8]
TM and GBS/AMAN	14-year-old male	Unknown	(Howell et al., 2007) [9]
TM and GBS	10-year-old female	Bartonellahenselae	(Zakhour et al., 2018) [10]
TM and AMSAN	7-year old female	Legionella pneumophila	(Canpolat et al., 2013) [11]
TM and GBS	5 pediatric cases (8-15 years old)	Flu-like	(Lin et al., 2011) [12]
ADEM and GBS	4 pediatric cases (5-16 years old)	Mycoplasma, EBV	(Bernard et al., 2008) [13]
Adult cases:			
TM, GBS and encephalitis	Adult female (24 years old)	Zika virus	(Mancera-Paez et al., 2018) [14]
TM and GBS	Adult female (28 years old)	Mumps virus	(Bajaj et al., 2001) [15]
TM and GBS	Adult female (62 years old)	Bartonellahenselae	(Rissardo and Caprara, 2019) [16]
TM and GBS	Adult female (34 years old)	Influenza virus	(Tripp, 2008) [17]
TM and GBS	Adult male (28 years old)	Unknown	(Schulze Beerhorst et al., 2007) [18]
TM and GBS	Adult male (32 years old)	Varicella	(Chua et al., 2001) [19]

Legend: TM – transverse myelitis, GBS - Guillain-Barre syndrome, AMSAN - acute motor-sensory axonal neuropathy, CIPNM - critical illness polyneuromyopathy, AMAN - acute motor axonal neuropathy, ADEM – acute disseminated encephalomyelitis, EBV–Epstein Barr virus

Discussion

In this case report, we described sequential occurance 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 summurized 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 ora 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 moefetil, 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 auto-antibodies 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 predisoposed 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 infeciton, 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 gangloside 1-like molecule [24]. That said, the viral examination in our patient did demonstrate postnatal recent Mycoplasma pneumonie 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, awarness 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. Succsesful managment 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

1. Agrawal, S., Peake, D., and Whitehouse, W.P. (2007). Management of children with Guillain-Barre syndrome. *Arch Dis Child Educ Pract Ed* 92**,** 161-168.
2. Ryan, M.M. (2005). Guillain-Barre syndrome in childhood. *J Paediatr Child Health* 41**,** 237-241.
3. Uncini, A., Manzoli, C., Notturno, F., and Capasso, M. (2010). Pitfalls in electrodiagnosis of Guillain-Barre syndrome subtypes. J Neurol Neurosurg Psychiatry 81, 1157-1163.
4. Hadden, R.D., Cornblath, D.R., Hughes, R.A., Zielasek, J., Hartung, H.P., Toyka, K.V., and Swan, A.V. (1998). Electrophysiological classification of Guillain-Barre syndrome: clinical associations and outcome. Plasma Exchange/Sandoglobulin Guillain-Barre Syndrome Trial Group. Ann Neurol 44, 780-788.
5. Chung, H., Joa, K.L., Kim, H.S., Kim, C.H., Jung, H.Y., and Kim, M.O. (2015). Concomitant acute transverse myelitis and sensory motor axonal polyneuropathy in two children: two case reports. Ann Rehabil Med 39, 142-145.
6. Tolunay, O., Celik, T., Celik, U., Komur, M., Tanyeli, Z., and Sonmezler, A. (2016). Concurrency of Guillain-Barre syndrome and acute transverse myelitis: a case report and review of literature. Korean J Pediatr 59, S161-S164.
7. Topcu, Y., Bayram, E., Karaoglu, P., Yis, U., Guleryuz, H., and Kurul, S.H. (2013). Coexistence of myositis, transverse myelitis, and Guillain Barre syndrome following Mycoplasma pneumoniae infection in an adolescent. J Pediatr Neurosci 8, 59-63.
8. Carman, K.B., Yimenicioglu, S., Ekici, A., Yakut, A., and Dinleyici, E.C. (2013). Co-existence of acute transverse myelitis and Guillain-Barre syndrome associated with Bartonella henselae infection. Paediatr Int Child Health 33, 190-192.
9. Howell, K.B., Wanigasinghe, J., Leventer, R.J., and Ryan, M.M. (2007). Concomitant transverse myelitis and acute motor axonal neuropathy in an adolescent. Pediatr Neurol 37, 378-381.
10. Zakhour, R., Mancias, P., Heresi, G., and Perez, N. (2018). Transverse Myelitis and Guillain-Barre Syndrome Associated with Cat-Scratch Disease, Texas, USA, 2011. Emerg Infect Dis 24, 1754-1755.
11. Canpolat, M., Kumandas, S., Yikilmaz, A., Gumus, H., Koseoglu, E., Poyrazoglu, H.G., Kose, M., and Per, H. (2013). Transverse myelitis and acute motor sensory axonal neuropathy due to Legionella pneumophila: a case report. Pediatr Int 55, 778-782.
12. Lin, J.J., Hsia, S.H., Wu, C.T., Wang, H.S., Lin, K.L., and Lyu, R.K. (2011). Risk factors and outcomes of Guillain-Barre syndrome with acute myelitis. Pediatr Neurol 44, 110-116.

13. Bernard, G., Riou, E., Rosenblatt, B., Dilenge, M.E., and Poulin, C. (2008). Simultaneous Guillain-Barre syndrome and acute disseminated encephalomyelitis in the pediatric population. J Child Neurol 23, 752-757.
14. Mancera-Paez, O., Roman, G.C., Pardo-Turriago, R., Rodriguez, Y., and Anaya, J.M. (2018). Concurrent Guillain-Barre syndrome, transverse myelitis and encephalitis post-Zika: A case report and review of the pathogenic role of multiple arboviral immunity. J Neurol Sci 395, 47-53.
15. Bajaj, N.P., Rose, P., Clifford-Jones, R., and Hughes, P.J. (2001). Acute transverse myelitis and Guillain-Barre overlap syndrome with serological evidence for mumps viraemia. Acta Neurol Scand 104, 239-242.
16. Rissardo, J.P., and Caprara, A.L.F. (2019). Transverse Myelitis and Guillain-Barre Syndrome Overlap Secondary to Bartonella henselae: Case Report. Prague Med Rep 120, 131-137.
17. Tripp, A. (2008). Acute transverse myelitis and Guillain-Barre overlap syndrome following influenza infection. CNS Spectr 13, 744-746.
18. Schulze Beerhorst, K., Klein, B., Oelerich, M., and Rieke, K. (2007). [The rare coincidence of Guillain-Barre syndrome and myelitis]. Nervenarzt 78, 445-450.
19. Chua, H.C., Tjia, H., and Sitoh, Y.Y. (2001). Concurrent myelitis and Guillain-Barre syndrome after varicella infection. Int J Clin Pract 55, 643-644.
20. Adamovic, T., Willems, A., Vanasse, M., D'anjou, G., Robitaille, Y., Litalien, C., and Gauvin, F. (2009). Critical illness polyneuromyopathy in a child with severe demyelinating myelitis. *J Child Neurol* 24**,** 758-762.
21. Cattano, D., O'connor, B., Shakir, R., Giunta, F., and Palazzo, M. (2008). Acute inflammatory demyelinating polyneuropathy and a unilateral babinski/plantar reflex. Anesthesiol Res Pract 2008, 134958.
22. Yuki, N., Handa, S., Tai, T., Takahashi, M., Saito, K., Tsujino, Y., and Taki, T. (1995). Ganglioside-like epitopes of lipopolysaccharides from Campylobacter jejuni (PEN 19) in three isolates from patients with Guillain-Barre syndrome. J Neurol Sci 130, 112-116.
23. Mckhann, G.M., Cornblath, D.R., Griffin, J.W., Ho, T.W., Li, C.Y., Jiang, Z., Wu, H.S., Zhaori, G., Liu, Y., Jou, L.P., and Et Al. (1993). Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 33, 333-342.
24. Yuki, N., Ang, C.W., Koga, M., Jacobs, B.C., Van Doorn, P.A., Hirata, K., and Van Der Meche, F.G. (2000). Clinical features and response to treatment in Guillain-Barre syndrome associated with antibodies to GM1b ganglioside. Ann Neurol 47, 314-321.
25. Susuki, K., Odaka, M., Mori, M., Hirata, K., and Yuki, N. (2004). Acute motor axonal neuropathy after Mycoplasma infection: Evidence of molecular mimicry. Neurology 62, 949-956.
26. Jakimovski, D., Weinstock-Guttman, B., Ramanathan, M., Dwyer, M.G., and Zivadinov, R. (2020). Infections, Vaccines and Autoimmunity: A Multiple Sclerosis Perspective. Vaccines (Basel) 8.
27. Martens-Le Bouar, H., and Korinthenberg, R. (2002). Polyradiculoneuritis with myelitis: a rare differential diagnosis of Guillain-Barre syndrome. Neuropediatrics 33, 93-96.