Child Neurology Open
October - December 2015: 1-2

DOI: 10.1177/2329048X15609606
cno.sagepub.com
SAGE

Guillain Barré Syndrome in a Child With X-Linked Adrenoleukodystrophy

Ron Jacob, MD[1], Hanna Mandel, MD[2], and Naim Shehadeh, MD[3]

Abstract

X-Linked adrenoleukodystrophy is the most common peroxisomal disorder with different phenotypes among patients carrying the same ABCD1 mutation. There were previously reported associations of X-linked adrenoleukodystrophy with autoimmune disorders. The authors describe Guillain Barré syndrome in a child with X-linked adrenoleukodystrophy. The available evidence does not permit conclusion concerning etiological linkage between the 2 diseases, but it warrants further study.

Keywords

pediatric, neurology, autoimmune, Addison's disease

Received June 30, 2015. Received revised August 3, 2015. Accepted for publication August 29, 2015.

A 2-year-old boy presented to the emergency department with 5 days of low-grade fever, progressive fatigue, and difficulty in breathing. Chest X-ray revealed right lower lobe consolidation. He was treated with antibiotics, bronchodilators, and systemic steroids. Two days later, he complained of a sudden pain in his arms and legs and worsening of weakness. He gradually lost consciousness and experienced respiratory failure necessitating mechanical ventilation. Brain computed tomography was unremarkable, and cerebrospinal fluid analysis revealed 10 white blood cells, with elevated protein and normal glucose levels. The next few days were characterized by altered state of consciousness, hemodynamic instability requiring vasoactive support, absence of tendon reflexes, and spontaneous limb movements. Extensive microbiologic and serologic studies were all negative. Motor and sensory nerve conduction studies of upper and lower limbs revealed multifocal slowing of nerve conduction, low amplitudes, elongated latencies, and absent F waves. Needle electromyography showed no spontaneous activity. In a working diagnosis of Guillain Barré syndrome, intravenous immunoglobulin course was given. When no significant neurological improvement was observed, another lumbar puncture was performed, unremarkable except for slightly elevated protein (56 mg/dL; normal range 0-40). Plasmapheresis was initiated with remarkable neurological improvement after the fifth course. During the following week, he was weaned off mechanical ventilation and medications and regained full neurological recovery after a few weeks.

Four years later, at age of 6, he presented to the emergency department with 2 days of diarrhea, vomiting, and a fever of 39.5°C. Shortly after admission, he developed bloody diarrhea, gradually became stuporotic, hypotensive (75 mm Hg systolic pressure), and hypoglycemic (serum glucose 30mg/dL). Fecal cultures were positive for *Shigella*. He was treated with antibiotics, systemic steroids, and hemodynamic support. Over the next 3 days, he improved rapidly and was discharged home.

Further investigation of the hypoglycemic episode revealed low morning serum cortisol level (43.3 nmol/L; normal range 138-690 nmol/L) and elevated adrenocorticotropin level (1230 pmol/L; normal range 1.1-10 pmol/L). These findings raised the diagnosis of Addison's disease, followed by the findings of abnormal profile of very long-chain fatty acids. This combination led to the diagnosis of X-linked adrenoleukodystrophy. Magnetic resonance imaging (MRI) of the brain was

[1] Department of Pediatrics B, Ruth Rapport Children's Hospital, Rambam Health Care Campus, Technion Faculty of Medicine, Haifa, Israel
[2] Metabolic Unit, Ruth Rapport Children's Hospital, Rambam Health Care Campus, Technion Faculty of Medicine, Haifa, Israel
[3] Department of Pediatrics A, Ruth Rapport Children's Hospital, Rambam Health Care Campus, Technion Faculty of Medicine, Haifa, Israel

Corresponding Author:
Ron Jacob, MD, Department of Pediatrics B, Ruth Rapport Children's Hospital, Rambam Health Care Campus, PO Box 9602, Haifa 31096, Israel.
Email: r_jacob@rambam.health.gov.il; ron.jacobb@gmail.com

unremarkable. Hydrocortisone replacement therapy was initiated. Evaluation of his asymptomatic 12-year-old brother revealed that he also has X-linked adrenoleukodystrophy, Addison's disease, and normal brain MRI. The diagnosis was confirmed by the findings of a previously reported c.1771C>T; p.591R>W mutation in the ABCD1 gene. The siblings are currently being followed by multidisciplinary medical experts and undergo brain MRI scanning every 6 months.

Discussion

Guillain-Barré syndrome is an acute polyneuropathy consisting of different subtypes. Acute inflammatory demyelinating polyradiculoneuropathy accounts for 90% of all cases with Guillain-Barré syndrome in the Western world. Acute motor axonal neuropathy and acute motor and sensory axonal neuropathy are axonal forms of Guillain-Barré syndrome that are more prevalent in Asia, South, and Central America, often preceded by *Campylobacter jejuni*. Acute motor axonal neuropathy and acute motor and sensory axonal neuropathy can be mediated by specific antiganglioside antibodies that inhibit transient sodium ion (Na+) channels. The efficacy of plasmapheresis and intravenous immunoglobulin has been established in large international randomized trials, with corticosteroids proven ineffective.[1]

X-linked adrenoleukodystrophy is the most common peroxisomal disorder with an estimated overall frequency of 1:17 000. The disease is caused by mutations in the ABCD1 gene that encodes the peroxisomal transporter of very long-chain fatty acids. A defect in the ABCD1 protein results in elevated levels of very long-chain fatty acids in the plasma and tissues.[2] The clinical spectrum in males with X-linked adrenoleukodystrophy ranges from isolated adrenocortical insufficiency and slowly progressive myelopathy to devastating severe inflammatory fatal cerebral demyelination.[3] Furthermore, patients carrying the same ABCD1 mutation can present with different phenotypes, a fact that led investigators to suggest the involvement of modifier genes or epigenetic factors that can modulate the clinical outcomes of the disease.[4]

The authors describe Guillain Barré syndrome in a child with X-linked adrenoleukodystrophy. The co-occurrence of these 2 diseases raised the question whether the authors are dealing with an anecdotal association or there might be a linkage between 2 diseases with immune dysregulation co-occurring in 1 patient. Of note, an association of other autoimmune phenomenon including vitiligo, ulcerative colitis, and multiple endocrine disorders have been previously reported in individuals with X-linked adrenoleukodystrophy.[5-7] Even more so, antiganglioside antibodies were shown to bind with enhanced affinity to gangliosides containing very long-chain fatty acids, which are theoretically differentially displayed on membranes, a fact that can lead to altered antigenicity.[8] Interestingly, other authors raised the hypothesis that accumulation of very long-chain fatty acids leads to myelin instability, which can trigger an inflammatory or immune-mediated process.[9]

It remains unclear whether clinical reports of comorbid immune diseases represent chance findings or true associations. The present report calls for increased awareness of physicians to the coexistence of X-linked adrenoleukodystrophy with other immune dysregulations and warrants further study.

Author Contribution

RJ wrote the first version of the manuscript. HM and NS were involved in patient management, revised the first draft, and approved the manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

References

1. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barré syndrome: an update. *J Clin Neurosci*. 2009;16(6):733-741. doi:10.1016/j.jocn.2008.08.033.
2. Kemp S, Berger J, Aubourg P. X-linked adrenoleukodystrophy: clinical, metabolic, genetic and pathophysiological aspects. *Biochim Biophys Acta*. 2012;1822(9):1465-1474. doi:10.1016/j.bbadis.2012.03.012.
3. Moser HW, Raymond GV, Dubey P. Adrenoleukodystrophy: new approaches to a neurodegenerative disease. *JAMA*. 2005;294(24):3131-3134. doi:10.1001/jama.294.24.3131.
4. Wiesinger C, Eichler FS, Berger J. The genetic landscape of X-linked adrenoleukodystrophy: inheritance, mutations, modifier genes, and diagnosis. *Appl Clin Genet*. 2015;8:109-121. doi:10.2147/TACG.S49590.
5. Sawaya RA, Mourad FH, Najjar S, Mikati M, Raymond GV. Adrenoleukodystrophy associated with vitiligo and ulcerative colitis. *Eur Neurol*. 1999;42(3):169-172.
6. Triantafyllou P, Economou M, Vlachaki E, et al. multiple endocrine disorders associated with adrenomyeloneuropathy and a novel mutation of the ABCD1 gene. *Pediatr Neurol*. 2014;50(6):622-624. doi:10.1016/j.pediatrneurol.2014.01.027.
7. Federico A, Dotti MT, Annunziata P, et al. Adrenomyeloneurodystrophy with late cerebral involvement and evidence of a multiple autoimmune disorder. *J Inherit Metab Dis*. 1988;11 Suppl 2:169-172.
8. Tagawa Y, Laroy W, Nimrichter L, et al. Anti-ganglioside antibodies bind with enhanced affinity to gangliosides containing very long chain fatty acids. *Neurochem Res*. 2002;27(7-8):847-855. http://www.ncbi.nlm.nih.gov/pubmed/12374222.
9. Singh I, Pujol A. Pathomechanisms underlying X-adrenoleukodystrophy: a three-hit hypothesis. *Brain Pathol*. 2010;20(4):838-844. doi:10.1111/j.1750-3639.2010.00392.x.