Non-Hodgkin Lymphoma and Guillain-Barré Syndrome: A Rare Association

Firas Seffo, MD[1]
Hamed A. Daw, MD[2]

[1]Department of Internal Medicine, South West General Hospital, University Hospitals of Cleveland, Cleveland, Ohio; [2]Department of Internal Medicine, Cleveland Clinic Cancer Center, Fairview Hospital, Cleveland, Ohio

Introduction

Non-Hodgkin lymphoma (NHL) is a neoplastic transformation of cells that reside predominantly within lymphoid tissues, which may be of B- or T-cell origin. There is a slight male-to-female predominance and a higher incidence in whites than blacks.

Incidence rises steadily with age, especially after 40 years. Extranodal lymphomas usually present as a mass, and sometimes as a fever of unknown origin. Primary central nervous system involvement results in headaches, seizures, lethargy, focal neurologic symptoms, or paralysis. Uncommon initial presentations of NHL include spinal cord compression and lymphomatous meningitis. Peripheral nervous system abnormalities occur in 5% of patients with lymphoma and have a wide differential diagnosis, with herpes zoster being the most common cause.[1] Direct lymphomatous involvement of the peripheral nerves (neurolymphomatosis) is a rare event, often occurring in the presence of widespread systemic disease.[2] Peripheral neuropathy is commonly attributed to the toxic effect of chemotherapeutic agents.[3,4] Another cause of central nervous system damage is radiation myelopathy. Paraneoplastic neurologic syndromes, such as Guillain-Barré syndrome (GBS), are rare in NHL.[5,6] We describe a rare case of NHL complicated by GBS.

Case Report

A 70-year-old, white, right-handed woman complained of bilateral leg weakness 3 weeks after her sixth cycle of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy for NHL. She gradually developed progressive bilateral leg weakness and had to use a wheelchair. She complained of some back pain, but denied any numbness or tingling in her legs, bladder or bowel dysfunction, or any shooting or radiating pains.

Four months prior, the patient had presented with left nasal mass infiltrating the left orbit and was diagnosed with T/NK-cell NHL, nasal type, stage Ie-A. She was treated with 6 cycles of CHOP and was in complete remission with total regression of the tumor 4 cycles into treatment. She also had hypertension, hyperlipidemia, anemia due to CHOP requiring blood transfusion, and anxiety disorder. Home medications included atenolol, atorvastatin, aspirin, bupropion hydrochloride, trazodone, multivitamins, propoxyphen, and zolpidem tartrate. The patient had quit smoking 30 years prior and denied alcohol or drug abuse. She had no other systemic symptoms. On exam, she was afebrile, with blood pressure of 108/66 mm Hg, heart rate of 80 beats per minute, respiration of 16 breaths per minute, weight of 128 pounds, and height of 5 feet, 6 inches. The head, ears, eyes, nose, and throat exam revealed no lymphadenopathy in the head, neck, or supraclavicular fossa, and no thyromegaly. The chest was clear to auscultation bilaterally, and the heart had regular rate and rhythm. The abdomen was soft and nontender to palpation, and bowel sounds were normoactive. No hepatosplenomegaly or masses were observed. No pitting edema, cyanosis, or clubbing were seen on the extremities. No percussion tenderness was seen when the back was checked. The neurologic examination revealed an alert and oriented (×3) mental status. Cranial nerve examination revealed normal visual fields; the fundi were grossly normal, and the pupils were normal. Pursuit eye movement testing uncovered left adductor limitation leading to a diplopia. Facial sensation was normal.

There was a slightly diminished left nasolabial fold. Hearing, palatal movement, pronation, resonation,

Address correspondence to:
Firas Seffo, MD, P.O. Box 45128, Westlake, OH 44145; Phone: 216-346-6740; E-mail: fseffo@swgeneral.com.

strength in trapezius, sternocleidomastoid, and tongue protrusion were normal. The motor exam revealed finger abduction 5 of 5 bilaterally, triceps 5 bilaterally, and deltoid 5 bilaterally, and toe flexion 5 bilaterally, toe and ankle dorsiflexion 5 right, 0 to 1 left, and plantar flexion 5 bilaterally. Ankle eversion was 5 right, absent left, and ankle inversion 5 right, 3 left. Knee flexion was 4 right, 2 left, and knee extension was 3 right, 3 left. Hip flexion was 3 bilaterally. Hip was adduction 3 bilaterally, and hip abduction 3 to 4 bilaterally. Tone, bulk, and posture were normal. There were no fasciculations, abnormal movements, or asterixis. Sensory exam showed that pain was diminished in the dorsums of the feet and lateral calves bilaterally. Vibration was diminished in both great toes and joint position, and sensation was diminished at the right great toe and absent in the left great toe. The patient had a loss of the left dorsiflexor phase with toe wrinkling and rapid alternating movements that were otherwise normal. Finger-to-nose was normal bilaterally, but gait was not tested due to profound weakness in the legs. Deep tendon reflexes were 2- left triceps and absent at the right triceps; both biceps, both knees, and both ankle jerks were absent. The plantars were equivocal bilaterally. Diagnostic data revealed serum calcium of 9.5 mg/dL, sodium of 138 mmol/L, normal serum vitamin B_{12} level >2000 pg/mL, hematocrit of 27%, platelet count 198 x 10^9/L, and creatinine 0.8 mg/dL. Magnetic resonance imaging (MRI) of the lumbosacral spine was unremarkable. Lumbar puncture revealed clear, colorless fluid; the opening pressure was 162 mm of water. Cerebrospinal fluid (CSF) examination exposed elevated protein (81 mg/dL), glucose 44 mM, and white blood cell count of 11×10^9 cells per liter, mostly lymphocytes. Electromyography demonstrated bilateral acute sensory motor polyneuropathy compatible with GBS. The patient developed quadriparesis, neurogenic bladder, neurogenic bowel, and right facial nerve palsy despite treatment, and was discharged to hospice.

Discussion

GBS is an idiopathic acute inflammatory demyelinating polyneuropathy that is believed to be immunologically mediated. Approximately two-thirds of the cases are related to a recent upper respiratory or gastrointestinal tract infection, especially infections due to *Campylobacter jejuni*, *Cytomegalovirus*, and Epstein-Barr virus.[7] Recent immunization has also been associated with GBS. The swine influenza vaccine, administered widely in the United States in 1976, is the most notable example; the mechanism is presumably immunization against neural antigens. GBS has been reported to be associated with some systemic diseases such as Hodgkin lymphoma, HIV, and systemic lupus erythematosis.[8,9] It is extremely rare in NHL, occurring in less than 0.3% of cases.[10] Table 1 summarizes the common causes of GBS.

Table 1. Common Causes of Guillain-Barré Syndrome

Infections
Campylobacter jejuni
Cytomegalovirus
Epstein-Barr virus
Recent Immunization
Swine influenza vaccine (1976)
Older types of rabies vaccine
Systemic diseases
Hodgkin disease
HIV
Systemic lupus erythematosis

GBS is manifested as an acute, ascending polyneuropathy, predominantly motor paralysis with respiratory failure, leading to death. In severe cases, the ocular motor nerves are involved and even the pupils may be unreactive. More than half of the patients complain of pain and an aching discomfort in the muscles—mainly those of the hips, thighs, and back—and therefore can be misdiagnosed with lumbar disc disease, back strain, and other orthopedic diseases. Sensory loss occurs to a variable degree during the first few days and may be barely detectable. Reduced and then absent deep tendon reflexes are consistent findings. The most important diagnostic studies are electromyography (EMG) and CSF examination. The CSF is under normal pressure and is acellular or contains only a few lymphocytes and 10–50 cells per mL at most, whereas protein levels are elevated (albuminocytologic dissociation, elevated proteins without cells). Abnormalities of nerve conduction are early and dependable diagnostic indicators of GBS. The most frequent early electrodiagnostic findings are reduction in the amplitude of muscle action potentials, slowed conduction velocity, and conduction block in motor nerves. Prolonged distal latencies (reflecting distal conduction block) and prolonged or absent F-responses (indicating involvement of proximal parts of nerves and roots) are other important diagnostic findings, all reflecting focal demyelination. Table 2 illustrates the diagnostic criteria for GBS.

Most peripheral neuropathies in NHL are attributed to local infiltration by lymphomatous cells causing axonal damage.[5] This disorder can affect nerve roots and cranial nerves, often associated with lymphomatous meningitis. NHL may also infiltrate peripheral nerves

Table 2. Diagnostic Criteria for Guillain-Barré Syndrome

Required
• Progressive weakness of 2 or more limbs due to neuropathy
• Areflexia
• Disease course <4 weeks
• Exclusion of other causes: vasculitis, toxins, botulism, diphtheria, porphyria, localized spinal cord or Cauda Equina syndrome
Supportive
• Relatively symmetric weakness
• Mild sensory involvement
• Facial nerve or other cranial nerve involvement
• Absence of fever
• Typical cerebrospinal fluid profile (acellular, increase in protein level)
• Electrophysiologic evidence of demyelination

and causes plexopathy, mononeuropathy, or generalized neuropathy. These neuropathies may resemble an asymmetric mononeuropathy multiplex or a generalized disorder such as chronic inflammatory demyelinating polyradiculoneuropathy. When NHL infiltrates diffusely, the term *neurolymphomatosis* is used. The initial differential diagnosis in our patient included cauda equina syndrome (which was excluded by the findings of MRI of the lumbosacral spine), chemotherapy drug toxicity (which could not explain her areflexia), lymphomatous (carcinomatous) meningitis, intramedullary lymphoma of the spinal cord, epidural compression of the cervical and thoracic cord, metastasis to the falx cerebri with involvement of the foramen magnum by affecting the leg decussation but not the arm decussation (rare possibility), and demyelinating neuropathy as a paraneoplastic entity (GBS). The presentation was more suggestive of a rapidly progressive entity such as cord compression (excluded by MRI) or a demyelinating polyneuropathy and was confirmed by the finding of cytoalbuminologic dissociation on CSF examination.

Conclusion

We believe that immune mechanisms triggered by NHL initiated the development of GBS in this patient. Although GBS is commonly seen in Hodgkin lymphoma, it is an extremely rare entity in NHL. Our literature review revealed some case reports of GBS associated with B-cell lymphoma and Burkitt lymphoma,[5,6,7,10] but we believe that this is the first report of T/NK-cell lymphoma, nasal type associated with GBS.

References

1. Hughes RA, Britton T, Richards M. Effects of lymphoma on the peripheral nervous system. *J R Soc Med*. 1994;87:526-530.
2. Ghobrial IM, Buadi F, Spinner RJ, et al. High-dose intravenous methotrexate followed by autologous stem cell transplantation as a potentially effective therapy for neurolymphomatosis. *Cancer*. 2004;100:2403-2407.
3. Carmona A, Alonso JD, de las Heras M, Navarrete A. Guillain-Barré syndrome in patient with diffuse large B-cell lymphoma, and rituximab maintenance therapy. An association beyond anecdotal evidence? *Clin Transl Oncol*. 2006;8:764-766.
4. Terenghi F, Ardolino G, Nobile-Orazio E. Guillain-Barré syndrome after combined CHOP and rituximab therapy in non-Hodgkin lymphoma. *J Peripher Nerv. Syst*. 2007;12:142-143.
5. Kelly JJ, Karcher DS. Lymphoma and peripheral neuropathy: a clinical review. *Muscle Nerve*. 2005;31:301-313.
6. Viala K, Behin A, Maisonobe T, et al. Neuropathy in lymphoma: a relationship between the pattern of neuropathy, type of lymphoma and prognosis? *J Neurol Neurosurg Psychiatry*. 2008;79:778-782.
7. Jacobs BC, Rothbart PH, van der Meche FG, et al. The spectrum antecedent infections in Guillain-Barré syndrome: a case control study. *Neurology*. 1998; 51:1110-1115.
8. Lisak RP, Mitchell M, Zweiman B, Orrechio E, Asbury AK. Guillain-Barré syndrome and Hodgkin's disease: three cases with immunological studies. *Ann Neurol*. 1977;1:72-78.
9. Julien J, Vital C, Aupy G, et al. Guillain-Barré syndrome and Hodgkin's disease: ultrastructural study of a peripheral nerve. *J Neurol Sci*. 1980;45:23-27.
10. Zuk E, Nowacki P, Fabian A. Guillain-Barré syndrome in a patient with Burkitt's lymphoma and type 2 diabetes mellitus. *Folia Neuropathol*. 2001;39: 281-284.

Review

The Immunopathogenesis of Guillain-Barré Syndrome

Sindhu Ramchandren, MD, MS, and Robert P. Lisak, MD

Department of Neurology, Wayne State University-Detroit Medical Center, Detroit, Michigan

Seffo and Daw report a case of Guillain-Barré syndrome (GBS) in a patient with T/NK-cell non-Hodgkin lymphoma (NHL), stage IE-A, after her sixth treatment cycle with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy.[1] The diagnosis was based on ascending motor weakness proximally and distally with cranial nerve involvement and nearly complete areflexia, albuminocytologic dissociation on cerebrospinal fluid (CSF) analysis, and electrodiagnostic studies demonstrating bilateral acute sensory motor polyneuropathy.

Address correspondence to:
Sindhu Ramchandren, MD, MS, 4201 Saint Antoine, UHC 8D, Detroit, MI 48201; Phone: 313-577-3515; Fax: 313-745-4216; E-mail: sramchan@med.wayne.edu.

Details of the therapy that was initiated are not provided; however, the patient reportedly had continued disease progression, and was discharged to hospice.

The diagnosis of GBS is clinical and is based on presentation, electrodiagnostic findings, and CSF analysis, as well as exclusion of other etiologies. In their discussion, Seffo and Daw have provided a succinct summary of clinical and electrodiagnostic features of GBS; readers are further advised to read the comprehensive review of GBS by Hughes and Cornblath.[2] GBS is an acute illness; the duration of symptoms from onset to nadir should be 4 weeks or less; if longer than 8 weeks, the diagnosis is probably chronic inflammatory demyelinating polyneuropathy (CIDP) or its variants. We are not provided with details on the progression of symptoms in the case report to know which category it belongs to. The clinical picture of GBS can be produced by several pathologic subtypes, often distinguished electrodiagnostically. The most common subtype of GBS in Europe and North America is acute inflammatory demyelinating polyradiculoneuropathy (AIDP); the acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN) subtypes are more prevalent in Asia and Central and South America, especially following *Campylobacter jejuni* infections. We are not provided sufficient detail on the clinical electrophysiologic studies to distinguish between the axonal and demyelinating forms in the case report. CSF evaluation should show elevated protein concentration with normal CSF white blood cell count (typically <5 cells/mm^3); variations should prompt investigations such as cytology for alternate etiologies. In the case report, the 11 cells/mm^3 and the degree of asymmetry, while not excluding GBS, is somewhat atypical.

Some researchers describing rare occurrences of GBS in patients with Hodgkin lymphoma[3,4] and NHL[5-8] have attributed the GBS presentation either to the underlying disease or its therapy, specifically vincristine, a key component of CHOP therapy. Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most important dose-limiting toxicities seen with vincristine exposure.[9-11] CIPN manifests as painful dysesthesias, length-dependent sensory loss to pain, temperature and proprioception (legs worse than arms), suppression of deep tendon reflexes in proportion to sensory loss, difficulty with balance and coordination, and distal muscle weakness, consistent with nerve pathology.[12] Patients with pre-existing neuropathies can develop life-threatening paralysis, even with low doses of vincristine.[13] Electrophysiologic studies show a distal axonal sensory-motor neuropathy,[14,15] but demyelination has also been seen.[16] This makes it difficult at times to separate a GBS presentation in malignancy from, or superimposed on, CIPN. Only 1 patient with NHL has been reported to develop GBS before the diagnosis and initiation of chemotherapy[5]; the rest developed GBS after initiation of CHOP or other chemotherapies. Nerve biopsy may sometimes be needed to distinguish the 2: neurofilamentous accumulations within axons are considered characteristic for vincristine neuropathy,[17] whereas GBS is characterized by intense lymphocytic inflammatory infiltrates in nerve roots and peripheral nerves (demyelinating type),[18] or macrophages invading the periaxonal space of myelinated nerve fibers (axonal type).[19]

Besides CIPN, direct lymphomatous infiltration of the nerve, vasculitis, paraproteinemic deposition, and paraneoplastic syndromes have all been postulated as the underlying etiology of acute neuropathies in NHL; these can be confirmed by morphologic and immunologic analysis.[5] Paraneoplastic neuropathy is a heterogeneous group of conditions that often presents as a subacute sensory neuronopathy. Less frequently seen paraneoplastic presentations include motor-sensory neuropathies, autonomic neuropathies, and lower motor neuron syndromes. The diagnosis is based on serum testing for known antineuronal antibodies (antibodies that react with antigens common to the peripheral nerve and the neoplasm).[20] It is not clear if GBS associated with lymphoma should be considered classically paraneoplastic, since the target antigen in most cases of AIDP is not known.

The pathogenesis of GBS is unclear, although there is strong evidence of immune dysfunction with delayed hypersensitivity to components of peripheral nervous system myelin.[21,22] In AIDP, macrophages invade intact myelin sheaths. This has been postulated to be due to a T-cell mediated process against one of the myelin proteins,[23] as seen in the animal model of GBS-experimental allergic neuritis[24-26]; a secondary enhancement of demyelination by an antibody-mediated process may be involved. Alternatively the initial event may be binding of antibodies to the Schwann cell surface and demyelination, perhaps prior to the cell invasion by macrophages.[27] On the other hand, in AMAN, there is strong evidence to support axonal destruction by antibodies to gangliosides on the nerve axolemma that target macrophages to invade the axon at the node of Ranvier as the result of molecular mimicry.[28,29]

Although the development of an immune-mediated disorder such as GBS in an apparently immunosuppressed individual may appear paradoxical, animal models such as the NZB mouse demonstrate that the depression of cell-mediated immunity and the T-cell system are associated with a humoral-mediated increase in autoantibodies and autoimmune diseases.[30-33] It is possible that selective

depression of cell-mediated immunity of any etiology might allow the development of a humoral and/or cellular immune reaction directed against peripheral nerve antigens. However, given the rare association between lymphoma (Hodgkin lymphoma or NHL) and GBS, we postulate that there must be other epigenetic factors that contribute to the development of GBS in any particular immunosuppressed patient.

Treatment of the patient with GBS requires a multidisciplinary approach, given the potentially fatal complications in patients with rapidly progressive disease and autonomic dysfunction.[34] In the acute phase, plasma exchange was accepted as the gold standard 20 years ago.[35,36] Studies done in the 1990s established the equivalence of plasma exchange with intravenous immunoglobulin (IVIg); no significant improvement was noted with the combination of both treatment modalities.[37,38] A Cochrane Database Review of 6 trials utilizing corticosteroids failed to show any benefit in GBS.[39] The American Academy of Neurology has published practice parameter guidelines recommending either plasma exchange or IVIg for the treatment of patients with GBS who have lost the ability to walk.[40] However, available treatment options still leave 20% of patients disabled, and persistent milder symptoms remain. Controlled clinical trials comparing best therapeutic options or developing new, targeted agents are needed. There is no mention in the case report of whether IVIg or pheresis was initiated in the patient; the fact that the patient continued to progress (potentially increasing the duration of symptoms to over 8 weeks) also raises the possibility of CIDP. Regardless, the above treatments are efficacious in CIDP as well as GBS.

In conclusion, although immune dysfunction is clearly associated with GBS, the underlying immunopathogenesis of its various subtypes are still being elucidated. The case reports of GBS associated with various immunosuppressed states such as lymphoma may provide further insight into the underlying etiology of this syndrome and lead to the development of targeted immunomodulatory therapies that are more specific, less toxic, and more beneficial than those currently available.

References

1. Seffo F, Daw HA. Non-Hodgkin lymphoma and Guillain-Barré syndrome: a rare association. *Clin Adv Hematol Oncol.* 2010;8:201-203.
2. Hughes RA, Cornblath DR. Guillain-Barré syndrome. *Lancet*. 2005;366: 1653-1666.
3. Lisak RP, Mitchell M, Zweiman B, et al. Guillain-Barré syndrome and Hodgkin's disease: three cases with immunological studies. *Ann Neurol.* 1977;1:72-78
4. Kelly JJ, Karcher DS. Lymphoma and peripheral neuropathy: a clinical review. *Muscle Nerve*. 2005;31:301-313.
5. Vallat JM, De Mascarel HA, Bordessoule D, Jauberteau MO, Tabaraud F, Gelot A, Vallat AV. Non-Hodgkin malignant lymphomas and peripheral neuropathies-13 cases. *Brain*. 1995;118:1233-1245.
6. Re D, Schwenk A, Hegener P, Bamborschke S, Diehl V, Tesch H. Guillain-Barré syndrome in a patient with non-Hodgkin's lymphoma. *Ann Oncol*. 2000; 11:217-220.
7. Magne N, Foa C, Castadot P, Otto J, Birtwisle-Peyrottes I, Thyss A. Guillain-Barré syndrome and non-Hodgkin's lymphoma. Report of one case and review of literature. *Rev Med Brux.* 2005;26:108-111.
8. Terenghi F, Ardolino G, Nobile-Orazio E. Guillain-Barré syndrome after combined CHOP and rituximab therapy in non-Hodgkin lymphoma. *J Periph Nerv Syst*. 2007;12:142-143.
9. Holland JF, Scharlau C, Gailani S, et al. Vincristine treatment of advanced cancer: a cooperative study of 392 cases. *Cancer Res*. 1973;33:1258-1264.
10. Vainionpaa L. Clinical neurological findings of children with acute lymphoblastic leukaemia at diagnosis and during treatment. *Eur J Pediatr*. 1993;152: 115-119.
11. Ocean AJ, Vhadat LT. Chemotherapy-induced peripheral neuropathy: pathogenesis and emerging therapies. *Support Care Cancer*. 2004;12:619-625.
12. Windebank AJ, Grisold W. Chemotherapy-induced neuropathy. *J Peripher Nerv Syst*. 2008;13:27-46.
13. Hildebrandt G, Holler E, Woenkhaus M, et al. Acute deterioration of Charcot–Marie–Tooth disease 1A (CMT 1A) following 2 mg of vincristine chemotherapy. *Ann Oncol*. 2000;11:743-747.
14. Sandler SG, Tobin W, Henderson ES. Vincristine-induced neuropathy. A clinical study of fifty leukemic patients. *Neurology*. 1969;19:367-374.
15. Casey EB, Jellife AM, Le Quesne PM, Millett YL. Vincristine neuropathy. Clinical and electrophysiological observations. *Brain*. 1973;96:69-86.
16. Hiser L, Harrington B, Lobert S. Effect of noscapine and vincristine combination on demyelination and cell proliferation in vitro. *Leuk Lymphoma*. 2008;49:1603-1609.
17. Shelanski MI, Wisniewski H. Neurofibrillary degeneration induced by vincristine therapy. *Arch Neurol*. 1969;20:199-206.
18. Wanschitz J, Maier H, Lassmann H, Budka H, Berger T. Distinct time pattern of complement activation and cytotoxic T cell response in Guillain-Barré syndrome. *Brain*. 2003;126:2034-2042.
19. Griffin JW, Li CY, HO TW, et al. Guillain-Barré syndrome in northern China. The spectrum of neuropathological changes in clinically defined cases. *Brain*. 1995;118:577-595.
20. Rudnicki SA, Dalmau J. Paraneoplastic syndromes of the spinal cord, nerve, and muscle. *Muscle Nerve*. 2000;23:1800-1818.
21. Asbury AK, Arnason BGW, Adams RD. The inflammatory lesion in idiopathic polyneuritis: its role in pathogenesis. *Medicine*. 1969;48:173-215.
22. Hughes RA, Hadden RD, Gregson NA, Smith KJ. Pathogenesis of Guillain-Barré syndrome. *J Neuroimmunol*. 1999;100:74-97.
23. Kieseier BC, Kiefer R, Gold R, Hemmer B, Willison HJ, Hartung HP. Advances in understanding and treatment of immune-mediated disorders of the peripheral nervous system. *Muscle Nerve*. 2004;30:131-156.
24. Waksman BH, Adams RD. Allergic neuritis: an experimental disease of rabbits induced by the injection of peripheral nerve tissue and adjuvants. *J Exp Med*. 1956;102:213-236.
25. Arnason BGW. Idiopathic polyneuritis and experimental allergic neuritis: a comparison. *Res Publ Assoc Res Nerv Ment Dis*. 1971;49:156-175.
26. Prineas JW. Acute idiopathic polyneuritis. An electron microscope study. *Lab Invest*. 1972;26:133-147.
27. Hafer-Macko CE, Sheikh HA, Li CY, et al. Immune attack on the Schwann cell surface in acute inflammatory demyelinating polyneuropathy. *Ann Neurol*. 1996;39:627-637.
28. Griffin JW, Li CY, Macko C, et al. Early nodal changes in the acute motor axonal neuropathy pattern of the Guillain-Barré syndrome. *J Neurocytol*. 1996;25:33-51.
29. Hafer-Macko C, Hsieh ST, Li CY, et al. Acute motor axonal neuropathy: an antibody-mediated attack on axolemma. *Ann Neurol*. 1996;40:635-644.
30. Lambert PH, Dixon FJ. Pathogenesis of the glomerulonephritis of NZB/W mice. *J Exp Med*. 1968;127:507-522.
31. Staples PJ, Steinberg AD, Talal N. Induction of immunologic tolerance in older New Zealand mice re-populated with young spleen, bone marrow or thymus. *J Exp Med*. 1970;131:1223-1238.
32. Levanthal BG, Talal N. Response of NZB and NZB/NZW spleen cells to mitogenic antigens. *J Immunol*. 1970;104:918-923.
33. Zatz MM, Mellors RC, Lance EM. Changes in lymphoid populations of aging CBA and NZB mice. *Clin Exp Immunol*. 1971;8:491-500.

34. Meythaler JM. Rehabilitation of Guillain-Barré syndrome. *Arch Phys Med Rehabil*. 1997;78:872-879.
35. Guillain-Barré study group. Plasmapheresis and acute Guillain-Barré syndrome. *Neurology*. 1985;35:1096-1104.
36. French Cooperative group in plasma exchange in Guillain-Barré syndrome. Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacement fluids. *Ann Neurol*. 1987;22:753-761.
37. Van der Meché FG, Schmitz PI. A randomized trial comparing intravenous immunoglobulin and plasma exchange in Guillain-Barré syndrome. Dutch Guillain-Barré Study Group. *N Engl J Med*. 1992;326:1123-1129.
38. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome. Plasma exchange/Sandoglobin Guillain-Barré syndrome trial group. *Lancet*. 1997;349:225-230.
39. Hughes RAC, van der Meche FG. Corticosteroids for treating Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2000;2:CD001446.
40. Hughes RAC, Wijdicks E, Barohn RJ, et al. Practice Parameter: Immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2003;61:736-740.