Guillain-Barré syndrome in an immunocompromised patient with Wiskott-Aldrich syndrome

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To the Editor,

Wiskott-Aldrich syndrome (WAS) is a primary immunodeficiency disorder with a classical triad of immunodeficiency, thrombocytopenia and eczema, with increased susceptibility to autoimmune diseases and malignancy[1]. It is caused by a mutation in the WAS gene encoding WAS protein (WASp), which has a role in actin cytoskeleton regulation during cellular activities and signal transduction[2]. Autoimmune hemolytic anemia, neutropenia, arthritis, skin vasculitis, cerebral vasculitis, inflammatory bowel disease and renal diseases are the frequently reported autoimmune and inflammatory diseases complicating WAS in up to 72% of cases[3].

Guillain-Barré syndrome (GBS) is an autoimmune, acute neuropathy with different pathological subtypes, the most common of which is acute inflammatory demyelinating polyradiculoneuropathy (AIDP)[4]. Immunocompromised patients with human immunodeficiency virus (HIV) infections, organ transplantation or malignancies can present with GBS[4]. However, to the best of our knowledge, GBS has not been reported previously in WAS patients. Here we report a WAS patient who developed GBS after a respiratory tract infection.

A 2.5-year-old boy, followed since nine months with the diagnosis of WAS (confirmed by mutational analysis), was on monthly intravenous immunoglobulin (IVIg) and daily steroid treatment for refractory thrombocytopenia. He was admitted to our hospital with difficulty in walking and progressive weakness of lower extremities for the previous week after a long-lasting cough and a respiratory tract infection. On physical examination, he had secretory rhonchi and rough rales and the liver was palpable 3 cm below the costal margin. Neurological examination showed absent deep tendon reflexes, and painful muscles were noted during motor examination. He was hospitalized and put on antibiotic treatment. Bone mineral density examination revealed a Z score of –2.94. Electromyographic examination and measurement of nerve conduction velocities showed severe motor and sensory polyneuropathy with accompanying slight axonal involvement without myopathic features (Table I). Spinal magnetic resonance imaging (MRI) done before lumbar puncture showed enhancement of the anterior motor nerve roots of the cauda equina bilaterally and symmetrically after IV gadolinium injection (Fig. 1). With diagnosis of GBS,

Table I. Nerve Conduction Studies Showing Normal Distal Latencies with Decreased Nerve Conduction Velocities

	Distal latency (ms)	Amplitude (mv)	Conduction velocity (m/s)	F waves (ms)
Right median nerve	4.5	1.0	16	58.1
Right ulnar nerve	3.2	1.0	20	–
Right tibial nerve	5.3	0.7	22	–

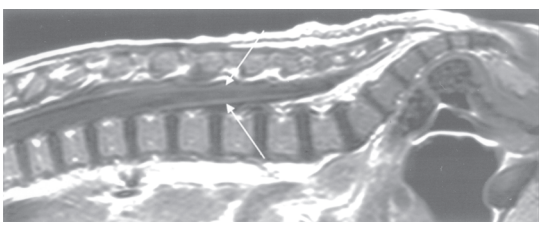

Fig. 1. Enhancement of the anterior motor nerve roots of the cauda equina bilaterally and symmetrically after intravenous gadolinium injection.

lumbar puncture was performed. Cerebrospinal fluid (CSF) protein was 58 mg/dl (N: 15-45) and CSF glucose was 46 mg/dl without any cells in microscopic examination. He was given IVIg treatment at a total dose of 2 g/kg. Gabapentin and calcium were started for treatment of pain and osteoporosis. One month after discharge, deep tendon reflexes were normoactive and he could walk without support.

As a primary immunodeficiency disorder, the occurrence of autoimmunity in WAS seems contradictory and the definitive mechanisms have not been clearly demonstrated. Interleukin-2 (IL-2) production is reduced in T cells of WAS patients and WASp knock-out mice[5]. IL-2 is a T cell growth factor with a regulatory effect on activation-induced T cell death and apoptotic mechanisms. IL-2 deficiency also leads to reduced generation of CD4+CD25+ regulatory T cells, which are important in autoimmune diseases[2,5,6]. Chronic inflammatory stimuli and impaired function of WASp-deficient T cells, B cells, macrophages or dendritic cells all could have important roles in developing autoimmunity by destabilizing the normal mechanism of immune function[2].

In the pathogenesis of AIDP, roles of both the humoral and cellular immune system have been discussed. Pathological studies have shown multifocal mononuclear cell infiltration throughout the peripheral nervous system, especially macrophage invasion to the myelin sheaths, as in experimental autoimmune neuritis[4,7]. Activated T lymphocytes are the major components in experimental autoimmune neuritis, by presenting antigens of the myelin sheath or Schwann cells to the activated macrophages. CD4+ T cell mediated immune response against myelin proteins P2, P0 or PMP22 is suggested to occur after loss of regulation of immune response[4,8]. Cross-reactivity between neural antigens and some microorganisms has also been extensively studied[4]. Loss of regulatory mechanisms in the cellular immune response, altered T cell function and defective interactions between T and B cells were discussed in the etiology of autoimmune neuropathy in immunocompromised patients with HIV or cancer[4].

We suggest that GBS, as a common autoimmune peripheral neuropathy seen in HIV, diabetes mellitus and cancer patients, may have been associated with altered immune function secondary to WAS in our patient.

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