The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

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Guillain-Barré syndrome

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1 Introduction

Guillain-Barré syndrome (GBS) is an autoimmune acute peripheral neuropathy, causing limb weakness that progresses over a period of days and up to 4 weeks. The syndrome was described in 1916 by three French neurologists: Guillain, Barré, and Strohl, and is considered to be the most common cause of acute generalized paralysis. The four most common subtypes of GBS are acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN) and the Miller Fisher syndrome (MFS), which is clinically distinct from the other three and is characterised by a triad of ophthalmoplegia, ataxia and areflexia. The four types differ in their pathophysiology and immunological profiles, as well as in their worldwide incidence. In Western countries AIDP accounts for about 90 % of all GBS cases, and AMAN accounts for most of the remaining 10 % [1].

GBS occurs throughout the world, affecting children and adults of all ages, with a median incidence of 1.3 cases/100 000 population (range, 0.4–4.0). Men are affected approximately 1.5 times more than women [1]. About two-thirds of GBS patients have had an infection within a 6-week period prior to the diagnosis, generally either a flu-like episode or gastroenteritis. The most frequent identifiable antecedent infectious organisms are Campylobacter jejuni (23–32 %), Cytomegalovirus (8–18 %), Epstein-Barr virus (2–7 %) and Mycoplasma pneumoniae (9 %) [2].

2 Pathogenesis

There is considerable evidence supporting an autoimmune mediated mechanism in GBS [3], though the pathophysiology is different in the various subtypes.

In AIDP the neuropathy is mainly demyelinating: macrophages invade the myelin sheaths and denude axons [1]. Axonal damage can occur secondarily when the inflammation is severe. The exact role of T-cell-mediated immunity in AIDP

remains unclear and there is also some evidence for the involvement of antibodies and complement [2].

In the axonal subtypes, AMAN and AMSAN, the main pathology is axonal injury rather than demyelinative one, and the pathophysiology is better understood. Strong evidence now exists that these axonal subtypes are caused by autoantibodies to gangliosides on the axolemma. An interesting observation is that the lipo-oligosaccharide from the Campylobacter jejuni bacterial wall contains ganglioside-like structures, thus promoting an immune response in some patients by the mechanism of molecular mimicry [1, 2]. There is also evidence indicating a small increase in the risk of GBS following vaccination, especially with the influenza vaccine.

Table 1. Asbury and Cornblath's clinical diagnostic criteria for Guillain-Barré syndrome [4] (Modified).

I. Features Required for Diagnosis
Progressive motor weakness of two or more limbs[1)]
Areflexia
II. Clinical Features Strongly Supportive of the Diagnosis (in order of importance)
Progression of symptoms over days, up to 4 weeks
Relative symmetry
Mild sensory symptoms or signs
Cranial nerve involvement
Recovery (usually begins 2–4 weeks after progression ceases)
Autonomic dysfunction
Absence of fever at the onset of symptoms
III. Features Casting Doubt on the Diagnosis
Marked, persistent asymmetry of weakness
Persistent bladder or bowel dysfunction
Bladder or bowel dysfunction at onset
Sharp sensory level
IV. Features That Rule Out the Diagnosis
Volatile solvents abuse
Acute intermittent porphyria
Recent diphtheria infection
Lead intoxication
Purely sensory syndrome, without motor weakness
A definite diagnosis of a condition such as poliomyelitis, botulism, or toxic neuropathy (e.g organophosphates)

1) Excluding Miller Fisher and other variant syndromes.

3 Diagnostic criteria

Guillain-Barré syndrome is a clinical diagnosis, supported by laboratory tests and requires exclusion of other mimics. Asbury and Cornblath's clinical criteria for the diagnosis of the Guillain-Barré syndrome [4] are widely accepted. A modified and simplified version of these criteria is listed in Table 1. Laboratory features supporting the diagnosis of GBS are listed in Table 2.

Table 2. Laboratory features supporting the diagnosis of Guillain-Barré syndrome.

I. Typical cerebrospinal fluid (CSF)
Normal pressure
High concentration of protein
< 50 mononuclear leuckocytes/mm^3 (typically < 10/mm^3)
No polymorphonuclear leukocytes in CSF
II. Typical electrophysiologic diagnostic features

4 Diagnostic measurements for experts

The most important laboratory aids to the clinical diagnosis, are the electrophysiological studies and the CSF examination. The CSF is typically under normal pressure, contains an increased protein content, and is acellular or contains only a few lymphocytes (usually less than 10, rarely more than 50 mononuclear leukocytes/mm^3) [1]. The protein content in the CSF may not be raised until 10 days after the onset of the disease and lumbar puncture may need to be repeated if the diagnosis remains doubtful.

Electrophysiological studies of both motor and sensory peripheral nerves play an important role in supporting the diagnosis, and help differentiate between the main subtypes of GBS — i.e. between the demyelinating form (AIDP) and the axonal forms (AMAN and ASMAN). However, electrophysiological studies are frequently normal or non-diagnostic at the onset of the disease and may need to be repeated after 1–2 weeks.

5 Serologic diagnostic tests

Several anti-ganglioside antibodies are associated both with AMAN (GM1, GM1b, GD1a and GalNac-GD1a in 64 %, 66 %, 45 % and 33 % of patients respectively) and with AMSAN (GM1, GM1b, GD1a) but not with AIDP [1, 2].

The Miller Fisher syndrome is associated with anti-GQ1b, a specific and sensitive anti-ganglioside antibody, present in more than 90 % of patients with MFS and absent in other forms of inflammatory neuropathy [2]. Anti-GQ1b have been

shown to damage the motor nerve terminal in vitro by a complement-mediated mechanism [2].

Anti-ganglioside antibodies may be tested in GBS, but their absence does not exclude the diagnosis. Of special diagnostic value are anti-GQ1b antibodies, which are sensitive and specific to MFS [1].

6 Requirements for family practitioners

Since GBS is a rapidly evolving and potentially life-threatening condition, family practitioners should be familiar with the symptoms and signs of GBS, and should immediately refer suspected patients to hospital. Paresthesias and slight numbness in the toes and fingers are the earliest symptoms of GBS. The major clinical manifestation is weakness that evolves more or less symmetrically, and reaches its nadir 2–4 weeks after onset of symptoms. The symptoms progress with an ascending pattern from the lower to the upper limbs in 56 % of patients, involve the four limbs simultaneously in 32 % of patients, and spread from the upper to the lower limbs in 12 % of patients [1]. The proximal as well as distal muscles of the limbs are involved. Involvement of the facial muscles is common, whereas the ocular motor muscles are usually spared, except with MFS. The weakness of the respiratory muscles may be severe enough to require assisted artificial ventilation in about 25 % of the patients. More than half the patients complain of pain and an aching discomfort in the muscles, mainly those of the hips, thighs and back. Autonomic involvement is common and may cause ileus, sinus tachycardia, hypertension, cardiac arrhythmia, and postural hypotension.

7 Follow up

Clinical observations

After a variable plateau phase, recovery begins with return of proximal, followed by distal strength over weeks or months.

Expectations

Most patients with GBS recover functionally within 6 to 12 months. Between 4 % and 15 % of patients die, and up to 20 % are left with a disabling motor deficit after a year, despite modern treatment [1, 2]. Poor prognostic factors include older age; severe, rapidly progressive disease; and electrophysiological features that suggest axonal involvement in AIDP [1]. Relapse may occur in a small percentage of patients.

Follow up studies

During recovery, improvement in clinical parameters such as muscle strength and ability to walk should be assessed. Commonly patient are treated and followed up in a rehabilitation facility for many months. Reports from these facilities help neurologists in the assessment of recovery and can be useful as reference points if a relapse is suspected. Electrophysiological studies may be used for follow up, especially if recovery is impaired or relapse is suspected. Blood tests are not routinely indicated.

8 Management

Treatment of GBS consists of both supportive care and specific therapy. All patients with GBS should be admitted to a hospital for close observation, in order to identify progression to respiratory failure necessitating endotracheal intubation and mechanical ventilation, as well as cranial nerve dysfunction, and autonomic instability. Prophylaxis for deep vein thrombosis should be provided because of prolonged immobilization. Intravenous immunoglobulins (IVIg) and plasma exchange (PEx) have been shown in randomised controlled trials to be similarly effective in accelerating the recovery, but do not significantly reduce mortality. IVIg has been found to be somewhat safer than PEx, having a lower frequency of multiple complications [5]. Thus, its efficacy, safety, and availability make IVIg the treatment of choice in many centers [1, 5]. A combination of PEx and IVIg does not seem to produce significant extra benefit. Corticosteroids are not effective in GBS. A recent Cochrane review [6] examined the evidence for the use of pharmacological agents other than steroids, IVIg and PEx, and found only very low quality studies that were unable to support their use.

Following discharge from the hospital, most patients are candidates for rehabilitation. A multidisciplinary rehabilitation program, with both occupational and physical therapy, is considered very important for recovery [2].

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