Guillain-Barré Syndrome Following Allogeneic Bone Marrow Transplantation

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70.1 Definition

Guillain-Barré Syndrome (GBS) is a clinical condition resulting from acute inflammatory demyelinating polyneuropathy (radiculopathy). It most frequently occurs after infection and immunizations and after malignancy. Allogenic bone marrow transplantation (BMT) is an important source.

70.2 Incidence

According to Tam et al. 2003 "Following the successful central and elimination of poliomyelitis in many regions of the world, GBS has become the most common cause of acute neuromuscular paralysis with estimated annual incidence ranging from 0.4 to 4 per 100,000 individuals in different populations."

70.3 Etiology

The majority of cases appear to have an infection as a trigger. The most common of these triggers is *campylobacter jejuni* infection. Evidence has accumulated linking GBS to campylobacter injection and Miller-Fisher syndrome. Miller-Fisher syndrome is a variant of GBS and comprises a clinical triad of ataxia, areflexia, and ophthalmoplegia autoantibodies against GQ1b have been considered archetypal anti-ganglioside auto-antibody-mediated neuropathy because the anti-GQ1b ganglioside antibody is detected in most patients with Miller-Fisher syndrome and decays with recovery. A related illness (Speed and Kaldor 1985; Jacobs et al. 1996; Rees et al. 1995) illustrated a link between *campylobacter* and

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serotypes in GBS were confirmed in Japan and in South Africa (see Tam et al. 2003). The mechanism is thought to be an autoimmune reaction against *c. jejuni* surface molecular with a structural similarity to gangliosides antigen on nerve endings (Hadden et al. 2001). Following *c. jejuni* infection the antibody level in the blood IgG isotype for up to 12 months, this is one of diagnostic criteria. In a Swedish study 30.1 cases of GBS per 100,000 confirmed *c. jejuni* cases. The same was found in England. In the U.S. *campylobacter* is one of the most common causes of diarrhea. About 15 cases are diagnosed each year per 100,000 population individuals. It is estimated that 1 million are infected annually in the U.S.; furthermore cases are not diagnosed or reported may be in addition. The bacteria are more isolated from infants and the young and more are males. It is estimated that probably a 100 persons die every year by *c. jejuni*. However, It is not know whether GBS in BMT subjects is equal to the GBS in the general population not definitive statistics are yet available

Two-thirds of GBS follow bacterial or viral infections. Lin et al. reported GBS after facial injuries and mentioned head injury as a possible precursor to GBS. It may follow general surgical procedures (see Merritt's Textbook of Neurology) and after delivery. GBS may follow allogenic BMT. This group of patients according to Wen et al. (1997) may have a higher risk of GBS. Neurologic complications are liable to develop in 50–70 % of patients having allogeneic BMT and less extent those having autologous BMT. Most of the complications are of central nervous system (CNS). Most of the peripheral nervous system (PNS) complications develop in the setting of graft-versus-host disease (GVHD). This includes chronic inflammatory demyelinating polyneuropathy as well as myasthenia gravis and polymyositis. GBS is acute inflammatory demyelinating disease of the peripheral nerves (polyneuropathy).

70.4 Pathology and Pathogenesis

The pathogenesis of GBS in patients after allogeneic BMT is not clear. It is believed to be a result of cellular immune response directed against components of the peripheral nerves. (Wen et al. 1997) According to Solare et al. GVHD is a frequent complication of allogeneic BMT; there is a possible relationship between neurological and MRI findings with a chronic GVHD. Solare et al., reported a case of allogeneic BMT resulting in central and peripheral neurological signs which correlates with chronic GVHD. Although rarely has this been confirmed in autopsy studies (Marosi et al. 1990; Mohrmann et al. 1990).

Pathology is the picture of chronic inflammatory demyelinating disease of the PNS. Histologically there is focal segmental demyelination with perivascular and endoneural infiltrations with lymphocytes and monocytes or macrophages. These lesions are scattered throughout the peripheral nerves, the roots and cranial nerves. There is segmental demyelination and axonal degeneration. During recovery there is regulation but lymphocytes remain.

70.5 Clinical Picture

The onset of the syndrome may be 10 days to 12 months after BMT (mean 3.8 months). According to Wen et al. (1997) GBS developed earlier in patients with autologous BMT. The same authors noted precipitating factors such as c. jejuni and cytomegalovirus. Before the onset there may be fever and GVHD. The CNS may also be involved. Solare et al. reported a case of cerebellar, pyramidal, and peripheral nerve involvement. The GVHD is manifested by skin rash and modest elevation of the liver function tests. GBS is characterized by acute onset of peripheral and cranial nerve dysfunction, which includes rapidly progressive weakness, loss of tendon reflexes, facial diplegia, esophageal and respiratory paresis, and impaired sensation in the hands and feet. The condition worsens in several days up to 3 weeks. The picture becomes stable for sometime and then improves gradually to normal or near normal condition. Sensory changes vary from normal to marked diminution in joint perception and vibration. There may be glove and stocking loss of pain and temperature sensation. The reflexes may be absent and occasionally transient positive Babinski's sign. Autonomic dysfunctions include hypotension, labile blood pressure, tachyarrhythmia, bradyarrhythmia, or resting tachycardia as well as cardiomyopathy as reported by Finkelstein and Melek 2006. Variants of GBS can be seen in Merritt's Neurology.

70.6 Diagnosis

Diagnosis is based on the following criteria:

1. History of BMT
2. History of respiratory or gastrointestinal infection
3. Neurological examination
4. Cerebral spinal fluid: Increased protein level, but may be normal early in the disease. Cytology is usually normal but monocytes may be high
5. Serological studies: Increased titres of IgG or IgA. GQ1b is a ganglioside antibody that is found in 90 % of Miller-Fisher syndrome
6. Symptoms of GVHD which are:
   (a) Anorexia
   (b) Diarrhea
   (c) Loss of hair
   (d) Leukocytopenia
   (e) Thrombocytopenia
   (f) Growth retardation
   (g) Sometimes death
   (h) The cause may be acute or chronic. The symptoms may develop 5–40 days after BMT in the acute form and after months in the chronic type
7. Nerve studies

70.7 Management

Methods adopted are:

- Plasmapheresis is helpful
- IV human immunoglobulin therapy as an alternative
- Steroid therapy is not so helpful
- Prevention of all kinds of infection in patients with BMT
- In severe GVHD immunosuppression may be considered

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