Guillain–Barré syndrome: a review

Guillain–Barré syndrome is an autoimmune disease which is a common cause of acute neuromuscular paralysis and should be suspected in all patients with unexplained motor weakness. Specific management strategies are more effective if given early in the course of the disease.

Guillain–Barré syndrome is a recognizable clinical entity characterized by rapidly evolving symmetrical limb weakness, loss of tendon reflexes, absent or mild sensory signs and variable autonomic dysfunction which occurs as an autoimmune response following a gastrointestinal or respiratory infection.

Guillain–Barré syndrome can be a severely debilitating disorder affecting 1–3 per 100 000 of the population per annum in the western world. It affects individuals of all ages, although there is a bimodal tendency towards young adults and the elderly. There is a slight male preponderance (Richards and Cohen, 2003).

Preceding events

Guillain–Barré syndrome is a prototype of a post-infectious illness. Two thirds of patients report an antecedent, acute infectious illness, most commonly a respiratory tract infection or gastrointestinal illness, that has resolved by the time neuropathic symptoms develop. The interval between the prodromal infection and the onset of Guillain–Barré syndrome symptoms varies between 1 and 3 weeks. Occasionally longer, it averaged 11 days in several large series (Hahn, 1998).

Campylobacter jejuni, a major cause of bacterial gastroenteritis worldwide, is the most frequent antecedent pathogen for Guillain–Barré syndrome, while cytomegalovirus is the most common viral trigger (Hahn, 1998).

Associations with Epstein–Barr virus and *Mycoplasma pneumoniae* are more often found in Guillain–Barré syndrome than in control patients (Seneviratne, 2000). Human immunodeficiency virus is a well-known association with Guillain–Barré syndrome, which can occur during seroconversion (Seneviratne, 2000).

Clinicopathological types

The main clinicopathological types of Guillain–Barré syndrome are acute inflammatory demyelinating polyradiculoneuropathy, acute motor axonal neuropathy and acute motor sensory axonal neuropathy. Acute inflammatory demyelinating polyradiculoneuropathy accounts for 85–90% of cases (Hahn, 1998; Seneviratne, 2000). Acute motor axonal neuropathy is a purely motor axonal form of neuropathy which involves a high proportion of paediatric patients (Newswanger and Warren, 2004). The disease course of acute motor sensory axonal neuropathy is typically fulminant, generally with slow and incomplete recovery.

Miller Fisher syndrome

In 1956, Fisher described three patients with ataxia, areflexia and ophthalmoplegia – the classical triad of signs in Miller Fisher syndrome (Seneviratne, 2000). Mild limb weakness, ptosis, facial palsy and bulbar palsy may also occur. In most patients with this syndrome, only the peripheral nervous system is affected, but some patients also have brainstem lesions (Hughes and Cornblath, 2005). Resolution occurs in 1–3 months (Seneviratne, 2000).

Pathophysiological role of antiganglioside antibodies

In about half of patients with Guillain–Barré syndrome, serum antibodies to various gangliosides in human peripheral nerves have been found. Most of these antibodies are specific to defined subgroups of Guillain–Barré syndrome (*Table 1*). Although there is a relationship between the presence of these antibodies and the clinical symptoms and severity of Guillain–Barré syndrome, the pathological significance of some of these antibodies is yet to be established (Doorn et al, 2008).

Diagnosis

Guillain–Barré syndrome usually occurs in otherwise healthy people and is not typically associated with an

Table 1. Target antigens for antiganglioside antibodies and the associated features

Serial no	Antigen	Clinical feature or Guillain–Barré syndrome type
1	GM1	Acute motor axonal neuropathy, pure motor Guillain–Barré syndrome
2	GD1a	Acute motor axonal neuropathy
3	GM1b	Pure motor Guillain–Barré syndrome
4	GD1b	Ataxia in Guillain–Barré syndrome
5	GQ1b	Miller Fisher syndrome, Guillain–Barré syndrome with ophthalmoplegia
6	GT1a	Bulbar palsy in Guillain–Barré syndrome

From Kaida et al (2009)

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autoimmune or other systemic disorder. The diagnosis of Guillain–Barré syndrome is based on typical clinical features. In 1993, the diagnostic criteria for Guillain–Barré syndrome were widened by the World Health Organization. The major criteria are now:

- The occurrence of symmetrical weakness
- Decrease or disappearance of the myotatic reflexes
- A nadir within 4 weeks
- Exclusion of other diagnosis (Vander Meche et al, 2001).

Electrodiagnostic examination shows features typical of Guillain–Barré syndrome and examination of CSF shows a high concentration of proteins.

Clinical course

Motor

The main features of Guillain–Barré syndrome are rapidly progressive bilateral and relatively symmetrical weakness of the limbs with or without involvement of respiratory muscles or cranial nerve innervated muscles (Doorn et al, 2008). Maximum weakness is reached within 4 weeks but most people have already reached their maximum weakness within 2 weeks. This is followed by a much slower recovery phase of varying duration which can range from days to months (Doorn et al, 2008).

Sensory

In typical cases, the first symptoms are pain, numbness, paraesthesia or weakness in the limbs. The weakness may initially be proximal, distal or a combination of both. Numbness and paraesthesia usually affect the extremities and spread proximally.

Autonomic

Autonomic involvement is common and can cause urinary retention and ileus. It can also cause cardiac arrhythmia and postural hypotension.

Prognosis

The outcome and prognosis of Guillain–Barré syndrome depends on factors such as *C. jejuni* infection, older age, need for mechanical ventilation and anti GM1 antibodies. Generally by 1 year about two thirds of patients have made a complete recovery (Seneviratne, 2000).

Patients with a rapid onset phase are more likely to do badly, while patients who can still walk at 14 days are likely to improve with or without treatment (Hughes and Cornblath, 2005). Between 4 and 15% of Guillain–Barré syndrome patients die and up to 20% are disabled after 1 year despite treatment (Hughes and Cornblath, 2005).

Management

Treatment for Guillain–Barré syndrome has two components: supportive care and specific therapy. Excellent multidisciplinary care is needed to prevent and manage potentially fatal complications of this disease.

Specific treatment

The two currently recognized disease-modifying modalities are plasma exchange and intravenous immunoglobulin therapy.

Plasma exchange

Plasma exchange became the gold standard treatment for Guillain–Barré syndrome almost 20 years ago. Plasma exchange is beneficial when used within the first 4 weeks of onset but the best effects are seen when it is started within the first 2 weeks (Doorn et al, 2008). Typically up to five exchanges are performed substituting 250 ml/kg of plasma with 4.5% human albumin solution. A Cochrane review states that plasma exchange helps speed recovery from Guillain–Barré syndrome, and is more beneficial when started within 7 days of disease onset (Raphael et al, 2002). Side effects include hypotension, hypocalcaemia, coagulation abnormalities and sepsis (Richards and Cohen, 2003).

Intravenous immunoglobulin

In recent years, intravenous immunoglobulin in a regimen of 0.4 mg/kg body weight daily for 5 consecutive days has replaced plasma exchange as the preferred treatment in many centres. A 2006 Cochrane review on intravenous immunoglobulin for Guillain–Barré syndrome states that in severe disease intravenous immunoglobulin started within 2 weeks of onset hastens recovery as much as plasma exchange. Treatment with intravenous immunoglobulin is more likely to be completed than plasma exchange because of its ease of administration. Giving intravenous immunoglobulin after plasma exchange does not confer any significant extra benefit (Hughes et al, 2006a).

Side effects of immunoglobulin therapy tend to be mild and include nausea, fever, headache, transient rise in liver enzymes, encephalopathy, meningism and malaise. More serious side effects include skin reaction (e.g. erythroderma), hypercoagulability, deterioration in renal function as a result of renal tubular necrosis and anaphylaxis (Richards and Cohen, 2003).

Treatment of patients with Miller Fisher syndrome

Miller Fisher syndrome has a good natural recovery and intravenous immunoglobulin or plasmapheresis have not been shown to influence the outcome (Mori et al, 2007). However, intravenous immunoglobulin therapy may be indicated in patients with swallowing and respiratory problems or those with autonomic dysfunction.

Supportive care

Patients with Guillain–Barré syndrome have a slow period of recovery. Patients are often hospitalized for months. It is essential to monitor their progression and prevent and manage complications.

Respiratory support

Respiratory failure occurs in 25% of patients and is more likely in those with rapid progression, bulbar palsy, upper limb involvement and autonomic dysfunction (Hughes and Cornblath, 2005). Regular monitoring of pulmonary function tests (vital capacity, respiratory frequency) should be carried out initially every 2–4 hours and in the stable phase every 6–12 hours (Doorn et al, 2008).

As respiratory muscles weaken, elective endotracheal intubation should be considered. This is usually converted to a tracheostomy. The presence of bulbar weakness may necessitate early tracheostomy to prevent aspiration pneumonitis and for safe provision of mechanical ventilation and tracheobronchial toilet.

Nutrition

Nutritional support and dietary input should be available, particularly for patients unable to swallow as a result of bulbar involvement and those requiring intubation and ventilation.

Thromboembolic prophylaxis

In non-ambulant adult patients, subcutaneous heparin and graduated compression stockings should be used to prevent deep vein thrombosis.

Analgesia

Pain has been described in up to 89% of patients with Guillain–Barré syndrome (Doorn et al, 2008). Recognition of pain is important, especially in patients who are unable to communicate as a result of intubation.

Narcotics should be used with caution because of the risk of ileus. Physical therapy including gentle massage, passive range of motion exercises and frequent position changes may provide pain relief (Newswanger and Warren, 2004). Carbamazepine and gabapentin have been used as adjuncts in pain management in Guillain–Barré syndrome (Newswanger and Warren, 2004).

Role of steroids

Oral steroids or intravenous methylprednisolone alone are not beneficial in Guillain–Barré syndrome. A Cochrane review concluded that oral corticosteroids may delay recovery from Guillain–Barré syndrome and intravenous corticosteroids do not produce significant benefit or harm (Hughes et al, 2006b). In combination with intravenous immunoglobulin, intravenous methylprednisolone may hasten recovery but does not significantly affect the long-term outcome.

Management of additional symptoms associated with Guillain–Barré syndrome

Autonomic failure

Autonomic dysfunction is a common complication in Guillain–Barré syndrome and occurs in approximately two thirds of patients. Frequent monitoring of autonomic functions should be carried out in all patients with Guillain–Barré syndrome. Vasoactive medications and morphine derivatives should be used with caution in all patients.

Fatigue after Guillain–Barré syndrome

Severe fatigue has been reported in 60–80% of patients after Guillain–Barré syndrome. Fatigue is independent of the severity of weakness during the initial phase of Guillain–Barré syndrome and may continue for many years (Doorn et al, 2008). Physical training programmes are effective for relief of fatigue.

Guillain–Barré syndrome and pregnancy

Guillain–Barré syndrome complicating pregnancy is a rare neurological event that has been associated with an increased incidence of respiratory failure (35%) and an increase in maternal mortality (10–13%) (Kocabas et al, 2007). A delay in presentation is common, maybe because initial non-specific symptoms mimic physiological changes in pregnancy (Chan et al, 2004).

Termination of pregnancy does not hasten the recovery of maternal disease nor improve maternal outcome, so Guillain–Barré syndrome on its own is not an indication for termination of pregnancy. There has only been one case reported of neonatal Guillain–Barré syndrome in a baby born to an affected mother (Luijckx et al, 1997). Several cases in the literature report successful management of Guillain–Barré syndrome during pregnancy and labour (Brooks et al, 2000; Kocabas et al, 2007).

There are no specific guidelines for the management of Guillain–Barré syndrome in pregnancy or management of labour or delivery in a patient with Guillain–Barré syndrome. The principles of management remain the same but meticulous attention should be paid to early identification and treatment of infection as these can be more severe during pregnancy.

General management

Because pregnancy itself is also a strong risk factor for thromboembolism, early administration of prophylactic anticoagulation and regular physiotherapy are important.

Normal uterine contractions are maintained and vaginal delivery is possible in the parturient who presents with Guillain–Barré syndrome. Therefore the presence of this syndrome is not an indication for caesarean section.

Caution should be exercised in the use of regional and general anaesthesia. Although there have been concerns regarding the possibility of Guillain–Barré syndrome being triggered by regional anaesthesia, there is no evidence that epidural anaesthesia causes this problem.

The future

New treatment options are required to improve the prognosis of Guillain–Barré syndrome treatment. This is especially applicable to mildly affected patients requiring

less aggressive treatment. Now the antiganglioside antibodies have been identified, research should be directed towards countering their pathological effects.

Conclusions

If recognized early, Guillain–Barré syndrome can be managed successfully. Although plasmapheresis or intravenous immunoglobulin is specific to management, patient outcome depends heavily on meticulous care of nutrition, analgesia and control of autonomic stability. Early recognition of Guillain–Barré syndrome during pregnancy can be a challenge but principles of its management remain unchanged. BJHM

KEY POINTS

- Although Guillain–Barré syndrome is a relatively rare pathological disease, it can be severely debilitating.
- On grounds of equal therapeutic benefit, greater convenience and similar overall cost, intravenous immunoglobulin may be preferable to plasma exchange. Immunoglobulin therapy is relatively easy to administer and is therefore suitable for use in smaller centres, reducing the need for interhospital transfers.
- Oral steroids or intravenous methylprednisolone alone are not beneficial in Guillain–Barré syndrome.
- Normal uterine contractions are maintained and vaginal delivery is possible in the parturient who presents with Guillain–Barré syndrome. Therefore the presence of this syndrome is not an indication for caesarean section. Caution should be exercised in use of regional and general anaesthesia.

Conflict of interest: none.

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