Guillain-Barr'e Syndrome

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Introduction

Guillain-Barr'e syndrome is the most common acute polyradiculopathy. While generally benign, spontaneously resolving condition, its course may be complicated by ventilatory failure and anythmias, with about 10-15% of patients being left with severe neurological deficits.

History

In 1830, Wardrop in England and Ollivier in France reported cases of patients developing severe ascending paralysis with subsequent recovery[1]. Landiy in 1859, described 10 patients with the features of Guillain-Barr'e syndrome[1]. The next significant development in our understanding of this condition came in 1916, when Guillain-Barr'e and Stohi documented the cerebrospinal fluid changes associated with the syndrome[2].

Epidemiology

All ages can be affected, but the frequency tends to increase in older age groups. There is a slight male predominance. Cases of the illness have been documented worldwide without seasonal association[3]. Overall, about 70% cases have a recognized preceding prodrotnal illness of other antecedent event . Such event[2] include viral and bacterial infections e.g., upper respiratory tract infection, diarrhoea, jaundice, as well as vaccination and surgical procedures. There has also been an association with a number of systenuc illnesses including certain malignancies and some connective tissue disorders. Infectious prodromes usually involve viral or bacterial agents. Cytomegalovirus (CMV) and Epstein Barre Virus (EBV) are the most conunonly associated viruses. The EMV infection may have manifested itself as an upper respiratory tract infection or as a gastroenteritis. Infectious mononucleosis due to EBV may also precede Guillain-Barr'e syndrome, as may infectious mononucleosis like picture due to CMV. Another virus that has been associated with Guillain-Barr'e syndrome is HIV[1]. Patients who are infected with the virus are more likely to develop Guillain-Barr'e syndrome in the earlier stages of the disease as contrast to the later more immunocompromised stages. Bacterial infections include Canipylobacterjejuni, Mycoplasma pneumoniae and Borrelia burgdorferi. Vaccination is also a well recognized antecedent event. The swine influenza vaccine of 1976, in particular, was associated with an increased incidence of Guilain-Barr'e syndrome (almost 20 times) . Likewise vaccinations with oral polio vaccine has also been associated with Guillain-Barr'e syndrome. Rabies vaccine and Guillain-Barr'e syndrome have also beenlinked. This is likely related to older preparations of the vaccine that were made from neural tissue, newer preparations have not been associated with the syndrome. Finally, many surgical procedures have been observed to be possible antecedent events.

Pathogenesis

The underlying pathogenesis of Guillain-Barr'e syndrome is not well understood. The condition is thought to be an inflammatory process involving an autoiminune response to schwanncells orpenpheral nerve myelinantigens. Pathologically, it is characterized by discrete foci of inflarnniation with segmental demyelination of peripheral nerves. It has now become recognized as a clinical syndrome that may be due to several pathological entities consisting of an acute inflammatory demyelinating polyradiculoneuropathy as well as an acute motor axonal neuropathy. Campylobacter Jejuni infection is a common preceding event and together with antiganglioside GM1 antibodies, is associated with axonal damage and a poor outcome. The mechanism by which such antibodies damage axons is not clear. The Miller Fisher syndrome is very closely associated with antibodies to ganglioside OQib that

may be important in pathogenesis. There may be multifocal loss of myelin throughout the peripheral nervous system with relative preservation of axons. Inflanunatoiy mononuclear cell infiltration is seen in peripheral nervous system. The extent and severity of cell infiltration is variable. Immunohistochemical studies with monoclonal antibodies have identified more leucocytes;(PD7/2BI 1+) and T cells (UCHL1+) in the endoneurium.

These findings and recent reports indicate that the pathology of Guillain-Barr'e syndrome is variable. This variability may reflect differences in pathogenesis, with greater cell-mediated immunity in some cases and greater antibody targeted macrophage mediated demyelination in others. Two major hypotheses which have been generated suggest that these inflammatory foci are secondary to either cellular immunity process orto humoral factor[2]. Early studies in fatal cases did not show evidence of any cellular infiltrates early in the illness, leading to the initial speculations about a humoral factor. Subsequently however, cellular infiltrates with lymphocytes and macrophages were detected in cases soon after the onset of the illness. More recently, with the advent of plasmapheresis, increased enthusiasm for a humoral basis for Guillain-Barr'e syndrome has developed. Plasmapheresis, however, can remove numerous inflammatory mediators in addition to antibodies and so the effect of plasma exchange in and of itself does not lend marked support to the hypothesis of a humomi basis for the illness.

Clinical features

The hallmark of Guilain-Baff'e syndrome is that of acute paralysis. There are, however, numerous other signs and symptoms that may be associated with the syndrome, as well as atypical variants of the classical ascending paralysis which may complicate diagnosis of the disorder. The most common and most widely recognized feature of Guillain-Barr'e sndmme is that of acute motorweakness. This usually begins in the lower limbs and progresses to a variable degree to involve the upper limbs, cranial nerves and thoracic musculature. Involvement is generally symmetrical though some asy mmetry may be seen. Limb involvement may be more proximal, more distal or about equal. Cranial nerve involvement is cOmmonwith signs of seventh nerve weakness being the most frequent. Laiyngeal and phaiyngeal weakness is less common, but can lead to severe complications such as difficulty in swallowing and aspiration pneumonia if undetected. Thoracic and diaphragmatic muscular weakness occurs in one-third of cases leading to respiratoty compromise. Reflexes am absent or severely reduced. This is true both for weakened muscle group and for muscles without marked clinical involvement. Symptoms of distal parasthesia and deep aching painare quite common, being present inabout two third of cases. Objective sensory loss, however, is less frequent and will most often involve propnoception and vibration, thoughpain and temperature modalities may also be affected. Autonomic nervous system dysfunction is another prominent aspect of Guillain-Barr'e syndrome. This may take the form of cardiac rythm disturbances, labile blood pressure, or altered gastrointestinal orgemto- urinary function. It is this aspect of the disease (especially the cardiovascular involvement) that accounts for the majority of fatalities. The most common cardiac arrythmia is persistent sinus tachycardia. Other dysrythmias, are bradycardias, atrioventricular blocks, atrial fibrillation and ventricular tachycardia. Blood pressure abnormalities may include marked postural hypotention and difficult to manage swings from hypertension to hy potension and vice versa. Finally, both the syndrome of inappropriate antidiuretic hormone and diabetes insipidus have been described and associated with autonomic involvement. With regard to the time course of the illness, the first symptoms of weakness generally appearabout two to three weeks after the prodromal illness and will progress over the course of next 1-3 weeks. Symptoms will remain stable for a similar period of time, after which slow recovery wiligenerally occur overa period of months. One of the less typical presentations is MillerFisher syndrome, a triad of ataxia, areflexia and opthalmoplegia. Itis generally thought tobe a morn benignform of illness but still has the potential for rapid respiratory compromise as well as autonormic dysfunction[1].

Diagnosis

No specific test is available to definitely diagnose Guillain- Barr'e syndrome. Rather, one needs to consider the signs and symptoms, course, cerebrospinal findings and electomyography results[5]. Features required for diagnosis include progressive motor weakness involving more than one limb. Weakness may be mild, or severe with total paralysis of all extremities and the trunk, bulbar and facial paralysis external ophthalmoplcgia and areflexia. Features strongly supportive of the diagnosis are clinical features of progression to maximal involvement by 2 tO 4 weeks, relative symmetery, mild sensory symptoms or signs, cranial nerve involvement; recovery is usually complete; begins 2 to 4 weeks after progression stops; autonomic dysfunction; absence offeverat onset of neuropathic symptoms. The cerebrospinal fluid findings strongly supporting the diagnosis are elevated CSF protein level and cell count of 10 or fewer mononuclear leukocytes per ml, now referred to as "albuminiocytologic dissociation".

Electrornyography is importantbothfordiagnosis of the conditionand also as atoolto assist in predicting the long term prognosis. The classical findings am those of reduced nerve conductionvelocities orconductionblock at some point in the illness. Prolonged distal latencies may be seen as well as absent I and II responses. Responses consistent with axonal degeneration may also be present. Patients with mean distal motor amplitudes of less than 20% of normal have a poor prognosis[4]. The diagnostic process is complicated by the wide range of possible clinical presentation like, marked persistent asymmetry of weakness,persistent bladder or bowel dysfunction more than 50 mononuclear leukocyte per ml in CSF and sharp sensory level.

The differential diagnosis of Guillain-Barr'e syndrome includes several infectious processes, toxic exposures and porphyria. Infections include poliomyelitis, a febrile illness associated with an asymmetrical pattern of weakness as well as memngeal irritation and a marked cerebrospinal fluid pleocytosis. Diptheric neuropathy is very similar to Guillian-Barre syndrome. The history of pharyngitis and the marked delay between this episode and the onset of weakness (often about three months) help to distinguish the two conditions. Other toxin conditions include botulism, hexane inhalation, arsenic ingestion, tick paralysis and ingestion of marine animal toxins. Hepatic porphyria also needs to be considered; these patients will have a history of abdominal painand the weakness will generally develop aflerexposure to barbiturates or other drugs.

Treatment

The treatment of Guillain-Barr'e syndrome is based on good supportive care and immune modulating therapies.

Supportive measures

These involve careful monitoring for respiratory compromise and autonomic instability. They also involve preventing and treating complications of immobility and altered pharyngeal and thoracic muscle function. Thus, patient needs to be admitted to a hospital and assessed frequently for progression of thoracic muscle weakness. Vital capacity is measured several times a day. Arterialbloodgases are not very useful markers as hypoxia and hypercathia am late signs of respiratory failure. Monitoring patients for impending respiratory failure is crucial even if they have minimal weakness, since thoracic muscle involvement may develop and progress very suddenly. Sinus tachycardia due to autonomic instability is frequent. Any other arrythmia, or blood pressure instability however, should be another indication for ICU admission. Thromboembolic disease prophylaxis is important, as is aggressive treatment of any thrombotic complications. Aspiration pneumonia is common and needs appropriate preventive and treatment strategies.

Immune modulating therapies

Apart from these supportive intervention there am three immune modulating therapies that have been evaluated in this condition: Plasma exchange, intravenous immune globulin and corticosteroids. Plasma exchange: Recent systemic overview of the trials evaluating the role of plasma exchange in Guillain-Barr'e syndrome[6] indicates that plasmapheresis hastens recovery and helps to prevent

respiratory failure. Plasma exchange volumes of 200-250 mI/kg are used over 7-14 days[7]. With regard to complications, the only significant difference that was noted was that the plasmapheresed patients had a higher rate of septicemia[8].

Immune globulin: The other immune modulating therapy that has been shown to benefit patients with Guillain-Barr'e syndnme is parentemi immune globulin (0.4 gm/kg daily for 5 days).

Corticosteroids: For many years, corticosteroids were believed to be beneficial in Guillain-Barr'e syndrome. Numerous studies suggested that they hastened recovery and improved overall outcome. In 1978 and 1993 however, two randomized controlled trials[9,10] assessed this question and arrived at a conclusion that corticosteroids did not play much role in the improvement of the condition.

Immunosuppressants

It has been observed that mortality among those who received immunosuppressants was significantly higher than those who did not receive them[11].

Conclusion

Guillain-Barr'e syndrome is an uncommon condition associated with peripheral nerve demyelination that leads to weakness, as well as sensory and autonomic symptoms. The condition generally begins several weeks after a prodromal illness and progresses over the next few weeks. A number of antecedent illnesses precede the muscular weakness, the commonest being fever before the onset of limb weakness. Guillain-J3arr'e syndrome generally has a good prognosis, reflected in an overall recovery rate of 80-85% by 12- 18 months. However, this leaves about 10-15% patients with severe long term disabilities such as, inability to perform selfcare activities or walk. Between 10-20% of patients will become ventilator dependent at some time duringthe course of their illness and about 3-4% of patients will die, usually because ofaspimtionpneumoniaorcardiovascularinstability. Treatment and careful observation are important for these patients to prevent the complications of immobility and to provide timely respiratory support, should it become necessary. Recently, immune modulating therapies, plasmapheresis and immune globulin have been shown to influence the course of Guillain-Barr'e syndrome.

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