DOI: http://dx.doi.org/10.5281/zenodo.4038305

REVIEW ARTICLE OPEN ACCESS

NEURONS
cmrasociety.org/neurons

Guillain-Barré syndrome: A review

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ARTICLE INFO

Received: 14 Mar 2020
Accepted: 20 May 2020
Published: 30 June 2020

Abstract

Introduction

Guillain-Barré syndrome (GBS) is a genetic condition that represents the most common cause of the acute flaccid symmetrical weakness of the limbs and areflexia that typically occurs within a month. The etiology and pathogenesis remain largely mysterious and despite immunotherapy, the syndrome leads to death or serious disability in 9-17 percent of cases. Guillain-Barré syndrome is related to Campylobacter infection in terms of etiology but the disease occurs in less than 0.1 per cent of infections. Activated macrophages and T cells, as well as serum antibodies to gangliosides, are identified in terms of pathogenesis but their meaning is unclear. Antiganglioside antibodies are present in 25 percent of patients with standard acute demyelinating GBS; 95 percent of patients in Miller-Fisher syndrome have antibodies to GQ1b ganglioside. The Guillain-Barré syndrome is a heterogeneous disease with various subtypes and recent evidence pointing to the role of immunohistochemical methods in ganglioside epitopes. GBS derives from a permissive genetic background from which disease is caused by environmental factors, including pathogens, vaccination and the effect of aging. Over 10 white cells in cerebrospinal fluid are likely to raise questions about alternative diagnoses like HIV. There are several treatment options, including plasma exchange and intravenous administration of the immunoglobulin. Most cases can be resolved without sequelae, but those that don't will leave substantial residual debility behind.

Conclusion

Biological therapies currently underway. The study includes monoclonal antibodies directed at components of the supplement pathway. Individuals are encouraged to communicate with their general practitioner and neurologist or to contact the GBS Support Group's information pages for general guidance on vaccine use after GBS.

KEYWORDS

Antibodies, diagnosis, Guillain-Barré syndrome, nerve, patients, weakness

INTRODUCTION

GBS may be challenging to diagnose at an early stage because it can show ambiguous signs of fatigue, neck or back pain and paraesthesia. In atypical situations, it can also be complicated, with an irregular distribution of weakness, such as presenting in the upper limbs or concentrating on respiratory muscles and interfere with limb strength. An initial casualty discharge is not unusual, but patients with suspected GBS should be hospitalized and closely monitored in cases where paralysis and life-threatening bulbar dysfunction is rapidly developing. Weakness can appear 'pyramidal,' with hip and knee flexor weakness without other features of associated with 'upper motor neurone.' [1-2] Total areflexia can develop from initial hyporeflexia within a few days. By definition, the progression of the two or more limbs weakness from regular to nadir should be less than four weeks and usually two weeks or less. A small number have the development of the subacute symptoms over 4–8 eight weeks, but no more would indicate an alternative diagnosis. There tends to be a relapsing form of GBS in sporadic patients. Sensory signs and symptoms are generally mild. Other variations include the Miller-Fisher syndrome (MFS), identified initially as ataxia, ophthalmoplegia and areflexia, but also patients with more severe involvement of the cranial nerve. The MFS functionality will overlap with GBS.

GBS usually does not cause vision impairment, hearing loss or early involvement in the sphincter, fever. Approximately two-thirds of patients reported anterior infection in the previous six weeks (e.g. diarrhoea, classically due to Campylobacter jejuni or upper respiratory tract infection); Anecdotal studies have documented GBS after vaccination, but only the vaccination program for swine flu in the USA in 1976 was causally related to GBS. [3, 4]

GBS is thought to be attributable to an inflammatory attack on peripheral nerves, occurring without evidence of other autoimmune disorders in previously safe patients. Some of the most frequently associated GBS-related antecedent infections (e.g. C. jejuni) are considered to share structural similarities with peripheral nerve components. Post-mortem tests and nerve biopsies indicate nerve penetration of the antibody and complement deposition, T cell and macrophage. In the acute phase of GBS, the most robust of which are antibodies directed against individuals or combinations of gangliosides, multiple immunological deranges have been identified.

The differential diagnosis of the syndrome is relatively broad early, with the initial emphasis on finding the disease in the nerve roots and peripheral nerves rather than anywhere else in the nervous system. If a neuropathy diagnosis is made, the differential diagnosis includes: infection (lyme, diphtheria), inflammatory (neurosarcoid), paraneoplastic, malignant (due to infiltration of nerve roots), vasculitic, metabolic (beri-beri due to vitamin B1 deficiency), postinfectious/autoimmune in origin (GBS). [5]

GBS is a clinical condition with the subsequent exclusion of other imitations and with accompanying tests. A cerebrospinal fluid (CSF) white cell count of over 10/µl raises the possibility of leptomeningeal malignancy, HIV or an alternative infectious diagnosis (e.g. Lyme disease or poliomyelitis). However, in clinical trials, CSF cell counts up to 50/µl are permitted. IvIg can very occasionally cause aseptic meningitis. Typically, the CSF protein is raised after the first week, often to more than 1 g/l.

Routine blood tests may contain levels of creatine kinase, biochemistry, and Ig. This is done to rule out other causes of weakness and to-ivIg risks. In renal failure ivIg is relatively contraindicated and in IgA-deficient patients it is more likely to induce anaphylaxis. [6-9]

Antiganglioside antibodies are normally measured in GBS, but the diagnosis is not removed due to their lack. evidence indicates that they are pathogenic. Gangliosides are prevalent in the nervous system helping to preserve the structure of the cell membrane:

Twenty-five per cent of patients with acute inflammatory demyelinating (AIDP) GBS have antiganglioside (usually GM1) antibodies, ninety-five per cent of patients with Miller-Fisher syndrome have anti-GQ1b antibodies, and 50 per cent of patients with axonal (acute motor axonal neuropathy) antibodies. Cardiac arrhythmias and declining respiratory function can be life-threatening. A cardiac monitor and regular vital capacity (VC) measurements are essential, at least until the patient is mobile. VC monitoring frequency (e.g. hourly to qds) should be adjusted to the clinical condition. No replacement for the peak expiratory flow rates. Intensive care should be notified early if there is the strong involvement of bulbars and elective intubation should be initiated as VC reaches 15 ml / kg. Declining oxygen saturations and changes in blood gas values can indicate imminent respiratory arrest. Prevention of deep vein thrombosis is important with stockages of thromboembolic disease and subcutaneous heparin. [10-14]

Treatment

Randomized controlled trials indicate that recovery of non-ambulant patients treated within two weeks of the onset of symptoms is accelerated by 0.4 g / kg / day ivIg for 5 days or 4–6 plasma exchanges.10,11Plasma exchange can benefit out-patients and patients with symptoms up to 30 days. A similar benefit could be

derived from ivIg by extrapolation, but experiments were not performed in these patient groups. [15]
Treatment should be begun as soon as possible, although there is no evidence to indicate that beginning it twelve hours sooner (e.g. overnight). First-line therapy is most generally ivIg due to its ease of administration. Some patients initially respond to ivIg but the impact will start to wear off within six weeks. Anecdotal evidence supports the use of additional ivIg in these 'therapeutic variations'. There is no indication that offering a second course of ivIg is of any benefit to those patients who do not respond to the medication. This is currently being investigated in a trial (personal communication; Collaboration on Inflammatory Neuropathy). [16]
There is no proof that steroids aid, although they don't impede this should be given if needed for other reasons, or that giving plasma exchange followed by ivIg is better than exchanging plasma alone.

Rehabilitation and news

Adequate pain management and a multidisciplinary therapeutic program are essential, as is patient education during slow but steady recovery, with progress expected to last up to two years. The GBS Support Network has a helpful website (www.gbs.org.uk) as well as phone line support. The US counterpart is the International GBS Foundation (www.gbs-cidp.org).
GBS is getting more media attention because of concern about whether the latest outbreak of swine flu will lead to more cases. Latest analyzes of historical evidence indicate that for seasonal influenza at least, the virus itself is much more likely to contribute to GBS than its vaccine. Individuals are encouraged to communicate with their general practitioner and neurologist or to contact the GBS Support Group's information pages for general guidance on vaccine use after GBS. A great deal remains to be done to reduce the disability burden following GBS. [14, 16] Early assessment of potential non- or poor responders may alter their management of current care. Recent work indicates that patients have different ivIg metabolism pharmacokinetics and may need different or repeated ivIg. [15] doses. Better understanding of the pathogenesis and target antigen in the normal AIDP GBS variant would be important for the immune response. Until symptoms emerge, treatment of a monophasic autoimmune disease such as GBS is hampered by the limited ability to shut off a mechanism already well under way. [17-19]

CONCLUSION

Biological therapies currently under study include monoclonal antibodies directed at components of the supplement pathway. Novel clinical trials are likely to be hampered to some extent. Individuals are encouraged to communicate with their general practitioner and neurologist or to contact the GBS Support Group's information pages for general guidance on vaccine use after GBS.

AUTHORS' CONTRIBUTIONS

a. Study planning: AU, GT
b. Manuscript writing: AU, GT
c. Manuscript revision: AU
d. Final approval: AU, GT
e. Agreement to be accountable for all aspects of the work: AU, GT

FUNDING

We have not received any funds for this review.

AVAILABILITY OF DATA AND MATERIALS

All data and materials are included in the manuscript, no separate data is available.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval is not required for this article type.

CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

None declared.

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