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Guillain–Barré syndrome (GBS) Clinical Guideline

Introduction

Guillain–Barré syndrome (GBS) is an inflammatory disease of the peripheral nervous system (PNS) and is the most common cause of acute flaccid paralysis, with an annual global incidence of approximately 1–2 per 100,000 person-years. The disease is much rarer in children and adolescents, with an incidence of 0.62 -0.75 cases per 100,000 PYs. In most patients the acute onset of neurological symptoms is preceded by an infective illness. It is monophasic illness.

The three phases of GBS are the progressive phase (lasting from days to 4 weeks), a plateau phase with little clinical change (lasting from days to months), and a recovery phase. By 7 days, about three quarters of patients will achieve their nadir in neurologic function, and 98% will do so by 4 weeks.

Treatments with immunotherapy accelerate recovery and decrease complications during the acute illness. Prognostic scales have been developed to predict patient outcome and to stratify treatment. Despite the proven effectiveness of these treatments in GBS, the care of patients in clinical practice is often complex due to lack of strong evidence and resultant variation in practice.

Guillain-Barré syndrome require close monitoring for disease progression, in particular for bulbar weakness, respiratory insufficiency, and autonomic dysfunction.

Holistic and multidisciplinary approach with involvement of the physiotherapists, occupational therapist, pain management and rehabilitative services earlier on are essential.

Note: Consider differential diagnosis of acute spinal cord compression or spinal cord lesion early.

All suspected cases of GBS need to be discussed with the Paediatric neurologist at the earliest opportunity.

Management approach at a glance

Diagnosis

When to suspect GBS:

- Rapidly progressive bilateral limb weakness and/ or sensory deficits
- Hypo/areflexia
- Facial or bulbar palsy
- Ophthalmoplegia

How to diagnose GBS:

- Check diagnostic criteria
- Exclude other causes
- Brain and spine MRI with contrast (unless contrast is contraindicated)
- Other investigations:
  - Blood laboratory tests (see below)
  - CSF examination
  - Electrophysiological studies
  - Respiratory function

Acute Care

When to consider admission to critical care / PICU

One or more:

- Rapid progression of weakness involving upper limbs
- Sever autonomic / swallowing dysfunction
- Evolving respiratory distress

When to start treatment:

One or more:

- Inability to walk independently
- Rapid progression of weakness
- Severe autonomic or swallowing dysfunction
- Respiratory insufficiency

Treatment options:

1. Intravenous immunoglobulin (0.4g/kg daily for 5 days or 2g/kg given over 3-5 days)

2. Plasma exchange (PLEX)

Monitoring:

Regularly assess

- Muscle strength
- Respiratory function
- Swallowing function
- Blood pressure
- Heart rate/rhythm
- Bladder/bowel control

Early complications:

- Aspiration
- Cardiac arrhythmias
- Infections
- DVT
- Neuropathic pain
- Depression
- Urinary retention
- Constipation
- Corneal Ulceration
- Weight loss
- Hyponatraemia
- Pressure ulcers
- Limb contractures

Clinical Progressions:

No initial response or incomplete recovery – No evidence for repeating treatment

Treatment related fluctuation – repeat same treatment.

Long-term Care

Rehabilitation:

- Start rehabilitation programme early
- Manage long-term complaints: fatigue, pain and psychological distress
- Contact GBS patient organisations

Typical Clinical Features:

Classic sensory motor form of GBS present with distal paraesthesia or sensory loss accompanied or followed by weakness that starts in the lower limbs and progresses to upper limbs and cranial/ bulbar muscles.

Reflexes are decreased or absent in most patients at presentation at time of severe weakness.

Dysautonomia is common and can include blood pressure or heart rate instability, pupillary dysfunction, and bowel or bladder dysfunction.

Pain is frequently reported (can be muscular, radicular or neuropathic.)

Disease onset is acute or subacute, and patients typically reach maximum disability within 2 weeks.

In patients who reach maximum disability within 24 h of disease onset or after 4 weeks, alternative diagnoses should be considered.

GBS has a mono- phasic clinical course, although TRFs (Treatment Related Fluctuations) and relapses occur in a minority of patients.

Atypical Clinical Features

Weakness and sensory signs, though always bilateral, can be asymmetrical or predominantly proximal or distal, and can start in legs, arms or simultaneously in all limbs.

Severe and diffuse pain or isolated cranial nerve dysfunction can precede the onset of weakness.

Young (<6 years old) children can present with nonspecific or atypical clinical features, such as poorly localized pain, refusal to bear weight, irritability, meningism, or an unsteady gait.

In a minority of patients with atypical GBS, particularly those with only motor signs (pure motor variant) and an AMAN (Acute Motor Axonal Neuropathy) subtype on electrophysiological examination, normal or even exaggerated reflexes might be observed throughout the disease course.

Variants

	Patterns of limb weakness	Sensory involvement	Cranial nerve involvement	CNS involvement	Serial neural conduction	IgG against ganglioside type	Proportion of patients with Guillain-Barré syndrome
Guillain-Barré syndrome spectrum							
Classic							
Demyelinating	Upper and lower limbs	Yes	Yes	No	AIDP	Unknown	69–90%
Axonal	Upper and lower limbs	Yes in AMSAN, no in AMAN	Yes	No	AMSAN, RCF	GM1, GD1a	<22%
Pure motor	Upper and lower limbs	No	Yes	No	AMAN, RCF	GM1, GD1a	5–70%
Pure sensory	None	Yes	No	No	Abnormal SNAPs	GD1b	<1%
Paraparetic	Lower limbs	Yes	No	No	Axonal	GM1, GD1b	5–10%
Facial diplegia and paraesthesia	None	Yes (distal)	Facial	No	AIDP	Unknown	<5%
Pharyngeal, cervical, brachial	Proximal upper limbs	Supportive	Bulbar	No	Equivocal	GT1a, GQ1b	<5%
Acute bulbar palsy	None	Supportive	Bulbar	No	Equivocal	GT1a	<1%
Guillain-Barré syndrome with hyperreflexia	Upper and lower limbs	Yes	Yes	No	Axonal	GM1	<1%
Miller Fisher syndrome spectrum							
Classic	None	Ataxia	Ocular motor nerves	No	Abnormal SNAPs	GQ1b, GT1a	4–25%
Acute ophthalmoplegia	None	Supportive	Ocular motor nerves	No	Normal	GQ1b	<1%
Acute ataxic neuropathy	None	Ataxia	No	No	Axonal	GM1	<5%
Acute ptosis	None	Supportive	Ptosis only	No	Normal	GQ1b	<1%
Acute mydriasis	None	Supportive	Dilated pupils	No	Normal	Unknown	<1%
Acute vestibular syndrome	None	Supportive	Nystagmus	Nystagmus	Normal	GQ1b	<1%
Bickerstaff brainstem encephalitis							
Classic	None	Supportive	Ocular motor nerves	Yes	Axonal	GQ1b, GT1a	<5%
Acute ataxic hypersomnolence	None	Ataxia	No	Yes	Normal	GQ1b	<1%

AIDP=acute inflammatory demyelinating polyneuropathy. AMAN=acute motor axonal neuropathy. AMSAN=acute motor and sensory neuropathy. RCF=reversible conduction failure. SNAP=sensory nerve action potential.

How to diagnose GBS

The diagnosis of GBS cannot be established by a single clinical parameter or test result. It is based on the combination of clinical and paraclinical findings, investigations with simultaneous exclusion of relevant differential diagnoses (See Appendix for list of D/D).

Two most commonly used sets of diagnostic criteria for GBS are NINDS & Brighton Criteria and later is validated in children as well.

Investigations

Laboratory testing is guided by the differential diagnosis in individual patients (See Appendix for the list of D/D) However, LP and NCS are part of the diagnostic criteria.

Commonly performed investigations: FBC, Ferritin, U&E, Bone profile, CRP, ESR, CK, LFT's, TFT's capillary blood gas (CBG). **Please save serum sample for potential future investigations**

CNS imaging (MRI Brain and whole Spine with contrast).

Lumbar puncture (LP): CSF for Protein, MC&S, viral PCR's, with matched plasma samples for Glucose, Oligoclonal bands, lactate. Please save CSF sample for potential future investigations

Nerve conduction studies (NCS)

CXR

ECG

Stool culture for Polio and Campylobacter jejuni.

Testing for preceding infections does not usually contribute to the diagnosis of GBS, but can provide important epidemiological information therefore consider sending NP swabs for viral infections like COVID 19. Some other agents to consider are CMV, EBV and Mycoplasma pneumoniae.

Consider repeat CSF and/or NCS at day 7-10 if initial results are normal.

Admission to PICU

As up to 22% of patients with GBS require mechanical ventilation within the first week of admission, it is recommended to consider mechanical ventilation in children and adolescents with GBS upon the first signs of respiratory exhaustion at an early stage before clinical decompensation occurs.

A state of imminent respiratory insufficiency is defined as clinical signs of respiratory distress, including breathlessness at rest or during talking, inability to count to 15 on a single breath, use of accessory respiratory muscles, increased respiratory or heart rate, vital capacity <15–20 ml/kg or <1 l, or abnormal capillary/ arterial blood gas or pulse oximetry measurements.

Treatment

IVIG therapy should be started if patients are unable to walk independently.

Evidence on treatment efficacy in patients who can still walk independently is limited, but treatment should be considered, especially if these patients display rapidly progressive weakness or other severe symptoms such as autonomic dysfunction, bulbar weakness or respiratory insufficiency.

1. **Intravenous immunoglobulin: 2 g/kg given over 3-5 days (calculate duration depending on rounding doses to nearest full vial size) or 0.4g/kg daily for 5 days. https://igd.mdsas.com/wp-content/uploads/Commissioning-Criteria-Policy-for-the-use-of-Ig-Version-Finala.pdf**
2. **Plasma exchange – consider early discussion with paediatric neurologist if clinically worsening.**

Monitoring Disease Progression

Regular assessment is required to monitor disease progression and to prevent complications.

1. Routine measurement of respiratory function is advised, as not all patients with respiratory insufficiency will have clinical signs of dyspnoea.

These respiratory measurements can include usage of accessory respiratory muscles, counting during expiration of one full-capacity inspiratory breath (a single breath count of declining pattern), forced vital capacity, and peak cough flow.

2. Muscle strength in the neck, arms and legs should be assessed using the Medical Research Council grading scale or a similar scale.

3. Patients should be monitored for swallowing and coughing difficulties.

4. Autonomic dysfunction should be assessed via electrocardiography and monitoring of heart rate, blood pressure, and bowel and bladder function. Formal swallowing assessment should be carried out. Consider nil by mouth (NBM) and naso-gastric tube (NGT) early.

Up to two-thirds of the deaths of patients with GBS occur during the recovery phase and are mostly caused by cardiovascular and respiratory dysfunction.

Therefore, it is advised to stay alert during this phase and monitor the patient for potential arrhythmias, blood pressure shifts, or respiratory distress caused by mucous plugs.

This monitoring is especially important in patients who have recently left the PICU.

Managing Early Complications

Complications in GBS can cause severe morbidity and death. Some of these complications, including pressure ulcers, hospital-acquired infections (for example, pneumonia or urinary tract infections) and deep vein thrombosis, can occur in any hospitalized immobile patient, and standard-practice preventive measures and treatment are recommended.

Medicinal and or (optional) physical thrombosis prophylaxis are recommended for adolescents during the period of limited mobility.

Other complications are more specific to GBS, for example, the inability to swallow safely in patients with bulbar palsy; corneal ulceration in patients with facial palsy; and limb contractures, ossification and pressure palsies in patients with limb weakness.

Adequate management of complications is best undertaken by a multidisciplinary team, which might include nurses, physiotherapists, rehabilitation specialists, occupational therapists, speech and language therapists and dietitians.

Consider monitoring for possible complications and immobility:

- Additional weight loss
- Psychological symptoms
- Electrolyte dysfunction
- Silent Aspiration
- Urinary retention (due to neuropathic bladder)
- Bowel dysfunction

Managing Clinical Progression

Discuss with neurology team at earliest opportunity if clinical progression is of concern.

APPENDIX :

1) Differential Diagnosis
2) Diagnostic criteria , Brighton score & features on NCS
3) MRC and GBS Disability scale
4) Link for diagnostic tools
5) References

The differential diagnosis of Guillain–Barré syndrome is broad and highly dependent on the clinical features of the individual patient. Here, we present an overview of the most important differential diagnoses categorized by location in the nervous system.

CNS
- Inflammation or infection of the brainstem (for example, sarcoidosis, Sjögren syndrome, neuromyelitis optica or myelin oligodendrocyte glycoprotein antibody-associated disorder)[a]
- Inflammation or infection of the spinal cord (for example, sarcoidosis, Sjögren syndrome or acute transverse myelitis)
- Malignancy (for example, leptomeningeal metastases or neurolymphomatosis)
- Compression of brainstem or spinal cord
- Brainstem stroke
- Vitamin deficiency (for example, Wernicke encephalopathy[a], caused by deficiency of vitamin B1, or subacute combined degeneration of the spinal cord, caused by deficiency of vitamin B12)

Anterior horn cells
- Acute flaccid myelitis (for example, as a result of polio, enterovirus D68 or A71, West Nile virus, Japanese encephalitis virus or rabies virus)

Nerve roots
- Infection (for example, Lyme disease, cytomegalovirus, HIV, Epstein–Barr virus or varicella zoster virus)
- Compression
- Leptomeningeal malignancy

Peripheral nerves
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
- Metabolic or electrolyte disorders (for example, hypoglycaemia, hypothyroidism, porphyria or copper deficiency)
- Vitamin deficiency (for example, deficiency of vitamins B1 (also known as beriberi), B12 or E)
- Toxins (for example, drugs, alcohol, vitamin B6, lead, thallium, arsenic, organophosphate, ethylene glycol, diethylene glycol, methanol or N-hexane)
- Critical illness polyneuropathy
- Neuralgic amyotrophy
- Vasculitis
- Infection (for example, diphtheria or HIV)

Neuromuscular junction
- Myasthenia gravis
- Lambert–Eaton myasthenic syndrome
- Neurotoxins (for example, botulism, tetanus, tick paralysis or snakebite envenomation)
- Organophosphate intoxication

Muscles
- Metabolic or electrolyte disorders (for example, hypokalaemia, thyrotoxic hypokalaemic periodic paralysis, hypomagnesaemia or hypophosphataemia)
- Inflammatory myositis
- Acute rhabdomyolysis
- Drug-induced toxic myopathy (for example, induced by colchicine, chloroquine, emetine or statins)
- Mitochondrial disease

Other
- Conversion or functional disorder

[a]Differential diagnosis for Bickerstaff brainstem encephalitis.

BRIGHTON DIAGNSOTIC CRITERIA :

- Level 1 of diagnostic certainty:
  - Bilateral and flaccid paralysis of the extremities
  - and diminished or absent tendon reflexes of the paretic extremities
  - and monophasic disease profile and 12 h to 28-day period between symptom onset and peak and subsequent clinical plateau phase
  - and electrophysiological findings indicative of GBS
  - and cyto-albuminological dissociation
  - and lack of alternative diagnosis for paresis
- Level 2 of diagnostic certainty:
  - All of the above-mentioned clinical criteria present
  - and electrophysiological findings indicative of GBS
  - or cyto-albuminological dissociation
- Level 3 of diagnostic certainty:
  - All of the above-mentioned clinical criteria present
  - Electrophysiological and CSF findings lacking/negative

Electrophysiological criteria for the diagnosis of GBS and its most important variants

- Electrophysiological criteria for AIDP.

At least 1 of the following findings derived from the measurement of at least 2 nerves, or at least 2 measurements on 1 nerve when all others are inexcitable and the amplitude of the distal compound muscle action potential (dCMAP) is >10% below the lower limit of normal (LLN):

1) motNCV <90% LLN (85% if dCMAP < 50% LLN).
2) Distal Motor Latency >110% of the upper limit of normal (ULN) (>120% in dCMAP < 100% LLN).
3) Amplitude ratio of pCMAP/dCMAP <0.5 und dCMAP >20% LLN.
4) F-wave latency >120% ULN.

- Electrophysiological criteria for AMAN.

None of the criteria for AIDP applies here except for 1 sign of demyelination at 1 nerve, if dCMAP <10% LLN. Normal amplitude of sensory nerve action potentials.

- Electrophysiological criteria for AMSAN.

None of the criteria for AIDP applies here except for 1 sign of demyelination at 1 nerve, if dCMAP <10% LLN. Amplitude of sensory nerve action potentials <10% LLN.

- Electrophysiological criteria for nerve inexcitability

dCMAP absent in all nerves, or dCMAP <10% LLN can be detected in 1 nerve.

AIDP = acute inflammatory demyelinating polyneuropathy, AMAN = acute motor axonal neuropathy, AMSAN = acute motor-sensory axonal neuropathy, motNCV = motor nerve conduction velocity, LLN = lower limit of normal, ULN = upper limit of normal, pCMAP = proximal compound motor action potential, dCMAP = distal CMAP.

MRC and GBS Disability scale :

Recommended functional assessment tools for monitoring the course of disease in GBS.

Medical Research Council (MRC) Scale for Manual Muscle Testing

5 – patient can maintain position against maximal resistance and through the entire physiological range of motion of the joint
4 – patient can maintain position against moderate resistance, and moves actively through the entire physiological range of motion of the joint
3 – patient cannot maintain position against resistance, but can move the extremity against gravity through the full range of motion
2 – patient can move the extremity through part of the physiological range of motion if gravity is eliminated
1 – muscle contraction can be detected by palpation if gravity is eliminated
0 – no contractions identifiable

GBS disability scale (Hughes und Cornblath) [redacted]

0 – healthy
1 – minor symptoms or signs of neuropathy, but capable of manual work and running
2 – can walk without the aid of a stick for 5 m across an open space, but is not capable of manual work or running
3 – can walk with a stick, orthosis or support (5 m across an open space)
4 – bedridden or wheelchair-bound
5 – ventilation assistance required (for any part of the day or night)
6 – dead

Modified Rankin Scale (MRS)

0 - no symptoms
1 - no significant impairment, despite some symptoms; able to carry out all usual activities
2 - slight impairment; not able to carry out all previous activities but can tend to own matters without the need for assistance
3 - moderate impairment; requires some help but able to walk without assistance
4 - moderately-severe impairment; unable to walk unassisted and cannot tend to bodily needs without assistance.
5 - severe impairment; bedridden, incontinent, requires constant nursing care and attention
6 - dead

LINK FOR DIAGNOSTIC TOOLS : *https://gbstools.erasmusmc.nl/prognosis-tool*

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