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GUILLAIN-BARRÉ SYNDROME ANAESTHESIA TUTORIAL OF THE WEEK 238

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CLINICAL SCENARIO

A 68-year-old man is admitted under the physicians with a 10 hour history of gradual onset of tingling and weakness in his arms and legs. This is associated with lower backache. He has recently returned from a two week holiday in Spain, during which time he suffered a self-limiting diarrhoeal illness that he attributed to the hotel food. He has no previous medical history and takes no regular medications. He drinks 12 units of alcohol per week and has never smoked.

His vital signs are as follows: blood pressure 100/60mmHg, pulse 120/min (sinus tachycardia on ECG), respiratory rate 24/min, saturations 95% on air and he is afebrile. On clinical examination there is symmetrically decreased tone and power in the upper and lower limbs. He is unable to move his legs and raises his arms with difficulty. The deep tendon reflexes are absent with down-going plantar reflexes.

QUESTIONS

1. Which investigations will aid in diagnosis of this condition?
 - a. Lumbar puncture
 - b. Muscle biopsy
 - c. Full blood count
 - d. Lumbar spine X-ray
2. What complication may be expected with this condition?
 - a. Arrhythmias
 - b. Respiratory failure
 - c. Sickle cell anaemia
 - d. Urinary retention
3. Which of the following are associated with a poor prognosis?
 - a. Precedent *Campylobacter jejuni* infection
 - b. Antinuclear antibodies
 - c. Insidious onset
 - d. Younger age

INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute demyelinating polyneuropathy first described in 1859. Its features are those of ascending motor weakness, sensory and autonomic dysfunction frequently following a prodromal illness (usually a respiratory or gastrointestinal infection). It is thought to be autoimmune in origin. GBS can cause significant morbidity requiring long hospital inpatient stay and significant periods of rehabilitation. Approximately 10–15% of patients require assistance with long-term residual disability.

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EPIDEMIOLOGY

The overall incidence of GBS worldwide is 1.1–1.8 cases per 100,000 per year, with higher rates in males than females. There is a bimodal age incidence, with peaks occurring in young adults and the elderly. The incidence rises to 3.3 cases per 100,000 per year after 50 years of age. [1,2]

There is an association with precedent infections in 70% of cases that are predominantly respiratory and gastrointestinal in origin. It has been suggested there has been an association between GBS and vaccinations, although the evidence for this is weak. [1]

CLINICAL FEATURES AND PATHOPHYSIOLOGY

Symptoms

The clinical features of GBS are variable. Weakness and sensory disturbance are the most common presenting symptoms. There is usually a progressive ascending motor weakness starting in the lower limbs ranging from difficulty walking to paralysis. The weakness may ascend to involve respiratory muscles and cause respiratory failure. Facial nerve palsies are common and there may be associated bulbar weakness and ophthalmoplegia. [3]

Sensory symptoms may include pain, numbness and paraesthesia. Pain commonly affects the lower back and may be severe. Numbness and paraesthesia starts distally and ascends in a similar fashion to the motor weakness in 80% of patients. [3]

Signs

On clinical examination a flaccid areflexic paralysis is found. Muscle wasting usually occurs within two weeks of the onset of symptoms and can be severe.

Autonomic dysfunction is common and may cause arrhythmias, swings in blood pressure, urinary retention, paralytic ileus and hyperhydriasis. If severe this may be associated with sudden death. [3]

GBS subtypes

GBS has a number of recognised subtypes that have differing clinical and pathophysiological features.

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common form and accounts for around 85–90% of cases. The clinical features are of symmetrical ascending motor weakness with hypo- or areflexia. The underlying pathological process involves inflammation and destruction of the myelin sheaths surrounding peripheral nerve axons by activated macrophages. This leads to slowing and blockage of conduction within peripheral nerves causing muscle weakness. Severe cases may develop secondary axonal damage. [3]

Acute motor axonal neuropathy (AMAN) is more common in Japan and China, amongst young people and in the summer months. It has an association with precedent infection with *Campylobacter jejuni*. Clinical features are similar to AIDP but tendon reflexes may be preserved. Electrophysiological testing may distinguish from other variants as selective motor nerve and axonal involvement is demonstrated. In AMAN the pathological process involves binding of antibodies to ganglioside antigens on the axon cell membrane, macrophage invasion, inflammation and axonal damage. [3]

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Acute motor and sensory axonal neuropathy (AMSAN) is a variant of GBS in which both motor and sensory fibres are involved and which can be demonstrated on electrophysiological studies. It is more severe and associated with prolonged or even partial recovery. Clinical features are similar to AMAN but also involve sensory symptoms. The underlying pathological process is similar to that for AMAN (i.e. antibody mediated axonal damage). [3]

Miller Fisher syndrome (MFS) presents with ataxia, areflexia and ophthalmoplegia. 25% of patients may develop limb weakness. Electrophysiological studies show primarily sensory conduction failure. Antiganglioside antibodies to GQ1b are found in 90% of patients and are associated with ophthalmoplegia. There have been limited pathological studies in MFS but demyelination of nerve roots has been demonstrated. [3]

A chronic form of GBS known as chronic inflammatory demyelinating polyradiculoneuropathy has been described. The clinical features are similar to that of AIDP but have a slowly progressive or relapsing course. [3]

INVESTIGATIONS [3]

Serum biochemistry

Urea and electrolytes are usually normal but may have evidence of the syndrome of inappropriate ADH secretion (SIADH) or renal dysfunction. ALT and gamma GT may be raised in 33% of patients. Creatine kinase may be raised.

Inflammatory markers

ESR is usually raised and CRP is sometimes elevated.

Antiganglioside antibodies

Anti-GM1 is positive in 25% of patients and is associated with a worse outcome. Anti-GD1a is associated with AMAN subtype of GBS. Anti-GQ1b is associated with Miller-Fisher syndrome.

Infection screen

Send serology for *Campylobacter jejuni*, Cytomegalovirus, Epstein-Barr virus, Herpes simplex virus, *Mycoplasma pneumoniae*. HIV antibodies should be considered. Stool cultures looking for evidence of gastrointestinal infections particularly *Campylobacter jejuni*.

Radiological

A CT brain is indicated to exclude other causes of symptoms and evidence of raised intracranial pressure prior to performing a lumbar puncture. An MRI of the spine may show selective anterior spinal nerve root enhancement with gadolinium and will exclude cervical nerve impingement.

Lumbar puncture

Cell count and glucose are usually normal with a raised protein, although the latter may also be normal in first two weeks.

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Nerve conduction studies

Findings depend on subtype of GBS. The majority show demyelinating pattern while some patients may show evidence of axonal loss with little or no demyelination.

Respiratory function tests

These may show reduced vital capacity, maximal inspiratory and expiratory pressures. Arterial blood gases may indicate progressive respiratory failure.

DIFFERENTIAL DIAGNOSIS [3]

Neurological

- Myasthenia gravis
- Eaton-Lambert (myasthenic) syndrome
- Multiple sclerosis
- Transverse myelitis

Metabolic

- Hypokalaemic periodic paralysis
- Hypermagnesaemia
- Hypophosphataemia
- Acute intermittent porphyria

Infective

- Post diphtheria neuropathy
- Polio
- Botulism
- Tick paralysis

Drugs / toxins

- Heavy metal poisoning (e.g. lead)
- Biological toxins (including snake and scorpion toxins)
- Drugs (including stavudine, nitrofurantoin and aminoglycosides)

Other

- Acute polymyositis
- Critical illness myopathy

MANAGEMENT

Multi-disciplinary input is important in all aspects of the care of patients with GBS both in the acute phase and rehabilitation of patients. Therapies may be classified as being supportive or immunomodulatory.

Supportive

Airway and respiratory

Around 30% of patients with GBS require ventilatory support. Deterioration in respiratory function may be rapid and frequent assessments should be made in all patients. Clinical markers suggestive of the need for ventilatory support include bulbar weakness, inability to lift the head, upper limb weakness and tachypnoea. [2,3]

Close monitoring of respiratory function tests is imperative. Vital capacity should be measured three times per day and can easily be assessed at the bedside. Measurement of vital capacity provides information about respiratory sufficiency. Maximal inspiratory and expiratory pressures may also be measured and provide information about the power of respective groups of respiratory muscles. Both tests may be difficult to interpret in patients with bulbar weakness, due to difficulty forming a seal around the mouthpiece.

Arterial blood gases may be measured to provide objective evidence of the development of respiratory failure. Oxygen saturations are easily monitored but desaturation can be a late sign.

Clinical indications for intubation and ventilation include:

- Vital capacity of less than 1L or less than 15 ml.kg⁻¹
- Maximum inspiratory pressure of less than 30cmH₂O
- Maximum expiratory pressure of less than 40cmH₂O
- Bulbar involvement with inability to cough, swallow and protect the airway
- Evidence of respiratory failure on arterial blood gases and autonomic instability. [3]

Tracheostomy should be considered if prolonged respiratory support is likely to be needed. Respiratory physiotherapy can be invaluable in aiding the clearance of secretions and prevention of hospital acquired pneumonias.

Anaesthetic considerations

Suxamethonium is absolutely contraindicated in patients with GBS. There have been a number of case reports of severe hyperkalaemia, life threatening arrhythmias, and cardiac arrest after its administration. [4]

Cardiovascular

Autonomic dysfunction occurs in around 70% of patients and may be life-threatening. Monitoring of the ECG, blood pressure and fluid balance is advisable. The most common arrhythmia seen is sinus tachycardia but various other ECG changes have been observed including atrial and ventricular tachyarrhythmias, prolonged QT interval, atrioventricular blocks and even asystole. [3]

Blood pressure may fluctuate between severe hypertension and hypotension. Orthostatic hypotension is common. Care should be taken when treating extremes of blood pressure with vasoactive drugs as patients may be particularly sensitive to their effects. Intubated patients with autonomic dysfunction may develop instability after tracheal suction. [3]

Gastrointestinal

Good nutrition is important particularly for those patients with bulbar weakness, and those who are sedated and mechanically ventilated. Poor oral intake may necessitate instigation of enteral or parenteral feeding. Dietician input is useful to ensure adequate calorific, micronutrient, fluid and electrolyte intake.

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Patients with autonomic dysfunction may be susceptible to the development of a paralytic ileus. This may be treated with prokinetic agents such as metoclopramide or erythromycin.

Neurological

Neuropathic pain is common and occurs in around 50% of patients. Non-opioid analgesics (paracetamol, NSAIDs) in combination with opioid analgesia should be instituted initially, but may provide inadequate pain relief. Adjunctive treatments such as anticonvulsants (e.g. gabapentin or carbamazepine), and tricyclic antidepressants may be effective.

Venous thromboembolism prophylaxis

Immobile patients are at very high risk of deep vein thrombosis and pulmonary emboli. Low molecular weight heparin in combination with either pneumatic compression devices or anti-embolism stockings, are recommended until patients are able to walk unaided.

Psychological

There is a high incidence of depression among patients with GBS. If available, it is important for the patient and their family to have access to support groups. In the UK the Guillain-Barré Support Group. It is also important that counselling and psychiatric help be available if needed. [3]

Rehabilitation

40% of patients who suffer from GBS will need admission for inpatient rehabilitation. Careful attention should be paid to limb positioning and posture as limb weakness can lead to compression nerve palsies, pressure sores and contractures. Extensive input from physiotherapists and occupational therapists is essential to provide tailored strengthening exercises and supportive aids. [3,5]

Patients may also suffer from persistent fatigue, which may respond to an exercise programme. [3]

Immunomodulatory

Intravenous immunoglobulin

Intravenous immunoglobulin (IVIg) is an effective treatment for GBS and has been demonstrated to be comparable to plasma exchange in accelerating recovery. It is most effective if administered within two weeks of the onset of symptoms. IVIg has a number of advantages over plasma exchange. It is more widely available, less labour intensive and has less side effects. Indications for IVIg include muscle weakness and respiratory depression.

IVIg contains pooled donor IgG antibodies and may reduce the severity of autoimmune inflammation in GBS by blocking Fc receptors. This prevents the Fc portion of antibodies binding and thus interrupts antibody mediated cell destruction. Complement activation is also altered.

Contraindications to IVIg include: previous anaphylactic reaction to IVIg and IgA deficiency (associated with anaphylactic reactions to blood products). Side effects of IVIg may be mild or severe and include nausea, headache, dermatological disorders including erythroderma, fluid overload, deranged liver function tests, venous thromboembolism, acute renal failure and anaphylaxis. There is no evidence that repeated courses of treatment are beneficial [3,9]

Plasma exchange

Plasma exchange is an effective treatment and has been shown to accelerate recovery in GBS. Improvements have been demonstrated in regaining muscle strength, ability to walk independently, and

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requirement for and duration of mechanical ventilation. It is more beneficial when commenced within one week of the onset of symptoms, but can be beneficial up to thirty days after the onset of illness. [9]

Plasma exchange has been successfully used in mild, moderate and severe cases of GBS with differing numbers of exchanges depending on severity. The indications for plasma exchange are the same as for IVIg.

Plasma exchange involves the passage of blood through an extracorporeal cell separator. The plasma fraction of the blood is removed then and replaced with FFP or human albumin solution. Anticoagulants are administered during the procedure. The aim of plasma exchange is to remove antibodies associated with the underlying autoimmune response.

Contraindications to plasma exchange include: coagulopathy, overwhelming sepsis, haemodynamic instability and shock. Side effects vary from mild to more severe and include nausea, vomiting, diarrhoea, fevers, coagulopathy, immunosuppression, hypocalcaemia which relates to the use of citrate and line related complications. [3,7,8]

Corticosteroids

Corticosteroids have been used historically, in order to suppress inflammation associated with Guillain-Barré syndrome. They are now no longer used. There is no evidence that they improve recovery or affect long-term prognosis. [6]

PROGNOSIS

Most patients with GBS recover fully but this may take many months of intensive therapy. 15% of patients suffer persistent disability. 10% are unable to walk unaided at one year. There may be a recurrence in 2–5% of cases. [2,3]

The mortality from GBS ranges from 2–12%. Common causes of death include venous thromboembolism, pneumonias, arrhythmias and complications related to dysautonomia. [12]

Markers of poor prognosis include age > 40 years, rapid onset of symptoms, severe weakness (especially if mechanically ventilation is required or there is marked upper limb weakness), association with precedent diarrhoeal illness or campylobacter infection, evidence of axonal damage on electrophysiological studies and lack of treatment with either plasma exchange or IVIg. [2,3]

MCQ ANSWERS

1. TFFT
2. TTFT
3. TFFF

REFERENCES AND FURTHER READING

1. Guillain-Barré Syndrome: Indications for Plasma Exchange. *Transfusion Science* 1999; **20**: 53–61.
2. A McGrogan, GC Madle, HE Seaman, C S deVries. Epidemiology of Guillain-Barré Syndrome Worldwide. A systematic literature review. *Neuroepidemiology* 2009; **32**: 150-63.
3. V Govoni, E Granieri. Epidemiology of the Guillain-Barré Syndrome. *Current Opinion in Neurology* 2001; **14**: 605-13.
4. R Hughes, D Cornblath. Guillain-Barré Syndrome. *The Lancet* 2005; **366**: 1653-66.
5. M Reilly, M Hutchinson. Suxamethonium is contraindicated in the Guillain-Barré Syndrome. *Journal of Neurology, Neurosurgery and Psychiatry* 1991; **54**: 1018-9.
6. JM Meythaler. Rehabilitation of Guillain-Barré Syndrome. *Archives of Physical Medicine and Rehabilitation* 1997; **78**: 872-9.
7. RAC Hughes, AV Swan, PA vanDoom. Corticosteroids for Guillain-Barré. *Cochrane Database of Systematic Reviews* 2010, Issue 2. Available at: <http://www2.cochrane.org/reviews/en/ab001446.html>
8. JC Raphael, S Chevret, RAC Hughes, D Annane. Plasma Exchange for Guillain-Barré Syndrome. *Cochrane Database of Systematic Reviews* 2002, Issue 2. Available at: <http://www2.cochrane.org/reviews/en/ab001798.html>
9. JC Raphael, S Chevret, I Auriant, T Sharshar, J Bouget, F Bolgert. Treatment of the Adult RAC Hughes, AV Swan, PA vanDoom. Intravenous immunoglobulin for Guillain-Barré Syndrome. *Cochrane Database of Systematic Reviews* 2010, Issue 6. Available at: <http://www2.cochrane.org/reviews/en/ab002063.html>