Polyradiculoneuritis

Polyradiculoneuropathy (**Guillain-Barré syndrome** = GBS, Acute inflammatory demyelinating polyradiculoneuropathy = AIDP) is **an acute inflammatory disease of the peripheral nerves**, including the spinal roots. Sensory, autonomic and cranial nerves are sometimes affected. GBS is characterized by **progressive muscle weakness (paralysis), paraesthesia and areflexia**. The typical form has an ascending, progressive course. Sensory, autonomic and stem lesions are also common. In severe conditions, respiratory failure with UPV is required due to respiratory muscle paralysis. Symptomatology usually follows febrile, most often viral disease. The maximum manifestations of paralysis usually come after 2 weeks from the onset of the disease. With the eradication of acute poliomyelitis, polyradiculoneuritis has become the most common acute muscular palsy in children.

The first description of the disease dates from Landry in 1859. In 1916, Guillain, Barré and Strohl further expanded the clinical description of the disease and were the first to reveal a typical laboratory finding – **proteinocytological dissociation in cerebrospinal fluid** (increased proteins at normal cell numbers). The cerebrospinal fluid finding, combined with a typical clinical picture, allows GBS to be distinguished from diseases with anterior horn cells.

Etiology

In 2/3 of patients, there is a history of gastrointestinal or respiratory infection, which preceded the development of the disease by 1-3 weeks. Infections include EBV, CMV, HBV, HIV, varicella, Mycoplasma pneumoniae, Chlamydia, Campylobacter jejuni. Influenza and rabies vaccination is considered a trigger. GBS has also been linked to malignancies such as Hodgkin's andnon-Hodgkin's lymphomas, pregnancy or the use of certain medicines (penicillamine, captopril, danazol) or drugs (heroin).

Patophysiology

Demyelinating and **axonal** forms of GBS have been described in terms of pathophysiology. In the demyelinating form, we find segmental demyelination of peripheral nerves in connection with infiltration of inflammatory cells. GBS with axonal degeneration can occur without demyelination or inflammation. Excitatory conduction block and motor nerve demyelination are responsible for progressive weak paresis, similarly affecting sensory nerves causes pain and paraesthesia. Many authors assume that **the disease is caused by an abnormal T-cell response associated with a previous infection or vaccination**. Induction of Th-lymphocytes by these pathogens is probably crucial. Specific endogenous antigens, such as myelin P-2, ganglioside GQ1b, GM1, GD1 and GT1a, also play a role. Molecular mimicry of these antigens may be the target of T-cell and macrophage-mediated immune responses. The result is then damage to the peripheral nerve fibers.

An epidemic of the disease has also been described in connection with Campylobacter jejuni infection. We often find antiglycolipid antibodies in these patients. Because in this case we find degeneration of peripheral axons without significant inflammatory infiltration, we call this type of GBS **acute motor axonal neuropathy** (**AMAN**). The prognosis is worse here than in the context of another infectious etiology.

Epidemiology

In the United States, the incidence of GBS in children is reported to be approximately **0.5–1.5 per 100 000 children under the age of 18**. Mortality is reported to be < 5 % and is most often associated with undiagnosed cases. Death is no longer most often due to respiratory failure (early diagnosis and the possibility of UPV), but in connection with **cardiac arrhythmia** or dysautonomia. Mortality in children is significantly lower than in adults. Complete recovery within 3-12 months is reported in 90-95% of patients. Conversely, 5-10% of patients may have permanent consequences. **The average age of occurrence of GBS is 4-8 years.** Recurrence of the disease is reported < 5%, relatively more often in the first 2-3 weeks after HDIVIG administration in a two-day course. Very rare is the chronic progressive course of the disease, known as **Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)**.

Clinical picture

The onset of the disease comes within 2-4 weeks after the acute illness or immunization . The main symptom is weak paresis (weakness in the English literature) with hypo- to areflexia, which typically begins on the lower limbs and progresses ascending to the torso (respiratory muscles may also be affected), the upper limbs. Eventually, the eye muscles may be affected. We call this typical course **Landry's ascending paralysis**. Patients with GBS complain of weakness, paraesthesia and imbalance. Progression comes in hours, days or even weeks. Paresis is mostly symmetrical, the physical correlate is hypo / areflexia. Proximal reflexes may still be in the initial phase of the disease. Pain and paraesthesia are more common in children than in adults, often before the development of paresis. Pain is usually the initial symptom in half of pediatric patients, the pain is most often reported in the shoulders, back, buttocks and thighs (children may prefer a position on the abdomen). It most often occurs in

patients with a sharp onset of the disease. Paresthesias usually begin on the fingers, then progress, as in paresis, ascending. Urinary retention due to sphincter disorders is described in 10–15% of children. Deep sensation is usually reduced.

Balance disorder is most often associated with weakness / paresis. However, ataxia may be part of the **Miller-Fisher variant of GBS** (ataxia, ophthalmoplegia, areflexia). Patients with these symptoms have a lower risk of respiratory failure, a common trigger of the disease is C. jejuni.

An even rarer variant of GBS is **BBE** (Bickerstaff´s brainstem encephalitis), which, like the Miller-Fisher variant, includes ataxia and ophthalmoplegia, and we find lethargy, loss of extensor plantar reflexes, or hemisensory loss. Patients usually have a good prognosis.

Other possible symptoms of the disease are **polyneuritis cranialis** (diplegia n. facialis, oculomotor nerves, nervus abducens). The clinical correlates are facial paresis (they may be asymmetric!), dysarthria, dysphasia, diplopia. Pharyngo-cervico-brachial syndrome, acute sensory neuropathy or acute pandysautonomy. Symptoms of **autonomic dysfunction** include orthostatic hypotension or hypertension, pupillary dysfunction, sweat gland dysfunction, arrhythmias (most commonly sinus tachycardia), paralytic ileus, hypothermia or hyperthermia.

Significant complications of GBS include pneumonia, ARDS, sepsis, constipation, gastritis, pulmonary embolism. Approximately 1% of patients may develop intracranial hypertension with papillary edema. These patients show symptomatology of the cerebral pseudotumor.

The remission of clinical difficulties is usually observed 2-4 weeks after the onset of clinical symptoms. Neurological functions appear in the opposite order than at the beginning of the disease, ie paresis of the eye muscles subsides first, then paresis of the lower limbs last. In children, the adjustment of neurological functions is usually complete. The consequences are more common in patients with cranial nerve damage, intubation and severe paresis at the time of diagnosis.

AMAN usually does not have a sensory disorder, respiratory failure is frequent and occurs within a week. Distal atrophy may occur. The period of difficulty can last up to 5 months.

The leading clinical symptoms are weak paresis (mostly symmetrical) and hypo / areflexia found in the physical examination!

Diagnostics

GBS diagnostics is based on:

- typical **clinical finding** (see table);
- examination of **CSF** lumbar puncture;
- **EMG**;
- in indicated cases by **MRI** examination.

In biochemistry, we can sometimes demonstrate hyponatremia with the development of SIADH (syndrome of inappropriate secretion of antidiuretic hormone), in 1/3 of patients transaminases may be elevated. Sometimes we can prove the positivity of antibodies against peripheral and central nerves. Anti-ganglioside antibodies, especially GM1 and GD1, are typical of axonal degeneration forms, anti-GM1 positivity often means a worse prognosis, anti-GQ1b detection may be positive in patients with Miller-Fisher variant or BBE and is an important differential diagnostic marker. . Anti-ganglioside antibodies are often associated with recent C. jejuni infection. Serological detection of antibodies is suitable for the detection of Campylobacter jejuni as a causative agent of GBS, because at the time of manifestation of polyradiculoneuritis, Campylobacter in the stool is usually already negative.

criteria *necessary* for diagnosis	**criteria *supporting* diagnosis**
progressive muscle weakness > 1 limb	progression within days - 4 weeks
areflexia / hyporeflexia of tendon reflexes	mostly symmetrical manifestations
	mild sensory impairment
	involvement of cranial nerves (n. VII)
	autonomic dysfunction
	absence of fever
	proteinocytological dissociation in CSF
	typical features of EMG (segmental demyelination)

Lumbar puncture supports the diagnosis of demyelination when proteinocytological dissociation is found (increase of proteinorachia within 3 weeks of the onset of the disease), without evidence of active infection (absence of pleiocytosis). In practice, it is important to think about the diagnosis of GBS even with initial cerebrospinal fluid negativity, because during the first 48 hours from the onset of typical symptomatology, cerebrospinal fluid may be completely negative. It is therefore not uncommon for repeated lumbar punctures to be necessary. Most patients have normal leukocyte counts, but mild pleiocytosis of up to 50 cells per milliliter is not uncommon. Conversely, > 50 leukocytes per milliliter may call into question the diagnosis of GBS.

Almost 2 weeks after the onset of the problem, a lumbosacral MRI scan shows increased gadolinium uptake. In patients with BBE, we find changes in up to 30% of patients.

Within examination methods, MRI remains a "substitute", indications are mainly conditions with an unclear clinic or EMG record. Conversely, follow-up MRI may predict the clinical course of the disease.

Spirometric examination of cooperating children is essential to detect initial respiratory insufficiency, a significant value is NIF = negative inspiratory flow, MIF = maximum inspiratory force and the value of vital capacity per kilogram of weight. Other tests include a chest x-ray and blood gas count. These examinations are also the basis for the diagnosis of respiratory distress in non-cooperating patients.

EMG examination shows a number of changes: pathological F response, increased distal latencies, conduction block, and decreased conduction velocity of the motor and sensory nerves. EMG is also useful in diagnosing axonal disease. Although EMG changes occur within the first week of the onset of symptomatology, it is prudent to wait at least 7-10 days for the test to be as valid as possible. Very early EMG can be negative, as with lumbar puncture.

Within cardiac disease, we can demonstrate a number of pathological findings on the ECG: second to third degree AV block, T wave abnormalities, ST depression, QRS complex enlargement.

Histological examination is not part of the standard of the examination plan. In the demyelinating form, we find signs of demyelination in the peripheral nerves, together with mononuclear infiltration by lymphocytes and macrophages.

The severity of neurological impairment is determined by scoring schemes (see Ordinal disability score). A sign of a serious course is the loss of the ability to walk independently.

Ordinal disability score

Score	functional ability
0	normal
1	able to run
2	able to walk 5 meters
3	able to walk with help
4	unable to walk, able to lift legs
5	unable to walk, unable to lift legs
6	need for intubation and artificial ventilation

Differential diagnostics

Differential diagnosis of GBS in childhood mainly includes a spectrum of progressive, symmetric paresis. **Botulism** must be considered. Here we find not only muscle weakness, but also extraocular muscle damage and constipation. Ophthalmoplegia is also present in **myasthenia gravis**. This diagnostic unit will help rule out a typical EMG (rapid action potential amplitude reduction after repeated pacing) finding. GBS-like symptoms are found in **Lyme disease** or HIV infection. Here is a characteristic finding of pleiocytosis in cerebrospinal fluid. Spinal cord abnormalities can sometimes manifest in progressive weakness, and physical examination can help distinguish spinal cord syndrome from diffuse neuropathy. **Transverse myelitis** can also manifest itself in progressive paralysis, hyporeflexia and back pain. Poliomyelitis and other enteric infections of the anterior horns of the spinal cord cause acute focal and asymmetric limb paresis, usually at the same time as pain and fever.

Another cause of acute neuropathy can be heavy metal **poisoning**, organophosphates, side effects of vincristine.

Rarely a sucking tick can cause ascending paralysis. Therefore, children should be carefully examined for ticks. After the tick is removed, the clinical difficulties subside quickly.

Therapy

As part of the monitoring of patients with GBS, we must record:

- body temperature,
- blood pressure,
- heart and respiratory rate,
- respiratory function (spirometry),
- diuresis.

GBS treatment is primarily focused on immunomodulation and includes two basic options:

- administration of high doses of intravenous **immunoglobulins**,
- **plasmapheresis**.

Previously recommended corticoids are no longer used today because their positive effect on the course of the disease has not been proven.

High-dose intravenous immunoglobulins

HDIVIG is administered at a total dose of 2 g / kg i.v. We use either a two-day course of administration in a single dose of 1 g / kg or we administer 400 mg / kg for 5 days. Some studies point to a better therapeutic effect of a two-day course or even administration in a single dose, especially in situations of rapid neurological deterioration. Other studies, on the other hand, point to more frequent early relapses using a short course of treatment. IVIGs reduce the severity of the disease as well as the duration of symptoms. However, the long-term outcome may not be fundamentally affected by IVIG.

The principle of action includes neutralization of circulating anti-myelin antibodies by anti-idiotypic antibodies, down-regulation of proinflammatory cytokines, blockade of Fc receptors for macrophages, suppression of T and B-lymphocytes, blockade of the complement cascade. HDIVIG also facilitates remyelination.

The side effects of HDIVIG are usually mild but not rare. These include allergic reactions, transient liver dysfunction, migraine headache, fever, rash ev. with pruritus, hypertension, aseptic meningitis syndrome, proteinuria, renal dysfunction, hemolytic anemia, increased serum viscosity (thromboembolic events), petechiae. If there is no danger of delay, it is appropriate to screen for IgA deficiency, the incidence of which in the population is 1:1 000. IgA - depleted IVIG is then indicated in these patients.

Plasmapheresis

The use of plasmapheresis also reduces the severity of the disease and shortens the course. The principle of action is the removal of antibodies, cytokines, complement components and other mediators from the circulation. Some pediatric centers prefer this method to HDIVIG, but the limit is body weight < 15 kg, where it is often difficult to provide central venous access for plasmapheresis because the method requires a large centerline diameter.

It is recommended to perform 4-5 plasmapheresis within 5-10 days. Disadvantages of plasmapheresis include unavailability, slightly higher cost, the need for a hemodialysis catheter and complications resulting from plasmapheresis (hypotension, hypercalcemia, bleeding from coagulation factor depletion, sepsis from Ig depletion, thrombocytopenia).

Aspects of the use of plasmapheresis

Advantages	Disadvantages
no allergic reactions	unavailability
lower frequency of relapses	slightly higher price
slightly higher effect therapy	the need for a hemodialysis catheter
optional outpatient treatment (USA)	complications (hypotension, sepsis from Ig depletion, thrombocytopenia)

Comparison of plasmapheresis and HDIVIG

There is no statistically significant difference between the efficacy of HDIVIG and plasmapheresis. Both methods accelerate the recovery of patients with severe disease, ie patients who require "walking assistance" (Cochrane Database Review, Grade A evidence). Concomitant use of plasmapheresis and subsequent administration of HDIVIG no longer increases the effectiveness of treatment.

Corticosteroids in the randomized trials did not show any therapeutic effect compared to the control (Cochrane Database Review, Grade A evidence).

The preference of HDIVIG or plasmapheresis depends a lot on the habits of the workplace and its possibilities. However, there are certain criteria when it is appropriate or necessary to opt for one or the other method.

Indications for plasmapheresis and HDIVIG in the treatment of GBS

Plasmapheresis	HDIVIG
congestive heart failure	atypical GBS (antiglycolipid Ig)
renal insufficiency	autonomic instability
pregnancy	symptomatology > 28 days
side effects in anamnesis	infectious diseases
previous IVIG treatment	diarrhea
IgA deficiency	relapse of disease

Indications for intubation and UPV

Intubation and mechanical ventilation are considered when reducing the vital capacity < 5 ml/kg t.h. or if hypoxia is detected (pO_2 < 70 mmHg). For cooperating children (usually children over 5 years of age) it is useful to determine the maximum (negative) inspiratory force, negative inspiratory force = NIF. A value of ≤ 20 cm H_2O predicts very limited inspiratory ability, respiratory distress and the need for UPV. Conversely, values ≥ 40 cm H_2O predict good spontaneous ventilation.

Other treatment modalities

Other treatment modalities include the administration of atropine in symptomatic bradycardia, or cardiac pacemaker in 3rd degree AV block. Tachycardia treatment is rarely required. Because autonomic dysfunction is characterized by its lability, we use short-acting antihypertensives β-blockers in hypertension and sodium nitroprusside in hypertensive crisis. Hypotension responds well to volume expansion. In long-term lower limb paralysis, we administer low molecular weight heparin to prevent deep vein trombosis. Attention should also be paid to the prevention and treatment of pressure ulcers, ensuring adequate nutrition, urinary retention and constipation, prevention and treatment of gastritis, adequate analgesia for pain and dysesthesia, anxiolytic therapy, prevention and treatment of infectious complications, prevention and rehabilitation of contractures in patients with prolonged course. Demonstration of Campylobacter jejuni in faeces or serological tests is not a reason to re-treat, as treatment will not affect the course of the disease.

Links

Related articles

- Polyradiculoneuritis/PGS
- Neuromuscular diseases
- Neuromuscular diseases (pediatrics)

Source

- HAVRÁNEK, Jiří: *Polyradikuloneuritidy*.