Acute bilateral weakness
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Acute bilateral motor weakness
Common causes
• Guillain-Barré syndrome GBS
• Acute myelopathy

Rare causes (random order)
• Acute myositis
• Acute polyneuropathy
• Myasthenia gravis
• Botulism
• Poliomyelitis
• Periodic paralysis
• Tick paralysis
• Others

GBS versus «transverse myelopathy»
Distinction important – investigations, treatment, prognosis differ
• GBS
  NO motor/sensory level
• Transverse myelopathy
  YES niveau
GBS spectrum disorders
(simplified – from Wakerley 2014)

• Classic GBS
• Paraparetic GBS
• Bifacial weakness with distal paresthesias
• Miller Fisher syndrome MFS
• Bickerstaff Branstem encephalitis BBE

→ «variants» - («GBS transverse myelitis overlap syndrome»)
overlaps

Diagnostic criteria for classic GBS

Core clinical features
• Weakness and areflexia/hyporeflexia in all four limbs

Supportive features
• Electrophysiological evidence of neuropathy

Notes
• Weakness usually starts in the legs and ascends, but may start in the arms
• Weakness may be mild, moderate or complete paralysis
• Cranial nerves innervated mm and respiratory muscles may be involved
• Muscle stretch reflexes may be normal or exaggerated on 10% of cases
GBS
• Clinical presentation: pain may be dominating
• Clinically «severe» GBS walking distance < 5 meters
• CSF cytoalbuminologic dissociation – may be delayed nonspecific result
• Nerve conduction studies - may be supportive
• MRI (spinal) - usually not indicated
• Most relevant DD Transverse myelitis Poliomyelitis Functional paresis

Miller Fisher Syndrome
Core clinical features
• Ophthalmoplegia
• Ataxia
• Areflexia/hyporeflexia
• Absence of limb weakness

Supportive feature
• Presence of anti-GQ1b IgG antibodies

GBS Treatment
• Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders
  Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

  Patwa HS et al Neurology 2012;78:1009-1015

  „Evidence is insufficient to support or refute use of IVIG in the treatment of....children with GBS.“

• IVIG dose total 2g/kg variable duration of administration – over 2 – 5 days
Axonal Guillain-Barré syndrome: concepts and controversies

- Kuwabara S and Yuki N, Lancet Neurol 2013
- Commonest form in Asia, Central and South America
- Often associated with campylobacter jejuni infection
- Molecular mimicry – cross-reactivity to carbohydrates of gangliosides
- Reflexes retained (- exaggerated)

<table>
<thead>
<tr>
<th>Subtypes and variants</th>
<th>IgG autoantibodies to</th>
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<tbody>
<tr>
<td>Guillain-Barré syndrome</td>
<td>None</td>
</tr>
<tr>
<td>Acute ascending demyelinating polyneuropathy</td>
<td>None</td>
</tr>
<tr>
<td>Acute motor-sensory axonal neuropathy</td>
<td>G4S, GQb, GQa</td>
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<tr>
<td>Miller Fisher syndrome</td>
<td>GQb, GQa</td>
</tr>
<tr>
<td>Incomplete forms</td>
<td>GQb, GQa</td>
</tr>
<tr>
<td>Acute ophthalmoplegia (without ataxia)</td>
<td>GQb, GQa</td>
</tr>
<tr>
<td>Acute axonal neuropathy (without ophthalmoplegia)</td>
<td>GQb, GQa</td>
</tr>
<tr>
<td>CNS variant: Bickerstaff brainstem encephalitis</td>
<td>GQb, GQa</td>
</tr>
</tbody>
</table>

Yuki and Hartung NEJM 2012

- "GBS-transverse myelitis overlap syndrome"
- Lower extremity weakness
- Areflexia
- Sensory ataxia
- Urinary retention
- MRI - myelopathy
GBS mimic PDHC deficiency

- Acute Flaccid Paralysis as Initial Symptom in 4 Patients with Novel E1α Mutations of the Pyruvate Dehydrogenase Complex

- Young age
- CSF: protein not elevated
- Persistent areflexia
- Normal NCV
- MRI inconsistent lesions in globus pallidus and brainstem
- Ev. relapse

Acute myelopathy - DD options

- «peracute» - vascular ischemic hemorrhage (AVM, cavernoma)
- «acute» - infectious – immunologic (NOT external compression)
- «subacute» infectious immunologic compression – tumor, skelettal dysplasia
Acute transverse myelopathy – initial management considerations

- Individual approach
- Imaging – very high significance
- CSF examination – significance in acute situation moderate
- Consider medical treatment before imaging is available
- Re-evaluation

Clinical Imaging

Spinal AVM

(Idiopathic) Transverse Myelitis

Occurrence
- Isolated - idiopathic
- Part of inflammatory disease (e.g. EBV, neuborreliosis)
- Assoc with rheumatol disorder

Presentation
- Acute onset (Nadir in minutes to few hours – to 21 days )
- Sometimes history of minor injury a few hours earlier
- Back pain
- Numbness
- Motor deficits
- Loss of bladder and bowel control
Transverse Myelitis

Imaging
- T2 hyperintensity of central cord
- Mostly > 3 segments
- 20-30 % enhancement

CSF
- Pleocytosis and protein elevation (inconsistent)

Treatment
- First line = iv steroids
- (if unresponsive IVIG ? plasma exchange?)

Outcome
- Residual lesions common
- Relapses depending on aetiology

Transverse Myelitis – Frohmann and Wingerchuk
NEJM 2010;363:567-72

Table 1. Diagnostic Criteria for Transverse Myelitis|
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>Bilateral (not necessarily symmetric) sensorimotor and autonomic spinal cord dysfunction</td>
</tr>
<tr>
<td>Spinal level</td>
<td>Clearly defined sensory level</td>
</tr>
<tr>
<td>Progression</td>
<td>Progression to nadir of clinical deficits between 4 hours and 21 days after symptom onset</td>
</tr>
<tr>
<td>MRI</td>
<td>Demonstration of spinal cord inflammation: cerebrospinal fluid pleocytosis or elevated IGG index; or MRI revealing a gadolinium-enhancing cord lesion</td>
</tr>
<tr>
<td>Exclusion</td>
<td>Exclusion of compressive, postirradiation, neoplastic, and vascular causes</td>
</tr>
</tbody>
</table>

A    Transverse Myelitis
B,C  Multiple Sclerosis
E,F  NMO
Myelitis (Courtesy Dr. D. Eckert)

Myelitis - Cervical - Lumbar
EBV infection

Myelopathy – unknown
10 year old boy
Back pain
«Stiff gait»
No neurological deficits
CSF 27 cells
Rapid recovery
(Steroids)
Same patient
Lesion extension into brainstem

Myelitis reality - expectations

- Often – no / no clear level
- Multi-level
- Extension into brainstem
- «Imaging often worse than patient»

NMO Neuromyelitis Optica
(from Devic disease to NMO spectrum)

Box 2
Diagnostic criteria for pediatric neuromyelitis optica
- Optic neuritis
- Transverse myelitis
- One of the following:
  - Longitudinally extensive spinal lesion (≥3 spinal segments)
  - NMO IgG seropositivity
NMO

- Simultaneous or sequential occurrence of ON and transverse myelitis
- Subacute onset
- Often severe course – marked morbidity
- Females >> males
- More common in non-Caucasian (Japanese, Afro-American, ...)
- CSF moderate pleocytosis (often > 50 cells), 10% oligoclonal bands (children)
- Antibodies against astrocyte water channel protein Aquaporin 4 (AQP4)
  «Astrocytopathy»
  According to distribution → lesions in brain prevalent
  (# not confined to ON + M)
  Diencephalon – brainstem – supratentorial wm (not periventricular)

NMO Imaging

Myelopathy
- > 3 segments (central / holocord involvement)
- Often cervical (may extend into brainstem)
- Enhancement variable

Longitudinally extensive myelopathy in children
Acute bilateral motor weakness

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MRI Findings in Children with Acute Flaccid Paralysis and Cranial Nerve Dysfunction Occurring during the 2014 Enterovirus D68 Outbreak

AJNR Feb 2015;36:245-50
Maloney JA et al Open access

11 patients in this study
> 1500 patients with seroconversion

GBS – Literature 1
Reviews
- Hughes R and Cornblath D
  Guillain-Barré syndrome
  Lancet 2005;366:1653
- Van Doorn PA et al
  Clinical features, pathogenesis, and treatment of GBS
  Lancet Neurol 2008;7:939
- Kuwabara S and Yuki N
  Axonal
  Guillain-Barré syndrome: concepts and controversies
  Lancet Neurol 2013;12:1180-8
- Wakerley BR et al
  Guillain-Barré and Miller Fisher syndromes
  – new diagnostic classification
  Nature Reviews Neurology 2014;10:537-44
GBS – Literature 2

• Recognizing Guillain-Barré syndrome in preschool children
  Roodboom J et al, Neurology 2011;76:807-810

• Yuki N, Hartung HP
  Guillain-Barré syndrome (Review article)

Additional references 1 (Myelitis and NMO)

• Deiva K et al
  Acute idiopathic transverse myelitis in children
  Neurology 2015;84:401-409

• Sorte D, Peretti A, Newsome et al
  Longitudinally extensive myelopathy in children
  Pediatr Radiol 2015;45:244-57

• Makhani L et al
  Diagnosing neuromyelitis optica
  Neuromuscl Clin N Am 2013;29:279-91

• Frohmann EM and Wingerchuk DM
  Transverse myelitis
  N Engl J Med 2010;363:564-72

• Reindl M et al
  The spectrum of MOG autoantibody-associated demyelinating diseases
  Nat Rev Neurol 2013;9:456-61

Additional references 2 (Myelitis and NMO)

• Zamvil SS, Slavin AJ
  Does MOG Ig-positive AQP4-seronegative optospinal inflammatory disease
  justify…
  Neurol Neuroimmunol Neuroinflamm 2015;2:e62

• Papadopoulos MC et al
  Treatment of neuromyelitis optica
  Nat Rev Neurol 2014;10:493

• Stettler S et al
  Non-traumatic spinal cord ischaemia in childhood: clinical manifestation, imagining…
  Eur J Paed Neurol 2013;17:176