Acute bilateral weakness

Eugen Boltshauser
Emeritus – Department of Pediatric Neurology
Children's Hospital Zürich
EPNS Training Course March 2015 Budapest

Acute bilateral motor weakness

Common causes
- Guillain-Barré syndrome GBS
- Acute myelopathy

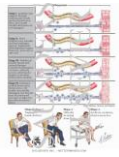
Rare causes (random order)
- Acute myositis
- Acute polyneuropathy
- Myasthenia gravis
- Botulism
- Poliomyelitis
- Periodic paralysis
- Tick paralysis
- Others

GBS versus «transverse myelopathy»

Distinction important – investigations, treatment,prognosis differ

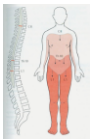
- GBS

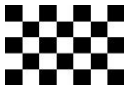
NO motor/sensory level

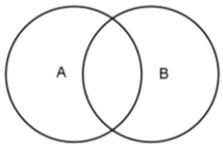


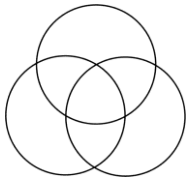
- Transverse myelopathy

YES niveau









Overlaps - Spectrum

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/hyporelfrexia 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."

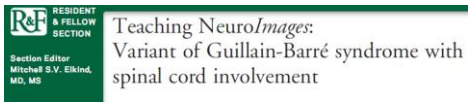
- IVIG dose total 2g/kg
  variable duration of administration – over 2 – 5 days

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)

Subtypes and variants	IgG autoantibodies to
Guillain–Barré syndrome	
Acute inflammatory demyelinating polyneuropathy	None
Facial variant: Facial diplegia and paresthesia	None
Acute motor axonal neuropathy	GM1, GD1a
More and less extensive forms	
Acute motor–sensory axonal neuropathy	GM1, GD1a
Acute motor-conduction-block neuropathy	GM1, GD1a
Pharyngeal–cervical–brachial weakness	GT1a > GQ1b >> GD1a
Miller Fisher syndrome	GQ1b, GT1a
Incomplete forms	
Acute ophthalmoparesis (without ataxia)	GQ1b, GT1a
Acute ataxic neuropathy (without ophthalmoplegia)	GQ1b, GT1a
CNS variant: Bickerstaff's brain-stem encephalitis	GQ1b, GT1a

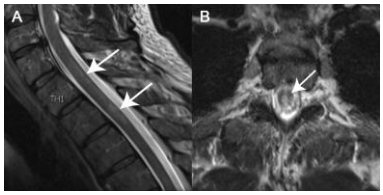
Yuki and Hartung NEJM 2012



- «GBS-transverse myelitis overlap syndrome»
- Lower extremity weakness
- Areflexia
- Sensory ataxia
- Urinary retention

- MRI - myelopathy

Imaging



Gaechter et al

GBS mimic PDHC deficiency

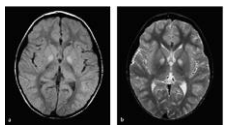
H. M. Strassburg[1]
J. Koch[2]
J. Mayr[2]
W. Sperl[2]
E. Boltshauser[3]

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

Neuropediatrics 2006;37:137-41

Particular

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

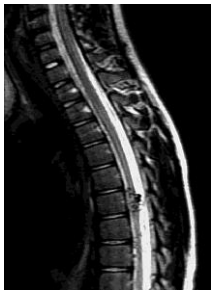


Acute myelopathy - DD options

- **«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, neurborreliosis)
- 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

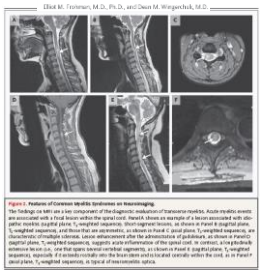
Transverse Myeltits – Frohmann and Wingerchuk
NEJM 2010;363:567-72

Table 1. Diagnostic Criteria for Transverse Myelitis.*

Bilateral (not necessarily symmetric) sensorimotor and autonomic spinal cord dysfunction
Clearly defined sensory level
Progression to nadir of clinical deficits between 4 hours and 21 days after symptom onset
Demonstration of spinal cord inflammation: cerebrospinal fluid pleocytosis or elevated IgG index,† or MRI revealing a gadolinium-enhancing cord lesion
Exclusion of compressive, postradiation, neoplastic, and vascular causes

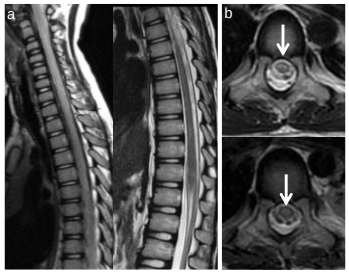
CLINICAL PRACTICE

Transverse Myelitis

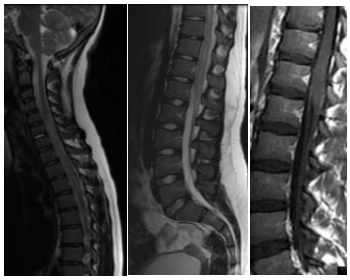


A Transverse Myelitis
B,C Multiple Sclerosis

E,F NMO

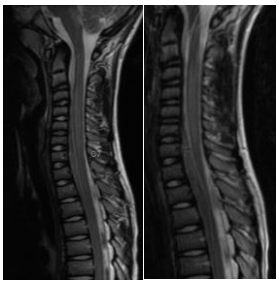


Myelitis (Courtesy Dr. D. Eckert)



Myelitis
- Cervical
- Lumbar

EBV infection

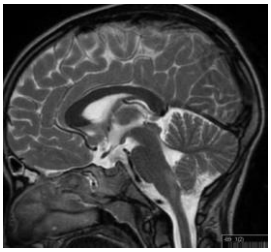


Myelopathy – unknown

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

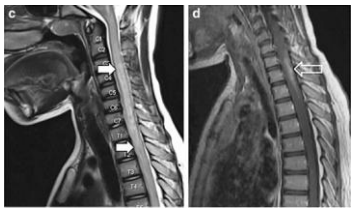
NMO

- 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



NMO

Longitudinally extensive myelopathy in children

Danielle Eckart Sorte · Andrea Poretti · Scott D. Newsome · Eugen Boltshauser · Thierry A. G. M. Huisman · Idem Izbudak

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

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 101410;537-44

GBS – Literature 2

- Recognizing Guillain-Barré syndrome in preschool children
  Roodbool J et al, Neurology 2011;76:807-810
- Yuki N, Hartung HP
  Guillain-Barré syndrome (Review article)
  N Engl J Med 2012;336:2294-2304

Additional references 1(Myelitis and NMO)

- Deiva K et al
  Acute idiopathic transverse myelitis in children
  Neurology 2015;84:341-49
- Sorte DE, Poretti A, Newsome et al
  Longitudinally extensive myelopathy in children
  Pediatr Radiol 2015;45:244-57
- Makhani L et al
  Diagnosing neuromyelitis optica
  Neuroimag Clin N Am 2013;23:279-91
- 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 opticospinal inflammatory diesease 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, imaging…
  Eur J Paed Neurol 2013;17:176