Chronic Inflammatory Demyelinating Polyneuropathy

or GBS?

- T and B cells in the pathogenesis
- Post-infection (viral hepatitis), -immunisation
- Progressive monophasic/relapsing deficits of p.nerves
- Motor, sensory, ataxic forms
  - proximal and distal weakness (usually symmetrical),
  - sensory involvement (numbness)
  - a/hyporeflexia.
- ENMG:

  prolonged distal motor latency, slowed conduction velocity, partial conduction block, delayed/absent F-wave

The value of electrophysiology:
studies in adults (USA)

- Electrophysiologic studies are frequently of poor quality
- nerve conduction studies: technically inadequate or misinterpreted,

These lead to misdiagnosis.

For example, small reductions of nerve conduction velocity are labeled “demyelinating” and technical issues lead to over-diagnosed “conduction block”s.

- The strict diagnostic criteria (specificity 100%, sensitivity 46%) for CIDP of the American Academy of Neurology

  have been replaced by slightly less specific (96%) but much more sensitive (81%) criteria that enable the recognition of atypical presentations, for which immunotherapy would have otherwise been delayed or withheld.

- BUT electrodiagnosis alone can never prove or exclude CIDP. Due to the patchy and diffuse demyelination, affected nerve parts may not be tested during electrophysiological examination. *McMillan et al 2013*

Clinical errors in interpretation: important in evaluating treatment results

Patients with stable or inactive disease, who are less likely to respond to novel treatments are not identified and excluded

- Recent research: 40% of CIDP patients are in remission or cured, but included in clinical trials.
- CIDP can exhibit spontaneous improvement.

CIDP is not always a chronic, lifelong disease.

Many patients continue to receive therapy for years when in fact their disease is no longer active.

active disease: worsens when treatment is tapered or discontinued

inactive disease: disability and examination findings are stable. NE is abnormal due to irreversible axonal degeneration. They do not require expensive and potentially toxic treatments anymore.

Cornblath et al 2013

Childhood cases from Turkey

Yüksel et al in preparation

Progressive neuropathic symptoms developing over weeks or months.
Preliminary diagnosis of CIDP. n=27

Seven patients were excluded: 2 metachromatic leukodystrophy,
3 hereditary neuropathy
1 spinal muscular atrophy type II
1 leukodystrophy.

Upon reviewing the EMG findings of the remaining patients, definitive diagnosis of CIDP **n=9**

n=3 presented subacute or acute onset; diagnosed when relapsed (n=1) or progressed >8 weeks (n=2)

Onset age	9.07± 5 (2-15) years
Gender (Female:Male)	3 Females 6 Males
Clinical onset	Acute (n=2), subacute (n=1), chronic (n=6)
Clinical progress	Monophasic (n=4) polyphasic (n=5)
Initial diagnosis of GBS	n=3 (n=1 recurrence, n=2 prolonged symptoms)
Duration of symptoms, months	5.40±7.71

Examination findings	Areflexia (n=7) Hyporeflexia (n=2) Symmetry (n=8) Asymmetry (n=1) Sensory defects (n=1) Stepping gait (n=5) Gowers sign (n=3) Inability to walk on heels (n=3)
Laboratory findings	CSF protein (n=4) 171±11 mg/dl (33-387) Brain MRI (n=5) all normal Spinal MRI (n=6), n=4 normal, n=2 roots thick, Gadolinium +

Treatment first-line	Corticosteroids (n=6), average 1mg/kg/day IVIG (n=2), once a month Combined Corticosteroids +IVIG (n=1)
Other treatments	Corticosteroids (n=8), average:1mg/kg/day, IVIG (n=7), once/twice a month Plasmapheresis (n=2), up to 25 cycles, ineffective* Azathioprine(n=6), average 1mg/kg/day Pulse Methyl Prednisolone (n=2), ineffective* Methotrexate (n=3), average 15mg/week Rituximab (n=1), 375mg/m^2/week Interferon (n=1), ineffective* Cyclosporine (n=1), ineffective*
Sequelae	Toe dorsiflexion defect (n= 3) Pes planus (n=1) Pes cavus (n=2) Muscle atrophy (n=2) Foot eversion (n=2) Hammer toe (n=1)
Follow-up months	27.22±1.69 (12-60)
MRS-first	3.14±0.69 (2-4)
MRS-end	1.43±0.97 (0-3)

Mc Millan et al 2013 Childhood series

60% relapsing, 40% monophasic
M=F
Most present with weakness of the legs, abnormal gait and falls. Difficulties with stair climbing can be the presenting symptom. Sometimes: UE only

Acute GBS-like start: 20%.
DTR absent 80%
Differential: Factors favouring the diagnosis of CIDP
longer time to initial clinical nadir,
longer time until first clinical deterioration
not as likely to need mechanical ventilation
more prominent initial sensory symptoms,
lower incidence of autonomic involvement and/or facial weakness
maintaining the ability to walk independently
ENMG asymmetrical demyelination

CSF prot 90%
80% good response to IVIg, 30% weaned off
Effect of IVIg similar to csteroids (84%) and superior to first-line PE

Treatment

- Loading dose of IVIg,
- maintenance every 3 weeks
- Steroids
- Other immunosuppressants
- Rtx-potential serious risks and lack of supporting evidence.

Trials have shown that:

up to 40% of patients receiving IVIg have inactive CIDP.

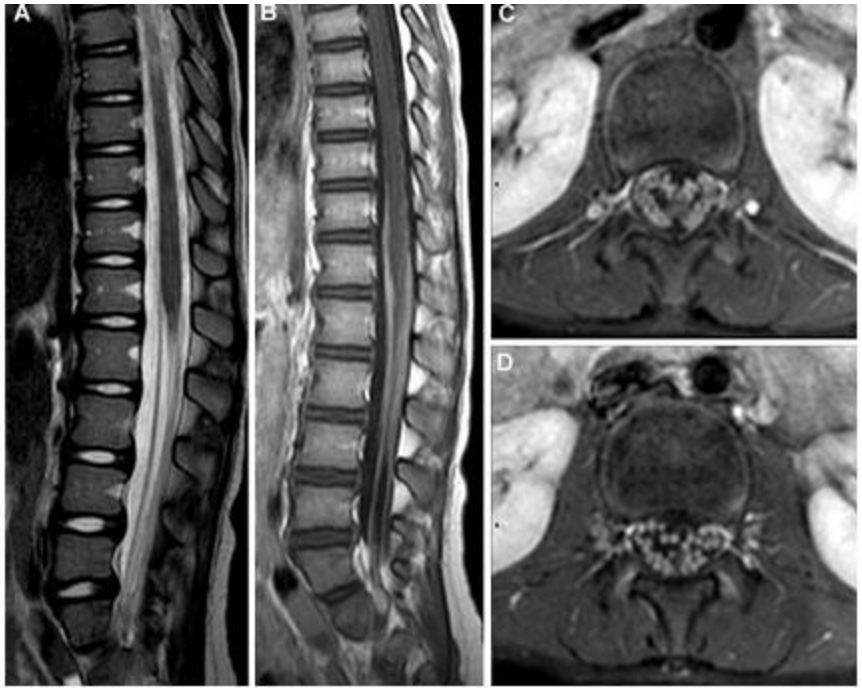
When patient becomes stable after IVIg: try to reduce dose to determine the lowest IVIg dose required to maintain stability.

Rossi et al 2013 Five y o girl.

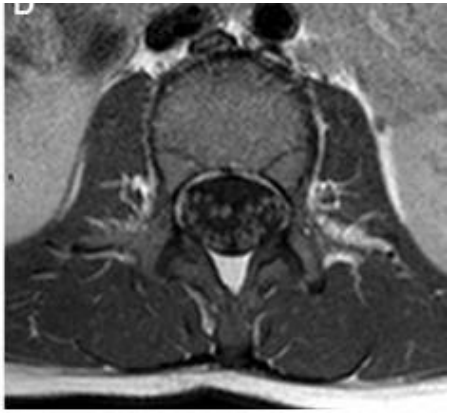
Sagittal T2W

Postcontrast sagittal T1W

Post Gd axial: diffusely thickened, enhancing caudal nerve roots



6 mo later



GBS, CIDP, hereditary polyneuropathies,metabolic diseases (leukodystrophies), infiltrative neoplasia, and toxic (i.e., methotrexate)

Riekhoff et al. European Journal of Pediatric Neurology 2012

Current practice in immunotherapy of childhood CIDP
as described in case reports and series.

1. First-line therapy - **IVIg** 0,4 g/kg/day for 5 days, repeat every 3-4 wks
   or
   Corticosteroids (oral prednisone) 1-2 mg/kg/day for 4-6 wks, then tapering.

2. Second-line therapy - Azathioprine 1-3 mg/kg/day
   Always consider **combining therapies**
   - Individual adjustments of treatment strategy

3. Alternative therapies: plasmapheresis, cyclosporine A, cyclophosphamide, mycophenolate mofetil, methotrexate, IFN alpha, RTX?