Update in Immune Axonal Neuropathies

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Objectives

• Learn the different causes of immune axonal neuropathies

• Learn the diagnostic work-up of immune axonal neuropathies

• Learn the best evidence-based options for when and how to treat immune axonal neuropathies
Outline

• Introduction to immune axonal neuropathies
• Rapid recognition of immune mediated neuropathy
• Differential diagnosis
• Discussion of illustrative cases of immune axonal neuropathies with brief overview/updates in specific subtypes of immune axonal neuropathies
• Take home messages
Immune Axonal Neuropathies: Introduction

• A diverse group of peripheral neuropathies (PN) where the immune system directly or indirectly damages the nerve axons (in contrast to an immune attack on the myelin covering of nerves)

• These are important to recognize and treat early, otherwise there is irreversible axonal loss

• Can be difficult to recognize in comparison to immune demyelinating neuropathies, which are recognized by changes in nerve conduction (e.g., Chronic Immune Demyelinating Polyneuropathy)

• Untreated, advanced demyelinating PN can be difficult to differentiate from axonal PN
Immune Axonal Neuropathies

**Associated with systemic disease**
- Vasculitis (autoimmune, infectious, drug-related)
- Connective tissue disease (e.g. Sjogren)
- Sarcoid disease
- Caused by cancer (e.g. anti-HU syndrome)
- Celiac disease

**Isolated to the nervous system**
- Axonal form of Guillain-Barré Syndrome
- Diabetic amyotrophy
- Non diabetic immune plexopathy (post surgical, Parsonage Turner syndrome, Hereditary Neuralgic Amyotrophy)
- Multifocal acquired motor axonopathy
Rapid recognition of immune mediated neuropathy
Danger signs in PN: ODS Criteria

- Onset-Develops quickly
- Distribution-Non length dependent
- Systemic features-Problems outside of nerves as well

- ODS POSITIVE if any of these criteria are present
Results

- ODS Sensitivity (detecting an inflammatory neuropathy) 96%
- ODS Specificity 85%
- ODS Positive Predictive Value 0.8, Negative Predictive Value was 0.97
Illustrative case 1: Use of ODS clinical criteria for autoimmune neuropathy screening
Illustrative Case #1: History

- 33-year-old man with **acute** left foot pain and weakness (Onset/Distribution)
- Episodes of **fever and sweating** (Systemic Symptoms)
- Testicular pain mistaken for torsion
- Muscle pain
- Abdominal pain
- Treated with minocycline for acne for 2 years
- Sister has Rheumatoid Arthritis

- This patient is ODS + due to acute onset and systemic symptoms
Illustrative Case #1: Exam and EMG

- Exam: left foot weakness in (in tibial nerve distribution) with sensory loss
- Electrical study of both tibial nerves shows that few nerve axons are firing on the left as compared to right nerve and some muscles contacted by tibial nerve have lost their incoming nerve signals

### EMG Summary Table

<table>
<thead>
<tr>
<th>Muscle Name</th>
<th>Spontaneous A</th>
<th>Fib</th>
<th>PSW</th>
<th>Fasc</th>
<th>H.F.</th>
<th>Amp</th>
<th>Dur</th>
<th>PPP</th>
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<tr>
<td>L. GASTROCN (MED)</td>
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<td>1+</td>
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<td>1+</td>
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<tr>
<td>R. GASTROCN (MED)</td>
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<td>None</td>
<td>None</td>
<td>N</td>
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<td>L. VAST LATERALIS</td>
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<td>None</td>
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<td>N</td>
<td>N</td>
<td>N</td>
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<td>N</td>
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<tr>
<td>L. BIC FEM (S HEAD)</td>
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<td>None</td>
<td>None</td>
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<td>1+</td>
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<td>Reduced</td>
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<td>L. TIB POSTERIOR</td>
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<td>1+</td>
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<td>1+</td>
<td>1+</td>
<td>1+</td>
<td>Stable</td>
<td>Reduced</td>
</tr>
</tbody>
</table>

### Nerve Conduction Studies (NCS)

- **Motor NCS R Tibial (Knee) - AH:**
  - Wave 1: 1
  - Wave 2: 2
  - Wave 3: 3

- **Motor NCS L Tibial (Knee) - AH:**
  - Wave 1: 1
  - Wave 2: 2
  - Wave 3: 3
Illustrative Case #1: Muscle Biopsy shows inflammation (arrow) around a blood vessel
Illustrative Case #1: Follow-up

- Most blood tests for potential causes (HBV and HCV, HIV, kidney function tests, ENA, CBC, LFTs, CK) were all normal or negative

- But blood test for vasculitis inflammation around blood vessels (Antineutrophil cytoplasmic antibodies (ANCA)) was positive perinuclear pattern

- Muscle biopsy confirmed inflammation around blood vessels (vasculitis), so treated with Cytoxan and prednisone to reduce inflammation

- Improvement of foot pain and resolution of weakness
Vasculitic neuropathy following exposure to minocycline

ABSTRACT

Objective: To report 3 patients with minocycline-induced autoimmunity resulting in peripheral nerve vasculitis.

Methods: We report 3 patients who, during minocycline treatment for acne vulgaris, developed subacute onset of pain and weakness caused by vasculitis in single and multiple mononeuropathy patterns.

Results: Each patient underwent either a nerve or muscle biopsy that confirmed vasculitis. One patient additionally developed systemic symptoms (including fever, fatigue, and night sweat) and another had a posterior circulation stroke. Symptoms developed with either early or prolonged use of minocycline. Despite withdrawal of minocycline, patients needed long-term immunotherapy to gain neurologic improvement.

Conclusions: Our findings suggest that the typical neuropathy associated with minocycline use is painful single or multiple mononeuropathy due to peripheral nerve vasculitis, which may also be accompanied by presumed CNS vasculitis (presenting as stroke). *Neurol Neuroimmunol Neuroinflamm* 2016;3:e180; doi: 10.1212/NXI.0000000000000180
Updates in Vasculitic Neuropathy
Systemic Vasculitis: Overview

- **Isolated**
  - Small vessel vasculitis (MPA, GPA)
  - Medium vessel (PAN)
  - Large vessel

- **Caused by other conditions**
  - Connective tissue disease
  - Sarcoid
  - Behcet’s
  - Infection: HBV, HCV, HIV, CMV, leprosy, Lyme, HTLV-1
  - Drugs
  - Malignancy
  - Inflammatory bowel disease
  - Hypocomplementemic urticarial vasculitis syndrome
ANCA Vasculitis-Related Peripheral Neuropathy

• Small blood vessels (arterioles, capillaries and venules)
• cANCA (PR3) → Granulomatosis with polyangiitis (Wegener's)
• pANCA (MPO) → Microscopic polyangiitis (MPA)
• ANCA PN
  • most common neurological complication in ANCA vasculitis
  • occurs in about 10-20% of patients
  • most common type is mononeuritis multiplex
  • Commonly first manifestation of the disease
  • 1/3 have complete resolution of neuropathy with appropriate treatment
Vasculitic PN: Typical Diagnostic Tests

- ANCA, cryoglobulin
- Rheumatological markers: ENA, ANA, RF
- Infectious diseases: HCV, HBV, HIV, Lyme
- Blood tests: CBC, SPEP/IFE, FLC
- Kidney function, Urine Analysis
- Inflammation markers: ESR, CRP, C3,4 levels
- CAT Scan chest (+/- Abdomen and pelvis) with contrast
- Nerve and muscle biopsy
- Brain MRI with contrast
Vasculitic PN: Utility of Nerve Conduction Study

• Important to determine the axonal nature of the neuropathy

• Important to help show asymmetry
  • Will miss multifocal neuropathy if done on only one side, even in normal values
  • Severe, advanced vasculitic PN will eventually look symmetric

• Can help determine which nerve to biopsy
Vasculitic PN: Nerve biopsy

- Essential for diagnosis of peripheral nerve vasculitis
- Can be avoided if patient already has a biopsy proven (other organ) systemic vasculitis
- Sensitivity for definite vasculitis around 30-50%
- Nerve + Muscle biopsy increases sensitivity for definite vasculitis ~ 20%
- Nerve + Muscle Biopsy probable or definite vasculitis ~85% sensitive

ANCA Vasculitis-Related PN: Treatment

• Classic 3-drug treatment: Steroids (oral or IV) or Plasma Exchange + cyclophosphamide (oral or IV) + azathioprine oral

• Recent: Using rituximab instead of cyclophosphamide for induction and rituximab for maintenance instead of azathioprine

• Future: ? Use of avacopan, a complement 5a inhibitor instead of steroids for induction and potentially maintenance (phase III study ongoing)
Non-ANCA Vasculitis-Related PN: Treatment

• Often similar to ANCA but some additional considerations

• Infectious vasculitis PN: Need to treat infection
  • HCV- Rituximab + interferon-α alone or combined with ribavirin

• Non-systemic vasculitic neuropathy (NSVN): may consider steroid monotherapy
Non-systemic Vasculitic Neuropathy (NSVN)

• No non-PNS organ involvement

• Serological markers usually negative

• Examples
  - Inflammatory neuropathy caused by surgery
  - Painful diabetic radiculoplexus neuropathy (cervical, thoracic or lumbosacral)
  - Painless diabetic radiculoplexus neuropathy
  - Non diabetic multifocal neuropathy
Illustrative case 2: Post-surgical inflammatory neuropathy

• HISTORY
  • A 58-year-old man undergoing cardiac bypass surgery

  • 3 days after surgery he developed pain in his left shoulder and forearm, numbness and tingling in the left hand and weakness of his left hand and fingers.

  • Symptoms have progressed and weakness has become more profound. He also developed atrophy in his left forearm. He has been requiring opiates for the pain.
Illustrative case 2: Post-surgical inflammatory neuropathy

• EXAM
  • Severe weakness in the hand (movement only without gravity)
  • Deep tendon reflexes were normal
  • Reduced sensation in the left hand

• STUDIES
  • MRI Cervical spine and brachial plexus +/- contrast: Normal
  • EMG: multiple, severe, acute, axonal mononeuropathies in the left upper extremity.
Post-surgical inflammatory neuropathy

• Important to differentiate from mechanical neuropathies

• Typically develops within 30 days post procedure

• Patients present with acute pain and weakness

• Nerve conduction study shows an axonal focal or multifocal neuropathy (including plexopathy)

• No randomized control trial evidence, but since most will have increased epineurial perivascular lymphocytic inflammation, a treatment trial with steroids is justified

Brain. 2010 Oct;133(10):2866-80
Updates on Management of Brachial Plexitis (Parsonage-Turner syndrome)

- No randomized control trials
- One large retrospective study
  - 50 treated patients (within 1 month of symptoms) vs 203 historical controls
  - 13-days oral prednisolone: 60 mg/day x 1 wk, tapered by 10 mg/day x 5 days, 5 mg on day 13

### Table 2  Outcomes for the study (prednisolone) group (SG) and the historical controls (HC)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Study group</th>
<th>Historical controls</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Median time (days) until initial pain relief (mean)</td>
<td>12.5 (17.1)</td>
<td>20.5 (37.2)</td>
<td>0.13</td>
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<tr>
<td>Recovery of strength within 1 month</td>
<td>9/50 (18.0%)</td>
<td>11/174 (6.3%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Full functional recovery within the first year</td>
<td>6/50 (12.0%)</td>
<td>2/189 (1.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Good (but not full) self-reported recovery within 6 months</td>
<td>16/50 (32%)</td>
<td>3/103 (2.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12 months</td>
<td>22/50 (44.0%)</td>
<td>11/103 (10.7%)</td>
<td>&lt;0.001</td>
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</table>
Updates in Axonal Guillain-Barré Syndrome variants
Illustrative case 3: GBS (Pharyngeal-cervical-brachial variant)

• 52-year-old diabetic woman with acute, progressive difficulty swallowing and speaking, upper extremity weakness and difficulty breathing

• HISTORY AND EXAM
  • Presented to outside emergency department for weakness and difficulty breathing.
  • Within one week, she required a ventilator to breath, then transferred to our hospital
  • Called the next day because of severe weakness in UE, face and neck
  • Normal strength in legs
  • Absent reflexes
Illustrative case 3: GBS (Pharyngeal-cervical-brachial variant)

• TESTING
  • MRI brain + c spine w/o contrast: Normal

• EMG :
  • ARMS ➔ Severe sensory motor polyradiculoneuropathy with absent motor responses
  • LEGS ➔ Normal motor responses

• LABS
  • CSF: RBC 2208/mm3; WBC 31/mm3, Protein 175mg/dL and glucose 62
  • Paraneoplastic panel: Slightly elevated antibodies to neuronal VGKC protein, with no LGi1 or CASPR2 abs
  • West Nile virus Ab: Negative
  • Ganglioside antibodies GD1b, GT1a, GQ1b: Negative
Illustrative case 3: GBS (Pharyngeal-cervical-brachial variant)

• MANAGEMENT
  • Treated with Intravenous Immunoglobulin (IVIG) (2 gms/kg)
  • Extubated 6 days later
  • Within 10 days, Deltoid strength went from 0/5 → 4+/5 and normal strength distally
### Guillain Barre Syndrome

- **Classic GBS**
  - AIDP (Acute Inflammatory Demyelinating Polyneuropathy)

- **Other GBS Variants**
  - AMAN (Acute motor axonal neuropathy)
  - AMSAN
  - Pharyngeal-cervical-brachial (PCB)
  - Acute Pharyngeal
  - Paraparetic (muscle weakness)
  - Bifacial weakness with paresthesia (abnormal skin sensations)

### Miller Fisher Syndrome

- **Classic MFS**
  - Ataxia, eye muscle weakness, absence of normal muscle reflexes

- **Other MFS Variants**
  - Acute eye muscle weakness
  - Acute ataxic neuropathy
  - Acute eyelid drooping
  - Acute pupil dilation
  - Bickerstaff brainstem encephalitis
  - Acute ataxic sleepiness

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<tr>
<th></th>
<th>GM1</th>
<th>GD1A</th>
<th>GT1a</th>
<th>GQ1b</th>
<th>GD1b</th>
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<td>ASAN</td>
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</tr>
<tr>
<td>PCB</td>
<td></td>
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<tr>
<td>MFS</td>
<td></td>
<td>x</td>
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</table>
Guillain-Barre Syndrome: General remarks

• This is a clinical diagnosis! Early in disease cerebrospinal fluid and nerve conduction tests may be normal
• Dynamic disease: One reassuring pulmonary function test early in the disease does not mean patient won’t need to be intubated
• Deep tendon reflexes can be present very early in the disease
• 5% patient have weakness spreading in a descending pattern
• Pain is common
• 20–30% of patients develop respiratory failure and need ventilation at an intensive care unit
• 15% patient have a mild increase in cells in cerebrospinal fluid (5 to 50 cells/μl CSF)
GBS general remarks

• 25% patients deteriorate during/shortly after treatment with IVIg or PE
• 10% patients relapse (“Treatment-Related Fluctuation” [TRF])
• 5% Mortality
• ~20% GBS patients cannot walk unaided 6 months after onset
• Most have residual pain and fatigue
• Most improvement happens in the first year, but some show further recovery even after 3 or more years.

Lancet 2016; 388: 717–27
Prediction of Respiratory Insufficiency in Guillain-Barré Syndrome

Christa Walgaard, MD,¹ Hester F. Lingsma, MSc,² Liselotte Ruts, MD,¹
Judith Drenthen, MD,¹ Rinske van Koningsveld, MD,³
Marcel J. P. Garssen, MD,⁴ Pieter A. van Doorn, MD,¹
Ewout W. Steyerberg, PhD,² and Bart C. Jacobs, MD¹,⁵

Objective: Respiratory insufficiency is a frequent and serious complication of the Guillain-Barré syndrome (GBS). We aimed to develop a simple but accurate model to predict the chance of respiratory insufficiency in the acute stage of the disease based on clinical characteristics available at hospital admission.

Methods: Mechanical ventilation (MV) in the first week of admission was used as an indicator of acute stage respiratory insufficiency. Prospectively collected data from a derivation cohort of 397 GBS patients were used to identify predictors of MV. A multivariate logistic regression model was validated in a separate cohort of 191 GBS patients. Model performance criteria comprised discrimination (area under receiver operating curve [AUC]) and calibration (graphically). A scoring system for clinical practice was constructed from the regression coefficients of the model in the combined cohorts.

Results: In the derivation cohort, 22% needed MV in the first week of admission. Days between onset of weakness and admission, Medical Research Council sum score, and presence of facial and/or bulbar weakness were the main predictors of MV. The prognostic model had a good discriminative ability (AUC, 0.84). In the validation cohort, 14% needed MV in the first week of admission, and both calibration and discriminative ability of the model were good (AUC, 0.82). The scoring system ranged from 0 to 7, with corresponding chances of respiratory insufficiency from 1 to 91%.

Interpretation: This model accurately predicts development of respiratory insufficiency within 1 week in patients with GBS, using clinical characteristics available at admission. After further validation, the model may assist in clinical decision making, for example, on patient transfer to an intensive care unit.

ANN NEUROL 2010;67:781–787
### TABLE 2: EGRIS

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<thead>
<tr>
<th>Measure</th>
<th>Categories</th>
<th>Score</th>
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<tr>
<td>Days between onset of weakness and hospital admission</td>
<td>&gt;7 days</td>
<td>0</td>
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<tr>
<td></td>
<td>4–7 days</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥3 days</td>
<td>2</td>
</tr>
<tr>
<td>Facial and/or bulbar weakness at hospital admission</td>
<td>Absence</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Presence</td>
<td>1</td>
</tr>
<tr>
<td>MRC sum score at hospital admission</td>
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</tr>
<tr>
<td></td>
<td>50–41</td>
<td>1</td>
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<tr>
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<td>40–31</td>
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<td></td>
<td>≤20</td>
<td>4</td>
</tr>
<tr>
<td>EGRIS</td>
<td></td>
<td>0–7</td>
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EGRIS = Erasmus GBS Respiratory Insufficiency Score; MRC = Medical Research Counsel.

### TABLE 3: Risk Categories for Respiratory Insufficiency According to EGRIS

<table>
<thead>
<tr>
<th>Category</th>
<th>Derivation Set</th>
<th>Validation Set</th>
<th>Combined Sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (EGRIS 0–2)</td>
<td>5/152 (3%)</td>
<td>5/116 (4%)</td>
<td>10/268 (4%; 95% CI, 1–6%)</td>
</tr>
<tr>
<td>Intermediate risk (EGRIS 3–4)</td>
<td>42/168 (25%)</td>
<td>13/60 (22%)</td>
<td>55/228 (24%; 95% CI, 19–30%)</td>
</tr>
<tr>
<td>High risk (EGRIS 5–7)</td>
<td>36/57 (63%)</td>
<td>9/12 (75%)</td>
<td>45/69 (65%; 95% CI, 54–76%)</td>
</tr>
<tr>
<td>Total</td>
<td>83/377 (22%)</td>
<td>27/188 (14%)</td>
<td>110/565 (19%; 95% CI, 16–23%)</td>
</tr>
</tbody>
</table>

Probability of respiratory insufficiency in the first week of hospital admission in the derivation, validation, and combined sets stratified for EGRIS and expressed as number of mechanically ventilated patients/total number of patients (%). EGRIS = Erasmus GBS Respiratory Insufficiency Score; CI = confidence interval for combined sets.
Management

• Equal efficacy of IVIg and plasmapheresis in terms of reducing the duration of mechanical ventilation, improving disability at 4 weeks, reducing residual disability and preventing death.
• No more benefit in doing plasma exchange then IVIG
• No benefit in giving corticosteroids
• In TRF, may repeat IVIG course
• Prevent deep vein thrombosis, dysautonomia and pain management
• Prevent bed sores and contractures
RCT: 34 pt, IVIg + either eculizumab (900 mg) or placebo (2:1)

Week 4 Independent Ambulation (functional grade ≤2):
- Eculizumab group → 61% (90% CI 42–78; n=14)
- Placebo group → 45% (90% CI 20–73; n=5)
- Did NOT meet primary end point

Week 24 Running: 74% Eculizumab vs. 18% in placebo

AE: Eculizumab group → Anaphylaxis x1, intracranial hemorrhage x1

Issues: Small number of patients, more severely affected than historical controls, IVIG may interfere with eculizumab
Update in Paraneoplastic Neuropathy
Illustrative case 5: Paraneoplastic PN
Illustrative case 5: Paraneoplastic PN

• HISTORY

• 62 y/o M with h/o DM, CKD, smoker who presented with 3.5 months of progressive painful dysesthesias.
• Started with uncomfortable tingling in his right face that then progressed to numbness.
• Developed feelings of burning and coldness that progressed from hands to shoulders, to elbows, to knees, to hips.
• Multiple episodes daily of feeling like his skin is on fire, requiring a cool cloth, alternating with abruptly feeling freezing cold.
Illustrative case 5: Paraneoplastic PN

- HISTORY CONTINUED
  - Endorsed 30lb unintentional weight loss, mild dry mouth, constipation, urinary changes, change in taste, early satiety and spasms in his hands.
  - Admitted to hospital and d/c with referral to psych for functional gait d/o
  - CT chest: New lung nodule from last year which was stable over 3 mos

This patient is ODS +
Illustrative case 5: Paraneoplastic PN

• EXAM
  • Loss of temperature, vibration in his extremities
  • Absent proprioception at the toes and impaired at the ankles
  • Pseudoathetosis
  • Ataxic gait with unsteady turns.
  • Diffusely areflexic
  • Normal strength
## Illustrative case 5: Paraneoplastic PN

### MNC

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Latency</th>
<th>Amplitude</th>
<th>Conduction Velocity</th>
<th>Neg Area</th>
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<tr>
<td></td>
<td>Onset Lat. ms</td>
<td>Normal ≤</td>
<td>Normal ≥</td>
<td>Distance mm</td>
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<td>Fibular (Peroneal).R Extensor digitorum brevis.R</td>
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<tr>
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<td>6.0</td>
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<td>Fibula (head)</td>
<td>12.5</td>
<td>3.6</td>
<td>430</td>
<td>52</td>
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<td>Above Knee</td>
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<td>80</td>
<td>42</td>
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<td>Tibial.R Abductor hallucis.R</td>
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<td>4.4</td>
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<td>Median.R Abductor pollicis brevis.R</td>
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<tr>
<td>Wrist</td>
<td>5.7*</td>
<td>3.8</td>
<td>4.7*</td>
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<td>3.8</td>
<td>310</td>
<td>46*</td>
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<td>Ulnar.R Abductor digiti minimi (manus).R</td>
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</tr>
<tr>
<td>Above elbow</td>
<td>9.8</td>
<td>4.6</td>
<td>100</td>
<td>59</td>
</tr>
</tbody>
</table>

### SNCS

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Peak Latency</th>
<th>Amplitude</th>
<th>Conduction Velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neg Peak Lat ms</td>
<td>Normal ≤</td>
<td>Normal ≥</td>
</tr>
<tr>
<td>Sural.R to Lat Mal.R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post Calf</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Median.R to Digit II (index finger).R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Ulnar.R to Digit V (little finger).R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Radial.R to Anatomical snuff box.R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forearm</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>
Illustrative case 5: Paraneoplastic PN

• ANNA-1 (anti-hu) Positive 1:7680
Neuropathies in cancer

• Neuropathies caused by cancer itself:
  • Paraneoplastic
  • Infiltrative

• Neuropathies caused by cancer treatment:
  • Toxic
  • Autoimmune
  • Opportunistic infections (CMV)
  • Trauma from surgery, bone fracture
  • Malnutrition, vitamin deficiency
  • Radiation
Paraneoplastic neuropathies

- Autoimmune neuropathy (mostly axonal)
- Tumor antigen is identical to the neural antigen
- Either neuronopathy or polyneuropathy
- Motor (rare), Sensory (common) with or without autonomic involvement
- Other syndrome may be associated such as LEMS, Encephalitis etc.
- Anti-Hu (ANNA-1) most common antibody, 2\textsuperscript{nd} comes anti-CRMP5 (CV-2) (may look demyelinating)
- The tumor is often occult, and the neurologic disorder typically precedes the diagnosis of cancer
- In patient felt to be in remission, paraneoplastic neuropathy usually means relapse

Arch Neurol. 2010;67(3):330-335
### Table 4. Tumor Types in the PNS Euronetwork Database

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Patients, No. (%) (n=899)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small cell lung cancer</td>
<td>345 (38.4)</td>
</tr>
<tr>
<td>Ovary</td>
<td>94 (10.5)</td>
</tr>
<tr>
<td>Breast</td>
<td>87 (9.7)</td>
</tr>
<tr>
<td>Non–small cell lung cancer</td>
<td>71 (7.9)</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>31 (3.4)</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>27 (3.0)</td>
</tr>
<tr>
<td>Thymoma</td>
<td>24 (2.7)</td>
</tr>
<tr>
<td>Prostate</td>
<td>23 (2.6)</td>
</tr>
<tr>
<td>Metastasis from unknown primary</td>
<td>18 (2.0)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>16 (1.8)</td>
</tr>
<tr>
<td>Esophagus or gastric</td>
<td>16 (1.8)</td>
</tr>
<tr>
<td>Testicular</td>
<td>15 (1.7)</td>
</tr>
<tr>
<td>Kidney or bladder</td>
<td>11 (1.2)</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Merkel carcinoma</td>
<td>6 (0.7)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Other</td>
<td>104 (11.6)</td>
</tr>
</tbody>
</table>
Paraneoplastic neuropathies

• Antibodies may be absent

• Patients with paraneoplastic neurologic disorders have a better prognosis than patients with histologically identical tumors but without paraneoplastic syndrome

• No evidence that immunosuppression for treatment of the paraneoplastic syndrome stimulates the growth of the tumor

• However immunotherapy is not very effective (unless, perhaps the patient is treated very early)

• Treatment of the tumor may stabilize the neuropathy
Take home messages

• Large groups of potentially treatable PN

• Use of clinical criteria may help early identification

• Laboratory testing can be helpful in some but not all cases

• Early recognition and treatment will help improve outcome