



Electrodiagnosis In Cancer

Christian M. Custodio, M.D.
Cancer Rehabilitation Fellowship Director
Memorial Sloan-Kettering Cancer Center

Assistant Professor
Weill Cornell Medical College



Disclosures

Nothing

Background

- 13.7 million cancer survivors in the US
- More primary and secondary complications noted

- True prevalence of neuromuscular disease in the cancer population is unknown

Neuromuscular complications

- From the cancer itself
 - Direct effects
 - Indirect effects
 - Paraneoplastic effects
- From treatments
 - Surgery
 - Chemotherapy
 - Radiation therapy
 - Transplantation

Peripheral Nervous System

- Anterior Horn Cell
- Root
 - Monoradiculopathy
 - Polyradiculopathy
- Plexus
- Multiple levels
- Peripheral Nerve
 - Mononeuropathy
 - Polyneuropathy
 - Mononeuritis multiplex
 - Large fiber
 - Small fiber
- Neuromuscular Junction
- Muscle

Purpose of EMG

- Confirmation
- Exclusion
- Detection
- Localization
- Chronicity
- Severity
- Pathophysiology
- Prognosis/progression/guide treatment

Limitations of NCS/EMG

- Does not directly assess small diameter fibers (a-delta, c fibers)
- Does not directly assess type II muscle fibers
- Inferring symptoms and neuropathic deficits
 - EMG severity \neq clinical severity
 - NCS/EMG changes may lag behind symptom onset
- Inferring underlying anatomical, biochemical, or other pathophysiologic derangements
 - Pre-existing conditions

NCS & EMG

Extension of the history and physical exam

Direct Effects of Cancer

Tumor Compression

- After disc disease and spinal stenosis, spinal tumors are the most common causes of radiculopathy
 - Metastases > Primary
 - Common metastases: breast, lung, prostate, thyroid, kidney, colon
 - Common primaries: multiple myeloma, plasmacytoma, Ewings, osteogenic sarcoma

Leptomeningeal Disease

- Polyradiculopathy Symptoms
 - Focal or radicular pain
 - Areflexia
 - Paresthesias
 - Lower motor neuron weakness
 - Nuchal rigidity
 - Upper motor neuron findings
 - Especially with concomitant brain involvement

(Poly)Radiculopathy

- Sensory NCS should be normal
- Motor responses (w/in affected myotomes) will be normal or reduced in amplitude
 - Prolonged or absent F-wave latencies
- Needle EMG = most sensitive test
 - Abnormalities in at least 2 muscles within same root innervation but with different peripheral nerve innervation.
 - Fibrillation potentials, reduced recruitment, large polyphasic motor unit potentials

Brachial Plexopathies

- Breast, lung most common primaries
 - Consider radiation-induced neoplasms
- Anywhere along the plexus, but preferentially lower trunk
 - Due to proximity to axillary nodes and superior sulcus of the lung
- Symptoms
 - Pain, paresthesias, numbness, weakness in a given distribution

Brachial Plexopathies

- Lower trunk NCS findings
 - Reduced amplitude median and ulnar CMAPs
 - Reduced amplitude ulnar SNAP
 - NORMAL median SNAP
 - Reduced amplitude medial antebrachial SNAP
- EMG abnormalities in lower trunk distribution (C8-T1)
 - FDI (ulnar), FPL (median), EIP (radial)
 - Paraspinal EMG normal

Lumbosacral Plexopathy

- Colon, GYN tumors, lymphomas, sarcomas
- Abnormal sural, superficial peroneal SNAPs
- EMG abnormalities in affected muscles
 - Esp proximal muscles (gluteal)
 - Normal paraspinals
- Asymmetry helps

Mononeuropathies

- Findings limited to distribution of the individual nerve
 - Radial neuropathy from humeral spiral groove involvement
 - Malignant nerve sheath tumors

Diffuse neuropathies

- Diffuse symmetric
- Mononeuritis multiplex
- Rare
 - Hematologic malignancies (CLL)
 - Amyloid deposition (multiple myeloma)

Focal myopathy

- Rare
 - Direct infiltration from underlying bony metastasis
 - Fibrillation potentials, CRDs, rapid recruitment, short duration, small amplitude, polyphasic MUPs

Paraneoplastic Syndromes

- ### Paraneoplastic Syndromes
- Often more severe and rapid in progression than would normally be expected in a non-cancerous etiology
 - Often precede the diagnosis of cancer
 - Early recognition may increase survival!
 - Treatment of tumor may result in improvement of symptoms
 - Neuronal antibodies

- ### Paraneoplastic Syndromes
- Any tumor
 - Any level of the nervous system
 - Any pattern of involvement

 - But some tumors and patterns are more likely than others...

Paraneoplastic Sensory Ganglionopathy

- Sensory neuronopathy
- Pain and sensory loss
 - Sensory ataxia, pseudoathetosis, areflexia
 - Upper > Lower extremities
- May be asymmetric
- Motor function preserved

- Small cell lung cancer (anti-Hu)
 - Breast, prostate, renal, lymphoma

Sensory Ganglionopathy

- Abnormal SNAPs
 - UE > LE
- Normal CMAPs
- Normal EMG
 - Poor activation due to proprioceptive loss

Lambert Eaton Myasthenic Syndrome

- Presynaptic disorder of neurotransmission
- Fatigue, proximal weakness, hyporeflexia, autonomic dysfunction
- “Warming-up” phenomenon

- 40-60% associated with small cell lung CA
 - Anti-voltage gated calcium channel antibodies (anti-VGCC)

LEMS

- Repetitive stimulation
 - Low frequency (2-3 Hz)
 - Low amplitude baseline CMAP
 - Decremental response
 - High frequency/post-10 second isometric exercise
 - Facilitation – 100-200% increase in CMAP amplitude
- SNAPs, EMG findings usually normal
 - Varying, unstable MUPs on EMG

Proximal Myopathy

- Symmetric, proximal weakness
- No sensory or reflex abnormalities
- Sensory and motor NCS normal
- EMG in proximal muscles
 - Fibrillation potentials, +/- CRDs
 - Rapid recruitment
 - Small, polyphasic MUPs
 - Usually no myotonic discharges

Proximal Myopathy

- True paraneoplastic association controversial
- Polymyositis and dermatomyositis associated with increased incidence of malignancy
 - Breast, lung, GYN

Motor Neuron Disease

- Rare
- Anti-Hu associated paraneoplastic encephalomyelitis/sensory neuronopathy/motor neuropathy syndrome
 - Small cell lung cancer
- No known association between ALS and cancer
 - Screening for cancer is part of the ALS workup

Motor Neuron Disease

- Normal sensory NCS
- Motor NCs either normal or low amplitude
- Diffuse needle EMG abnormalities
 - Fibrillation potentials
 - Fasciculation potentials
 - Reduced recruitment
 - Varying, large, polyphasic MUPs

Indirect Effects

- Critical illness neuromyopathy
- Steroid myopathy
- Metabolic associated neuropathies
 - Weight loss associated compressive neuropathy
 - Malnutrition/vitamin B12 deficiency
 - Renal failure due to myeloma/amyloid

Treatment Related Neuromuscular Issues

Surgery
Chemotherapy
Radiation Therapy
Stem Cell Transplant

Surgery

Perioperative Injuries

- Uncommon, but thought to be more likely in cancer due to the complexity of surgeries
- Occasionally nerves are intentionally sacrificed
 - Spinal accessory nerve in radical neck dissection
 - Trapezius weakness, branch to SCM usually spared

Upper Limb Injuries

- Lower trunk brachial plexus
 - Thoracotomy, mastectomy
- Ulnar neuropathy at the elbow
 - Arm boards used to secure IVs
- Radial neuropathy at the spiral groove
 - Prolonged lateral decubitus positioning
- Median/radial neuropathies at the elbow
 - IV infiltrations

Upper Limb Injuries – EDX findings

- Focal slowing, temporal dispersion, conduction block across the site of injury
- Reduced recruitment within the affected distribution (distal to the lesion), rare fibrillation potentials, MUP changes depending on chronicity.

Lower Limb Injuries

- Pelvic Surgery
 - Femoral neuropathy
 - Lumbar plexopathy
- Hip/acetabular surgery
 - Sciatic neuropathy (peroneal division)
- New, acute symptoms 24-48 hours post surgery – think delayed post-op hematoma
 - Get an ultrasound or CT, not an EMG!

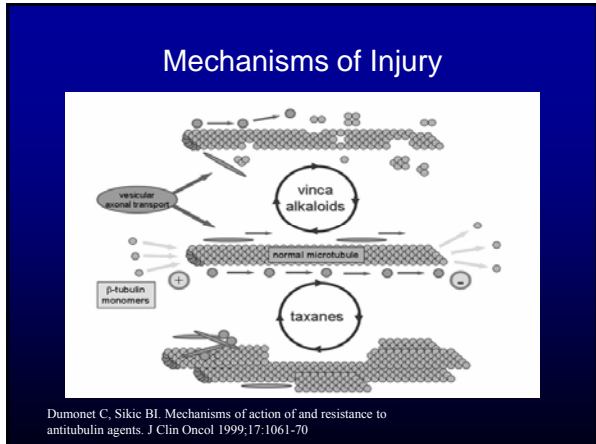
Chemotherapy

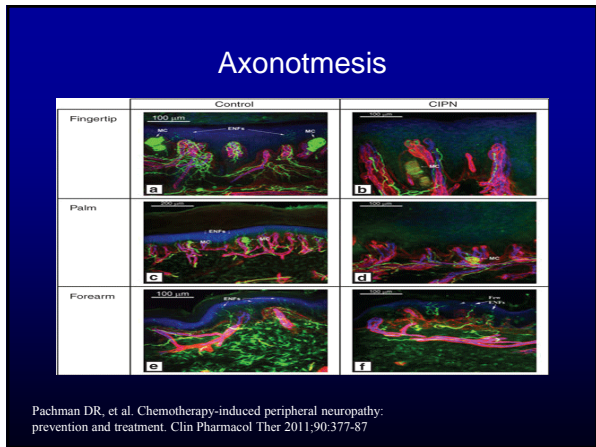
Neurotoxic Agents

- **Vinca alkaloids**
 - Vincristine, vinblastine, vinorelbine, vindesine
- **Taxanes**
 - Paclitaxel, Abraxane, docetaxel, tesetaxel
- **Platinum compounds**
 - Cisplatin, carboplatin, oxaliplatin
- **Others**
 - Bortezomib
 - Thalidomide
 - Lenalidomide
 - Ixabepilone
 - Capecitabine
 - Cytarabine
 - Suramin
 - Interferons

Mechanisms of Injury

<u>Axonotmesis</u>	<u>Neurotmesis</u>
• Microtubule dysfunction <ul style="list-style-type: none">– Binds tubulin<ul style="list-style-type: none">• Arrests dividing cells in metaphase– Axonal transport<ul style="list-style-type: none">• Large and small fibers	• Direct cytotoxic effects (apoptosis) <ul style="list-style-type: none">– Binds/cross-links DNA<ul style="list-style-type: none">• Inhibits protein synthesis– Dorsal root ganglion preference<ul style="list-style-type: none">• Blood-brain barrier
• Mitochondrial disruption	• n.b. - Myelinopathy <ul style="list-style-type: none">– Damage to Schwann cells





- ### Mechanisms of Injury
- | <u>Axonotmesis</u> | <u>Neurotmesis</u> |
|---|---|
| <ul style="list-style-type: none"> • “Stocking-glove”
– Sensory > motor | <ul style="list-style-type: none"> • “Glove-stocking”
– Sensory >>> motor |
| <ul style="list-style-type: none"> • Variable recovery | <ul style="list-style-type: none"> • Permanent impairment |
| <ul style="list-style-type: none"> • Seen w/ all agents | <ul style="list-style-type: none"> • Seen esp. w/ platinum agents |

Typical NCS/EMG findings in Axonal Neuropathies (Taxanes, Vinca alkaloids)

- Sensory NCS
 - Decreased SNAP amplitudes, +/- mildly slowed conduction velocities
- Motor NCS
 - Normal vs. reduced amplitude, +/- mildly slowed conduction velocities
- EMG
 - Normal vs. fibrillation potentials and large, polyphasic motor unit potentials in distal muscles

Typical NCS/EMG findings in Ganglionopathies (Platinum compounds)

- Sensory NCS
 - Absent or reduced SNAP amplitudes, slowed conduction velocities
 - Usually more severe UE > LE
- Motor NCS
 - Normal
- EMG
 - Normal
 - Poor activation (pseudoelectrodes)

Radiation Therapy

Radiation Injury

- Can occur at any level of the nervous system
- Delayed, late complication
- Brachial plexopathy
- Radiation induced myopathy

“Classic” Plexopathy

- | Neoplastic | Radiation-induced |
|---|---|
| <ul style="list-style-type: none">• Painful• Lower trunk• Less associated with lymphedema• Not progressive (if treated)• Absence of myokymic discharges• Absence of fasciculation potentials | <ul style="list-style-type: none">• Painless• Upper trunk• Greater association with lymphedema• Progressive• Myokymic discharges• Fasciculation potentials |

Caution!

- Absence of myokymia does not exclude a radiation-induced injury
- Presence of myokymia does not exclude a neoplastic-induced injury
- External compression from areas of soft tissue fibrosis can cause pain

Myopathy

- Affected muscles limited to radiation treatment field
 - e.g. “Dropped-head” syndrome following mantle field radiation therapy
- EMG findings:
 - Decreased insertional activity
 - Rare (if any) fibrillation potentials
 - Rapid recruitment, small polyphasic MUPs

Hematopoietic Stem Cell Transplantation

All bets are off

Stem Cell Transplantation

- Patients often receive pre-transplant chemotherapy and/or radiation therapy
- High incidence of metabolic derangements
 - Steroid induced diabetes
 - Malnutrition/malabsorption syndromes

Graft vs. Host Disease

- 40% of 100+ day post-transplant survivors will develop GVHD
- High incidence of autoimmune neuromuscular disorders
 - Polymyositis > dermatomyositis
 - Myasthenia gravis
 - Autoimmune neuropathies
 - Distal symmetric axonal
 - Multifocal demyelinating (similar to AIDP)

Special Safety Considerations

- Thrombocytopenia/anticoagulation issues
 - My cutoff: 15,000/mcl
 - Caution < 50,000/mcl
 - Careful, limited selection of muscles for EMG
 - Minimal exploration within each muscle
 - Avoid deep, difficult to compress muscles, muscles near major vascular structures
 - Iliopsoas, posterior tibialis, supinator, paraspinals
 - Avoid facial muscles
 - Document maintenance of hemostasis

Special Safety Considerations

- Lymphedema/peripheral edema
 - NCS are safe
 - May need higher stimulus intensities
 - Needle EMG
 - Actual risk of cellulitis unknown
 - Well controlled lymphedema generally ok
 - Again, careful muscle selection, minimal exploration
 - Balance potential risks with the need to obtain the necessary information

“In life, there are more questions than there are answers. So try to be the one who asks the questions.”
– Charles Schulz
