A Complex Diagnosis

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Objectives

- To use a case study of a true patient to better understand disease presentation, pathology, and treatment
- To review the differential diagnosis of foot drop
- To review the anatomy and distribution of the lumbosacral nerve plexus and selected pathologic presentations
- To discuss the pathophysiology, clinical presentation, evaluation, and current treatment modalities of complex regional pain syndrome
- To briefly discuss the additional quality of life, medical, psychiatric, and social implications of a chronic pain syndrome
Clinical vignette

- 24 yo female, new patient to establish care
- Also seeking treatment of LLE pain and immobility, occurred after a major MVA ~8 months prior
- Pain in left foot and lower leg, burning. Pain worse with touch and weight bearing, unable to wear a shoe on that foot. Left ankle had become severely limited in motion with a left foot drop.
- MVA resulted in significant pelvic crush injury with surgical repair, increasing trouble with the left leg since then
- Only medication was Gabapentin 600 mg TID which helped some, did not resolve the pain.
Clinical vignette cont...

PMH: Obesity; OSA
PSH: T&A; Pelvic reconstruction surgery (ORIF)
Social history: <1 ppd cigarettes. No EtOH/illicit drug use. Recent move from out of state, now living with her mother. Recently ended an engagement. Currently unemployed; was an LPN prior to the MVA.
Family history: Mother with HTN.
ROS: Was completed, nothing further in addition to the presenting complaints.
Clinical vignette cont...

- Physical Exam:
  - VS: BMI 40.9  BP 134/85  T 97.9  F oral  P 89  O2 97%
  - GEN: young adult female, obese, appears stated age, NAD and pleasant
  - Heart and lungs unremarkable (rrr, no murmurs, CTAB)

- Remarkable MSK exam:
  - Left patellar reflex 1+/4. Unable to elicit Achilles reflex on the left. RLE reflexes 2+/4.
  - Strength of proximal BLE 5/5. Distal left leg and foot with contracture, purple discoloration, 1+ pedal pulse, allodynia, and cooler temperature in comparison to the right foot. Severely limited ROM left ankle with all directions (both active and passive), sustained in plantar flexion at ~180 degrees. Left foot drop.
  - No abnormalities of the upper extremities.
“Foot drop is a deceptively simple name for a potentially complex problem.” - Medscape
FOOT DROP: Involved structures

- **TIBIALIS ANTERIOR MUSCLE**

- Can also involve extensor hallucis longus, extensor digitorum longus
FOOT DROP: Pathophysiology

1. Compression $\rightarrow$ reversible ischemia with repositioning
   - Compression continues $\rightarrow$ demyelination starts to occur
   - Nerve conduction slows then is completely blocked
     $\rightarrow$ THIS IS WHEN SYMPTOMS OCCUR

2. Transection

3. Ischemia: vasculitis and atherosclerosis
   - Axonal injury pattern (no slowing of conduction)
     - Basement membrane remains intact: regrowth may occur if disease controlled

4. Radiation (can occur years later)

5. Inflammation (ex. Viral infection)

6. Degeneration (axonal polyneuropathies)
Foot Drop: DDX

Table 1 Causes of peroneal neuropathy

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1.</td>
<td>External compression (casts, immobilization)</td>
</tr>
<tr>
<td>2.</td>
<td>Direct trauma (fracture)</td>
</tr>
<tr>
<td>3.</td>
<td>Traction injuries (forcible ankle inversion)</td>
</tr>
<tr>
<td>4.</td>
<td>Masses (ganglion, tumor)</td>
</tr>
<tr>
<td>5.</td>
<td>Entrapment (fibular tunnel)</td>
</tr>
<tr>
<td>6.</td>
<td>Vascular conditions</td>
</tr>
<tr>
<td>7.</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>8.</td>
<td>Leprosy</td>
</tr>
<tr>
<td>9.</td>
<td>Idiopathic</td>
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</table>

Foot Drop: DDX cont...

- Central causes should also be considered:
  - 52-67% of pts with spinal UMN disease
  - 2 case studies:
    - One with thoracic stenosis
    - One with a brain tumor
  - Strokes (usually lacunar)

<table>
<thead>
<tr>
<th>Clinical</th>
<th>UMN</th>
<th>LMN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle tone</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Hyperreflexia</td>
<td>Hyporeflexia</td>
</tr>
<tr>
<td>Babinski sign</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>

UMN: upper motor neuron; LMN: lower motor neuron.
Foot Drop cont...

- L4-L5 radiculopathy is the most common cause

- **Areas of compression/trauma/traction:**
  - Most commonly: along fibular head
  - Popliteal fossa: Baker’s cyst
  - Ligamentous knee (ACL) injuries
  - Hip: sciatic nerve lateral fibers most susceptible to injury → forms common peroneal nerve at the knee
  - Ankle: tight shoes; ankle sprain or fracture tx
  - Tibial plateau fracture, total knee arthroplasty (rare), operative positionings
  - Weight loss association (ex. After bariatric surgery)
  - Osteoarthritis: nerve stretch or compression with varus knee deformity, osteophytes
Foot Drop cont...

- **Masses**
  - Consider intraneural ganglion cyst, schwannoma, neurofibroma, others
  - MC site in the PNS of an intraneural ganglion cyst is the Common Peroneal Nerve
  - Evaluate with plain films, MRI

- Ganglion cyst: benign, develop in areas of chronic local mechanical irritation, close to joints or tendons
Foot Drop cont...

- **Vascular conditions:**
  1. Immune-complex deposition: ex. Mixed cryoglobulinemia; polyarteritis nodosa
  2. Cell-mediated immunity: ex. ANCA-associated diseases
  - Not mutually exclusive
  - Vasa nervorum blood vessels become occluded/Ischemia
  - Neurologic vs Nonneurologic features
    - Mononeuritis multiplex, Polyneuropathy, Radiculopathy and/or plexopathy
      - **FOOT DROP is MC presentation of M.M.**
      - Fever, malaise, weight loss, other specific organ involvement
  - Typically vascular conditions that involve small-medium sized arteries and arterioles
    - Occurrence with pure small-vessel or large-vessel diseases should prompt reconsideration of the dx
Vasculitic neuropathy begins by involvement of both sensory (hashed areas) and motor nerve (black areas) distribution. As the process progresses (moving left to right on the figure), it becomes more confluent and symmetrical.

*Courtesy of John H Stone, MD, MPH.*
Foot Drop cont...

- Determining the underlying etiology is important for prognostication
  - Demyelination vs axonal loss
  - Determined with NCS
- **Demyelination:**
  - Conduction block with slowing across the lesion
  - Underlying axon is intact $\rightarrow$ remyelination can occur over several weeks
- **Axonal Loss:**
  - Needs regrowth of the terminal axon
  - Recovery over several months, with possibility of incomplete recovery
Foot Drop cont...

- EMG/NCS best choice
- Imaging – MRI usually best choice for neurologic imaging
- Serology – look at the clinical picture
  - Reasonable to check Hb/Hct (anemia), Chemistry panel (liver, renal), TSH
  - If suspect mononeuritis multiplex – multiple other studies warranted
  - ?Lyme - if endemic
- Unusual presentations – consider LP
- Nerve bx may help – usually not needed
Foot Drop cont...

- Complications if left untreated:
  - Equinovarus foot deformity
    - DAILY STRETCHES REQUIRED TO PREVENT CONTRACTURE
  - Loss of MSK function/ankle and foot starts to affect other areas in the patient’s life
    - Job, Recreation, Exercise, complications of limited mobility
Clinical vignette cont...

- **Hx of extensive LLE trauma**, this was the presumed cause of her symptoms based on the H&P.

- **Same day of initial visit**: plain film of the ankle, with follow up MRI, as well as referred for a NCS of the peroneal nerve/LLE. Past medical records requested.

- **Lab studies**:
  - CBC: WBC 12.2, Hb 15.6, Hct 45.4, Platelets 388, Neutrophil #7.5, Monocyte #1.1
  - CMP: Unremarkable
  - Lipids: TC 196, TG 207, HDL 46, LDL 109, VLDL 41
  - TSH: 6.67 (0.47 – 4.68)

- Continued current dose of Gabapentin pending further studies
<table>
<thead>
<tr>
<th>Time Frame after MVA</th>
<th>Study</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 months</td>
<td>Plain film left ankle (3 views)</td>
<td>Osteopenic changes, no other abnormality</td>
</tr>
<tr>
<td>5 months</td>
<td>EMG LLE</td>
<td>Severe sciatic mononeuropathy</td>
</tr>
<tr>
<td>6 months</td>
<td>MRI L-S spine</td>
<td>unremarkable for foraminal stenosis, foraminal compromise, or nerve abnormality of L1-S1</td>
</tr>
<tr>
<td>8 months</td>
<td>Plain film left ankle (3 views)</td>
<td>Severe osteoporosis; Moderate-size calcaneal spur at insertion of Achilles tendon</td>
</tr>
<tr>
<td>8 months</td>
<td>MRI left ankle/foot</td>
<td>Partial tear at Achilles tendon insertion (~50%) and measured 1.2 cm. Abnormal positioning of the foot d/t paralysis</td>
</tr>
<tr>
<td>8 months</td>
<td>EMG LLE</td>
<td>“Probable peroneal nerve injury (study terminated d/t pt. intolerance). Probable Reflex Sympathetic Dystrophy.”</td>
</tr>
</tbody>
</table>
Imaging: Ankle Plain Film
ER visit for uncontrolled and worsening pain (~9 months post-MVA)
- Left ankle 3 view: “Marked periarticular osteopenia consider reflex sympathetic dystrophy”
- Left knee 4 view: “Periarticular osteopenia consider reflex sympathetic dystrophy or osteoporosis from decreased usage”
- Lumbar spine 3 view: “Normal study” – hardware partially visible in left pelvis – recommended MRI if sx’s persist, which pt had already completed
- Pelvis 2 view: “No acute osseous abnormality”
- Pt. was instructed to f/u with her primary doctor
Imaging from ER visit
Clinical vignette cont...

- Subsequent Clinic Visits:
  - ~9 months: Starting having anxiety attacks; pain/neuropathy increasing
    - Had seen podiatry, who recommended pain management referral prior to surgical repair
    - Discussed CBT and started SNRI (venlafaxine XR) for both pain control and anxiety
  - ~10-11 months: Anxiety improved with SNRI, pain with mild improvement, requested a second opinion regarding LLE
    - Started physical therapy
    - Bone scan obtained
Clinical vignette cont...

- NM Bone Scan results
COMPLEX REGIONAL PAIN SYNDROME: What is it?

- Consensus Definition:
  - "CRPS describes an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings. The syndrome shows variable progression over time."

- 2 Subtypes:
  - CRPS Type 1: ~90%; no evidence of peripheral nerve injury
  - CRPS Type 2: evidence of peripheral nerve injury
CRPS: Pathophysiology

- Formerly called “Reflex Sympathetic Dystrophy”
- Characterized by:
  - “limb-confined sensory, autonomic, motor, skin, and bone changes”
- #1 symptom = Pain out of proportion/duration to the initial event

- Complete pathogenesis unknown – proposed mechanisms:
  - Inflammation (classic vs neurogenic)
  - Central sensitization
  - ? Role of sympathetic nervous system
CRPS Pathophys cont...

- Significant increases in proinflammatory cytokines
  - In tissues that are affected, plasma, and CSF
- Inflammatory mediators and pain-producing peptides released
  - Offers explanation for **allodynia** (normally painless stimulus produces significant pain)
- ? Catecholamine hypersensitivity and formation of a reflex arc
CRPS: Epidemiology

- F>M
- Inciting event in most cases: fractures, sprains, crush injuries, surgery
  - Up to 10% have no inciting event
CRPS: When to suspect dx

- Symptoms weeks after trauma
- Not explained by the inciting event
- Distal limb, extend beyond the trauma region, and not associated with a single nerve or root
CRPS: Clinical Presentation

- Budapest Consensus Criteria
  - For a clinical diagnosis:
    1. Continuing pain, which is disproportionate to any inciting event.
    2. At least 1 symptom in 3 of the 4 following categories:
       A. Sensory: Reports of hyperesthesia and/or allodynia
       B. Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
       C. Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry
       D. Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
CRPS: Criteria cont...

3. Must display at least 1 sign at time of evaluation in 2 or more of the following categories:

   **A. Sensory:** Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)

   **B. Vasomotor:** Evidence of temperature asymmetry (>1C) and/or skin color changes and/or asymmetry

   **C. Sudomotor/Edema:** Evidence of edema and/or sweating changes and/or sweating asymmetry

   **D. Motor/Trophic:** Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, skin, nail)

4. There is no other diagnosis that better explains the signs and symptoms
CRPS: Criteria cont...

- For research purposes:
  - At least 1 symptom in all 4 symptom categories
  - At least 1 sign (observed at evaluation) in two or more sign categories
  - Results in a sensitivity of 70% and specificity of 94%

Table 4
Summary of decision rules considered (modified from [12])

<table>
<thead>
<tr>
<th>Criteria/Decision Rules for Proposed Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>2+ sign categories &amp; 2+ symptom categories</td>
<td>0.94</td>
<td>0.36</td>
</tr>
<tr>
<td>2+ sign categories &amp; 3+ symptom categories</td>
<td>0.85</td>
<td>0.69</td>
</tr>
<tr>
<td>2+ sign categories &amp; 4 symptom categories</td>
<td>0.70</td>
<td>0.94</td>
</tr>
<tr>
<td>3+ sign categories &amp; 2+ symptom categories</td>
<td>0.76</td>
<td>0.81</td>
</tr>
<tr>
<td>3+ sign categories &amp; 3+ symptom categories</td>
<td>0.70</td>
<td>0.83</td>
</tr>
<tr>
<td>3+ sign categories &amp; 4 symptom categories</td>
<td>0.86</td>
<td>0.75</td>
</tr>
</tbody>
</table>

CRPS: Evaluation

- No “Gold Standard”
- Bone scintigraphy
- Plain films: patchy osteoporosis
- Autonomic testing (resting sweat output, resting skin temperature, quantitative sudomotor axon reflex test)
CRPS: DDX

1. Infection
2. Compartment syndrome
3. Peripheral arterial disease
   - RF include increasing age, diabetes, and smoking
   - Presents usually with claudication (reversible muscle ischemia)
4. DVT
5. Peripheral neuropathy
6. Inflammatory processes (ex. RA)
7. Raynaud phenomenon
8. Erythromelalgia
   - Repeat CBC with normal H/H
CRPS: Treatment Modalities

- Education, education, education
- “An ounce of prevention is worth a pound of cure”
  - Vitamin C supplementation following fracture or surgery
    - 500 mg for 50 days
  - Early mobilization
- Interdisciplinary approach

CRPS: Treatment cont...

- Goals of pain treatment: allow active participation, restore functionality
- NSAIDS
- Anticonvulsants
- TCAs; Antidepressants
- Bisphosphonates
- Topical lidocaine/capsaicin
- Calcitonin
- ? Glucocorticoids
- Use whatever works to control pain to restore functionality and ability to participate in physical therapy
CRPS: Treatment cont...

- Less-used drugs: alpha-adrenergics, ketamine, IVIG, opioids

- Interventional procedures:
  - Trigger point injections
  - Regional sympathetic nerve blocks
  - Spinal cord stimulation
  - Epidural clonidine
CRPS: Prognosis

- Recurrences can be triggered by: cold, a new trauma or surgery, or occur spontaneously
- Relatively uncertain prognosis: rates of recovery vary among the trials
  - Many patients will have prolonged symptoms with disability
Clinical vignette cont...

- Subsequent clinic visits:
  - ~12 months: Anxiety worsened (? Related to anniversary of MVA)
    - Increased venlafaxine dose
    - Discussed trying bisphosphonate therapy, started Vit C
  - ~13 months: IV zoledronic acid 5 mg
  - ~14 months: Pain significantly improved
    - Anxiety persisted, though mostly controlled
    - Limited in most activities – wanted to work, limited social circumstances
- Surgical solution of the foot/ankle at this time:
  - Percutaneous Achilles tendon lengthening (left); Flexor tenotomies 1-5 (left); MPJ arthroplasty (left first MPJ)
Tenets of Osteopathic Medicine

1. The body is a unit; the person is a unit of body, mind, and spirit.

2. The body is capable of self-regulation, self-healing, and health maintenance.

3. Structure and function are reciprocally related.

4. Rational treatment is based upon an understanding of the basic principles of body unity, self-regulation, and the interrelationship of structure and function.
Clinical vignette cont...

- Weight-bearing activities were slowly increased, pt. began to ambulate w/o assistance
- Pain increasing in left knee and hip with improved pain in left foot
  - went to urgent care for pain, with repeat knee imaging
  - Prescribed tramadol
Clinical vignette cont...

- Other modalities for pain control
  - Short term NSAIDs, Muscle relaxants, OMT, Physical therapy

- Other medical implications: obesity, HTN, HLD (metabolic syndrome)
  - BMI: 40.9 → 47.74
  - Weight 269 lb → 314 lb
  - Started on antihypertensives (BP 150s/92)
  - Repeat lipid panel: TC 196, TG 190, HDL 38, LDL 120, VLDL 38

- Anxiety and depression: effect on mind and spirit


