Complex Regional Pain Syndrome

Managing a poorly understood condition

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CRPS

- Hypersensitivity to touch
- Swelling
- Changes in skin temperature
- Changes in skin color
- Continuous burning or throbbing pain usually in hand or foot
- Changes in skin texture
- Changes in hair or nail growth
- Motor symptoms
- Abnormal sweating
History

- Ambroise Pare treated King Charles ix for smallpox by lance. Subsequently the King developed progressive atrophy and contracture of the limb.
History

• Described in Civil War after battlefield injuries
  • Trauma to limb, amputation, immobilization
  • Heart attack or stroke

Various names over the years:
• **Causalalgia**—Mitchell’s original term
• **Sudek’s atrophy**—1900. Sudek noted spotty osteopenia and suggested abnormal inflammatory response
• **RSD**—Coined in 1946 after work suggesting sympathetic dysfunction
• **CRPS**—IASP term defined in 1994
• Budapest Criteria—2007
CRPS

- CRPS I—most common (90%). Previously referred to as RSD

- CRPS II—Involves distinct nerve injury. Previously “causalgia”
CRPS Epidemiology

• Incidence 5-26:100,000
• Female to Male 3:1
• Peak incidence ages 35-50
• Major or minor injury
• Immobilization
• Described after MI, Stroke
• CRPS I>>>CRPS II

• 44% CRPS follows fracture
  • Radial, tibial, foot
• Upper extremity>Lower extremity
• CRPS II 1-5% after peripheral nerve injury
  • Barron 2005
Symptoms/Signs

• Hypersensitivity to touch
• Swelling
• Changes in skin temperature
• Changes in skin color
• Continuous burning or throbbing pain usually in hand or foot
• Changes in skin texture
• Changes in hair or nail growth
• Motor symptoms
• Abnormal sweating
**Table. Budapest Criteria for CRPS**

All of the following statements must be met:
- The patient has continuing pain that is disproportionate to any inciting event
- The patient has at least 1 sign in 2 or more of the categories below
- The patient reports at least 1 symptom in 3 or more of the categories below.
- No other diagnosis can better explain the signs and symptoms.

<table>
<thead>
<tr>
<th>No.</th>
<th>Category</th>
<th>Signs/Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sensory</td>
<td>Allodynia (pain to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement) and/or hyperalgesia (to pinprick)</td>
</tr>
<tr>
<td>2</td>
<td>Vasomotor</td>
<td>Temperature asymmetry and/or skin color changes and/or skin color asymmetry</td>
</tr>
<tr>
<td>3</td>
<td>Sudomotor/edema</td>
<td>Edema and/or sweating changes and/or sweating asymmetry</td>
</tr>
<tr>
<td>4</td>
<td>Motor/trophic</td>
<td>Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nail/skin)</td>
</tr>
</tbody>
</table>

Based on reference 3.
Allodynia

• Pain experienced with stimuli that are not usually painful
  • 70-80% of patients
Washington State L&I Diagnostic Criteria


- Positive bone scan can substitute for one as one of the positive physical exam findings
Evolution of CRPS over time

• Typically, CRPS I is subdivided into the following 3 phases:

  • Acute stage - Usually warm phase of 2-3 months
  • Dystrophic phase - Vasomotor instability for several months
  • Atrophic phase - Usually cold extremity with atrophic changes

• This classic description is highly variable. “spreading” CRPS debated. Contiguous, random and mirror image spreading described.
Differential Diagnosis

• Nerve injury
• DVT
• Occult fracture
• Arterial insufficiency
• Raynaud’s phenomenon
• Plexopathy
  • Pancoast tumor
• Acute neuropathy
• Infection
• Erythromelalgia
• Somatoform disorder
• Factitious disorder
Theories of pathophysiology in CRPS

- Sympathetic
- Neurological maladaption
- Inflammatory
- Behavioral
- Primary bone disease
Pathophysiology

• Autonomic dysregulation
• Distinct from autonomic dysreflexia
• Rationale for sympathetic blockade in CRPS
• Catecholamine levels lower in limbs with CRPS
Maladaptive Neuroplasticity

• Spinal—aka windup
  • Increased mRNA for alpha receptors in DRG following injury

• Brain—changes in cortical sensory areas and limbic areas
Pathophysiology

Aberrant inflammation
Neurogenic Inflammation

- Nervous system and immune system are interconnected
- Rapid behavioral response to injury
- Rapid immune response to injury
  - Chiu, Nature NS 2012
Antidromic Actions—wound healing and immune defense

- **CGRP**—vasodilation
- **SP**—Increases capillary permeability and recruits immune cells
- Denervation of joint attenuates synovitis in RA
- Sensory neurons implicated in allergic pulmonary dz, colitis, psoriasis
Diagnostic studies

• Blood tests—primarily to r/o alternative processes
• Xray—osteoporosis or periarticular bone loss
• Bone scan—specific pattern of periarticular uptake
• MRI—similar periarticular pattern of marrow changes
  MRI may have higher sensitivity but lower specificity than bone scan
Imaging studies
Prevention

- Early mobilization—reduced incidence of CRPS after stroke

- Vitamin C 500mg/day for 50 days
  - Reduced incidence of CRPS following radial, foot and ankle fx
    - Zollinger
      - RCT after wrist fracture Lancet 1999
      - RCT and dose response study JBJS 2007
Treatment of CRPS--Systematic Reviews


Treatment--corticosteroids

• Several low quality studies in 1970s and 1980s
• Suggest benefit within first 12 weeks of onset
• Unlikely benefit at later stages
Treatment

• **Calcitonin**
  - Goberlet Pain 1992

• **Bisphosphonates**
Treatment

- TCAs—no studies
- Opioids—no studies
- NSAIDs—no studies
- IV lidocaine—low quality studies
- Topical lidocaine—low quality studies
- Gabapentin—weak evidence for benefit
- Oral sympatholytics—case reports only
- Clonidine—weak evidence
Sympathetic blocks

• Up to 70% of patients report some immediate relief
• Systemic review: “literature inadequate to draw any conclusions”
IV Regional Blocks

- Guanethidine—7 trials showed little analgesia
- Bretylium—one trial suggested superiority to lidocaine
- Droperidol, reserpine, atropine—no clear benefit
IV infusions

Ketamine

--2004 Uncontrolled study-- 76% of 33 patients improved
   Correll GE. *Pain Med.* 2004 Sep. 5(3):263-75

--2009  60 patients five days IV ketamine v. placebo. No sustained difference in pain or improvements in function

--2009 RCT  10 days of iv ketamine vs. placebo showed improvement in pain parameters
Spinal Cord Stimulation

- Kemler — 36 patients comparative study. Described improvement in pain and economic benefits at 6 mo and 1 yr.
  - NEJM 2000

- 3 year retrospective study of two different types of SCS systems in 101 patients suggests that newer systems may offer more benefit.
  - Poree L, Krames E, Pope J, Deer TR, Levy R, Schultz L. Spinal cord stimulation as treatment for complex regional pain syndrome should be considered earlier than last resort therapy. Neuromodulation. 2013
Psychological Interventions

• Single blind study of CBT resulted in significant improvements in pain and function in both adults and children

• Graded exercise and exposure to movement therapy resulted in reduced pain and pain-related disability
Physical therapy

• Patients with better pain control and support are more likely to benefit from therapy
• Sustained attention to injured limb may be part of maladaptive process.
• Protocol involving mirror therapy, motor planning activities reduced disability in CRPS
Treatment Recommendations—L&I 2011

- Treatment should include elements of the following:
  - Physical therapy (PT) or occupational therapy (OT)
  - Medication for pain control
  - Psychological or psychiatric consultation and therapy
  - Sympathetic blocks
  - Multidisciplinary Program for Pain Management
2011 L&I Guideline

- The Department will not authorize the following interventions for CRPS:
- Sympathectomy -- no effect/no improvement in function
- Ketamine infusions -- no effect/no improvement in function, serious adverse events
Treatment Principles
WA LNI Guideline

1. Establish an early and accurate diagnosis
2. Exclude common masquerading conditions
3. Avoid over diagnosis
4. Evaluate whether patient is recovering normally
5. Refer to specialty care early if CRPS suspected or patient is not recovering normally.