Complex Regional Pain Syndrome

Complex regional pain syndrome is a chronic neuropathic pain syndrome characterized by spontaneous and evoked pain, with superimposed vasomotor, sudomotor, and trophic changes.

ANESTHETIC CONSIDERATIONS:

- Chronic pain syndrome with autonomic and trophic features
- Psychological factors
- Opioid addiction
- Multimodal management

ANESTHETIC GOALS:

- Optimize pain control
- Improve function and quality of life

HISTORY

- Initiating event (may be remote to onset of Sx)
  - Trauma (neuro or MSK) – crush, laceration, sprain, fracture, burns (?work-related), post-surgical
  - Neurologic insult – CVA, tumor, SCI, peripheral nerve injury
  - Other – MI, malignancy, Herpes zoster
- Clinical features (CRPS diagnosis requires ≥1 symptom in ≥3 categories AND ≥1 sign in ≥2 categories)
  - Sensory – spontaneous pain, stimulus-evoked pain (allodynia, mechanical hyperalgesia, thermal hyperalgesia, deep somatic hyperalgesia); quality of pain burning, crushing, stabbing; aggravated by any movement or pressure
  - Vasomotor – vasodilation, vasoconstriction, skin temperature asymmetry, skin color changes
  - Sudomotor – swelling, hyperhidrosis, hypohidrosis
  - Motor, trophic – motor weakness, tremor, dystonia, coordination deficits, nail/hair changes, skin atrophy, joint stiffness, soft tissue
- Severity and duration of symptoms
- Cognitive, behavioural, and affective components of the pain syndrome
  - Depression, anxiety, personality disorder, stressful life events
- Functional capacity
- Response to previous Tx
  - Identify opioid addiction/dependence
- Review of systems – must rule out dDx of CRPS
  - Local pathology (fracture, sprain)
  - Compartment syndrome
  - DVT
  - Cellulitis
  - Vasoocclusive disease – vasospasm, Raynaud's disease, thromboangiitis obliterans
  - Radicular pain syndrome
- PMHx, PSHx
  - ?Prior back surgery

PHYSICAL

- VS
- Derm
  - Changes in skin color and temperature, hyper/hypohidrosis, edema
  - Skin temperature difference (>0.6-0.8°C) during sympathetic stimulation (
  - Atrophy of skin (smooth, glossy), lack of hair, thick nails
- MSK
  - Weakness, tremor, dystonia
  - Joint pain and stiffness with ↓ROM
- CNS/PNS
  - Focal neurologic deficit in CRPS II

INVESTIGATIONS

Labs

- CBC including platelets, lytes, urea, Cr, INR, PTT

Imaging of affected extremity

- Radiograph (chronic stages) – patchy bone demineralization
- Bone scan (acute stages) – periarticular uptake
- MRI – nerve lesion in CRPS II

Other

- NCS – normal until late
- EMG – normal until late

OPTIMIZATION

- Consult multidisciplinary pain clinic

ANESTHETIC OPTIONS

- **For Tx of CRPS**
  - Sympathetic blocks – diagnostic/prognostic, neurolytic

- IVRA
- **For surgery unrelated to CRPS**
  - Local, regional, GA

ANESTHETIC SETUP

- **Drugs**
  - Standard emergency drugs
- **Equipment**
  - Standard CAS monitors
  - Resuscitation equipment available when placing blocks

MANAGEMENT OF ANESTHESIA

- **For treatment of CRPS**
  - Procedural sedation
- **For surgery unrelated to CRPS**
  - As required for procedure
  - Protect limb affected by CRPS – avoid iv, BP cuff

DISPOSITION & MONITORING

- Chronic pain service to follow on ward

COMPLICATIONS

- Infection
- Ulceration
- Chronic edema
- Dystonia
- Myoclonus

PATHOPHYSIOLOGY

- **Definitions**
  - **Allodynia**: Pain due to a stimulus which does not normally evoke pain.
  - **Hyperalgesia**: An increased response to a stimulus which *is* normally painful
  - **Hyperesthesia**: Increased sensitivity to stimulation, excluding special senses. Note that hyperesthesia includes both allodynia and hyperalgesia (but the most specific term should be used whenever applicable)
  - **Dysesthesia**: An unpleasant abnormal sensation, whether spontaneous or evoked (special cases include allodynia and hyperalgesia).
  - **Paresthesia**: An abnormal sensation, whether spontaneous or evoked. A paresthesia is not unpleasant (or else it would be a dysesthesia).
  - **Hyperpathia**: A painful syndrome characterized by an abnormally painful reaction to a stimulus, especially a repetitive stimulus, as well as an *increased* threshold. May occur with hyperesthesia, hyperalgesia and allodynia. (Note: I don't really see the difference between hyperalgesia and hyperpathia except that the stimulus seems to be *repetitive and the threshold is raised not lowered*).
  - **Neuralgia**: Pain in the distribution of a nerve or nerves.
  - **Neuropathy**: A disturbance of function or pathological change in a nerve: in one nerve, mononeuropathy; in several nerves, mononeuropathy multiplex; if diffuse and bilateral, polyneuropathy.

- **Epidemiology**
  - CRPS I – incidence 5.5 per 100,000 person-yrs at risk; prevalence 21 per 100,000
    - Occurs in 1-2% of fractures
  - CRPS II – incidence 0.8 per 100,000 per 100,000 person-yrs at risk; prevalence5 per 100,000
    - Occurs in 2-5% of peripheral nerve injuries
  - F: M = 2:1 – 4:1
- **Risk factors**
  - Female, work-related injury, trauma, surgery
  - Peak age at time of Dx 40-50y, peak incidence 61-70y
  - Nerve injury (for Type II)
- **Proposed mechanisms of CRPS**
  - Somatomotor changes likely generated by central changes in motoneuron activity – disturbed integration of visual and proprioceptive inputs in posterior parietal cortex
  - Immune cells (Langerhans cells) may stimulate inflammation and cytokine release (TNFa, IL-1, IL-6, IL-1B)
  - Postinfectious autoimmune mechanism (5%)
  - Sympathetically-maintained pain features – cutaneous nociceptors may develop catecholamine sensitivity after partial nerve lesions (although some CRPS patients have sympathetic-independent pain)
  - Injured afferent nociceptive and non-nociceptive neurons undergo sprouting, shrinkage, death, and up- or down-regulation of neurotransmitters, ion channels, and a-adrenoceptors
    - Coupling may occur b/w nociceptive and non-nociceptive afferent neurons
- **Classification** – CRPS I vs CRPS II
- CRPS type I
  - Asymmetrical distal extremity pain and edema *without* an overt nerve lesion; preceded by minor injury to extremity (most common), a CNS lesion (SCI, CVA) or cardiac ischemia
  - Burning spontaneous pain, aggravated by dependent position, movement, and joint pressure
    - Not related to individual nerve territory or site of inciting lesion
  - Autonomic changes – edema, changes in sweating (hyperhidrosis > hypohidrosis) and skin blood flow
    - Acute: affected limb warmer
    - Chronic: affected limb cooler (v/c induced by endothelial damage)

- Trophic changes (most prominent in chronic phase) – abnormal nail growth, or hair growth, fibrosis, thin glossy skin, osteoporosis, restricted ROM, weakness of all muscles of affected distal extremity, tremor, dystonia, neglect
- Subdivided into 3 stages
  - Stage 1 (acute) – extremity warm and erythematous; duration 2-3 mo
  - Stage 2 (dystrophic) – vasomotor instability; duration several mo
  - Stage 3 (atrophic) – cold extremity with pallor/cyanosis, atrophic changes

- CRPS type II
  - Similar characteristics as CRPS I, although with preceding peripheral nerve injury
    - Major nerve trunk injury involving rapid deformation of nerve (eg: GSW)
    - Subsequent focal deficits corresponding to nerve injury
  - Sx/signs spread are not necessarily limited to distribution of injured nerve; may spread beyond innervation of the injured peripheral nerve and often occur remote from site of injury
- **Clinical presentation**
  - Sensory, motor, sudomotor, vasomotor
  - Severity and duration of Sx exceed expected clinical course of inciting event
- **Diagnostic criteria**

General definition of the syndrome:
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

To make the *clinical* diagnosis, the following criteria must be met:
1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in *three of the four* following categories:
   Sensory: Reports of hyperesthesia and/or allodynia
   Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
   Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry
   Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Must display at least one sign **at time of evaluation** in *two or more* of the following categories:
   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)
   Vasomotor: Evidence of temperature asymmetry (>1°C) and/or skin color changes and/or asymmetry
   Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
   Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms

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- **Psychiatric comorbidities**
  - Depression, anxiety, personality disorders
  - Stressful life events in close relationship to onset of CRPS in 40%
- **Treatment options**
  - Physical therapy
    - Physiotherapy effective in reducing pain and improving mobility and function
  - Psychologic
    - Cognitive-behavioural therapy may be helpful in some patients
    - Tx of coexisting psychiatric conditions
  - Pharmacologic
    - NSAIDs – not studied in CRPS, may help control mild to moderate pain
    - Opioids – not studied in CRPS, beneficial in other neuropathic pain syndromes
    - TCAs, SSRIs – not studied in CRPS, beneficial in other neuropathic pain syndromes
    - Sodium-channel blockers – iv lidocaine effective analgesic in CRPS
    - GABA-agonists – baclofen intrathecal effective for dystonia in CRPS
    - Gabapentin – mild effect on pain, good effect on sensory deficits
    - Corticosteroids – improve entire clinical status in CRPS
    - NMDA antagonists – ketamine, memantine, dextromethorphan not studied in CRPS, beneficial in certain other neuropathic pain syndromes
    - Calcitonin intranasal effective analgesic in CRPS
    - Bisphosphonates – alendronate ↓s pain/swelling, improves ROM
    - Free-radical scavengers – DMSO, NAC effective analgesics; vitamin C?
    - Clonidine – transdermal effective for small areas of hyperalgesia
  - Interventional
    - Sympathetic blockade for acute phase (limited evidence; paravertebral ganglion block probably best); pain relief after block does *not* guarantee sympathetically-mediated component to pain
      - Stellate ganglion block
      - Celiac plexus block
      - Sympathetic paravertebral ganglion block; local anesthetic
      - IV regional anesthesia (IVRA) sympatholysis of extremity isolated with tourniquet (depletes NEpi in postganglionic axon); bretylium + lidocaine or ketorolac
    - Stimulation techniques (neuromodulation)

        - TENS may be effective in some cases
        - Epidural spinal cord stimulation – may relieve pain and allodynia in some patients
        - Other stimulation techniques (peripheral nerve electrodes, transcranial, magnetic stimulation, deep brain stimulation) – may be effective in some cases
    - Neuraxial techniques – epidural clonidine effective analgesic in CRPS although significant side-effects, intrathecal baclofen effective for dystonia
  - Surgery (neuroablation)
    - Sympatectomy – may provide only temporary relief, risk of post-sympathectomy neuralgia
    - Amputation – risk of phantom-limb pain
- **Approach to Tx**
  - Goals
    - Optimize pain control (necessary for all other interventions)
    - Restore full function of extremity
    - Improve quality of life
    - Treat comorbid psychologic factors
  - Medical therapy
    - First-line analgesics – opioids, TCA, antidepressants, gabapentin, carbamazepine
      - Consider corticosteroids if inflammatory signs/Sx
    - Perform sympatholytic procedure (preferably sympathetic ganglion block) to identify any component of sympathetically-maintained pain
      - If block ↓s pain, further options include intermittent regional sympathetic block, sympathetically active systemic drugs (eg: clonidine, prazosin), neurolytic treatment, or surgical sympathectomy
    - Calcium-regulating agents for refractory pain
    - Spinal cord stimulation and epidural clonidine for refractory pain
    - Intrathecal baclofen for refractory dystonia
  - Physical therapy
    - Progress from passive ROM → active isometrics → active isotonic training until full motor function achieved
  - Psychological therapy
    - To develop coping strategies and identify contributing factors

- **Prevention of recurrence**
  - To reduce risk of recurrent CRPS with surgery on affected extremity
    - IVRA with lidocaine + clonidine may reduce recurrence rate
- **Prognosis**
  - Variable duration; may persist for decades
  - In rare cases causal therapy (eg: decompression of nerve entrapment) may lead to complete recovery
  - Disease course determined by severity; not affected by etiology, age, gender, or affected side
  - Fractures associated with higher resolution rate than other causes
  - Unfavorable course and outcome may be predicted by low skin temperature at onset of disease
  - If syndrome longstanding (>2yrs), treatment results are uniformly poor

REFERENCES

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