A Complicated Case of CRPS after THA

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Terms

- These are older terms not felt to be an adequate representation of the full scope of the signs and symptoms
  - Reflex sympathetic dystrophy
  - Causalgia
- Complex Regional Pain Syndrome has been the preferred term since 1995 per IASP (International Association for the Study of Pain)

History

- Originally described in the American Civil war
- Reflex sympathetic dystrophy
  - based on the theory that sympathetic hyperactivity was involved in the pathophysiology
- Causalgia
  - Greek for heat and pain
Pathophysiology

- Reference:
  Anesthesiology: September 2010 - Volume 113 - Issue 3 - pp 713-725
  An Update on the Pathophysiology of Complex Regional Pain Syndrome
doi: 10.1097/ALN.0b013e3181e3db38

Pathophysiology

- Seems to be multifactorial, which may include: (poorly understood)
  - Altered cutaneous innervation after injury
  - Central sensitization
  - Peripheral sensitization
  - Altered sympathetic nervous system function
  - Circulating catecholamines
  - Inflammatory factors
  - Brain plasticity
  - Genetics
  - Psychologic Factors

Pathophysiology

- Sensory abnormalities
  - Numerous exist and are not limited to the pain area but may include the entire half of the body
  - Several hypothesis exist regarding the sympathetically mediated pain and describe both central and peripheral mediated components as well as a feedback loop involving primary afferent neuron, spinal cord neurons, sympathetic neurons, and a pathologic sympathetic coupling
Pathophysiology

- Altered cutaneous innervation after injury
  - Decrease in A and C fiber density
  - Abnormal innervation around hair follicles and sweat glands
- This occurs even in CRPS I where there are no clinical signs and symptoms of peripheral nerve damage

Pathophysiology

- Central Sensitization
  - Mediated by Substance P, Bradykinin, N-methyl-D-aspartic acid receptors
  - Results in hyperalgesia, allodynia and wind up
  - Wind up meaning that repetitive tactile stimulation may cause increasing pain, pain may continue after stimulation is stopped

Pathophysiology

- Peripheral sensitization
  - Tissue injury cause primary afferent fibers to release substance P and bradykinin that increase background firing of nociceptors, increase firing in response to nociceptive stimuli and decrease firing threshold of thermal and mechanical stimuli
  - Contributing to hyperalgesia and allodynia
Pathophysiology

- Sympathetic Nervous System (SNS) Dysfunction
  - Classic explanation of symptoms of CRPS
  - Excessive SNS outflow causing vasoconstriction resulting in cool, bluish limb (chronic CRPS)
  - This supports the rationale for using sympatholytic blocks

Pathophysiology

- SNS dysfunction:
  - It has been suggested that adrenergic receptors are expressed on nociceptive fibers
  - May contribute to sympotho-afferent coupling
  - Findings may indicate that sympotho-afferent coupling may contribute to CRPS pain and symptoms which may be linked to SNS activity in some cases

Pathophysiology

- While sympotho-afferent coupling is linked to SNS activity it does not imply that excessive SNS outflow is responsible
- Human studies do not support this common clinical assumption
### Pathophysiology

- **SNS dysfunction**
  - Studies have shown that there is SNS impairment
  - Reduced SNS flow would account for vasodilation (warm, red extremity) seen in early CRPS
  - CRPS patients have dysfunctional SNS thermoregulatory activity

- **Catecholamines**
  - Circulating catecholamines released by stress or by pain may lead to exaggerated sweating and vasoconstriction in the affected extremity

- **Inflammatory Factors**
  - Classic inflammatory mechanisms can contribute through actions of immune cells such as lymphocytes and mast cells, which, after tissue trauma, secrete proinflammatory cytokines including interleukin-1β, -2, -6, and tumor necrosis factor (TNF)-α. One effect of such substances is to increase plasma extravasation in tissue, thereby producing localized edema similar to that observed in CRPS.
Pathophysiology

- Brain Plasticity
  - Reorganization of the somatotopic maps
  - Reduction in size of the representation of the CRPS, affected limbs in the somatosensory cortex compared with the unaffected side
  - Return to normal after successful CRPS treatment
  - This could explain nondermatonal distribution of pain and sensory symptoms

Pathophysiology

- Genetics
  - Studies examining familial CRPS occurrence patterns indirectly support genetic contributions
- Psychogenic Factors
  - Life stressors/depression may exacerbate or make a patient more susceptible to CRPS
  - Though some patients without stressors/depression developed CRPS and some with stressors/depression did not

Incidence and Prevalence

- Two studies
- Population based
  - Olmsted County, MN
  - Netherlands
Incidence and Prevalence

- Sandroni (2003)
  - Mayo Clinic and Olmsted Medical group looked at all medical records with codes of Reflex Sympathetic Dystrophy (RSD), Complex Regional Pain Syndrome (CRPS) and compatible diagnosis 1989-1999
  - Each potential case then classified according to International Association for the Study of Pain (IASP) data

Incidence and Prevalence

- 389 charts reviewed
- 74 cases of CRPS identified
  - Most common trigger point sprain or fracture 46%
  - 74% of patients underwent resolution often spontaneously
    - This is controversial because 90% received PT and nearly half received sympathetic blocks and pharmacological intervention

Incidence and Prevalence

- Incidence 5.46/100,000 person years at risk
- Prevalence 2,057/100,000 person years
- Female : male ratio 4 : 1 with median age at 46 years at onset
- Upper limbs affected twice as commonly as lower limbs
<table>
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<th>Definition</th>
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<td>• <strong>Incidence proportion</strong> (also known as cumulative incidence) is the number of new cases within a specified time period divided by the size of the population initially at risk. For example, if a population initially contains 1,000 non-diseased persons and 28 develop a condition over two years of observation, the incidence proportion is 28 cases per 1,000 persons, i.e. 2.8%</td>
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<td>• de Mos (2007)</td>
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<td>• Source population comprised 190,902 persons from 46 practices</td>
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<td>• Potential cases were identified in Integrated Primary Care Information Project (IPCI) using a list of synonyms and abbreviations CRPS, Sudecks dystrophy, RSD, dystrophy, etc.</td>
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<td>• Each potential case was classified according to the IASP (very sensitive), the Bruehle criteria (highly specific) and the Veldman criteria (the only criteria, that theoretically allows a diagnosis of CRPS in the absence of pain)</td>
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<td>• 238 incident cases of CRPS could be identified</td>
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### Incidence and Prevalence

- **Incidence (in the Netherlands)**: 26.2 cases/100,000 years
- **Female : male ratio**: 3.4 : 1
- **Peak incidence at 61-70 years of age**
- **16.4% result of orthopedic surgery**
- **44% after fracture**

### Incidence and Prevalence

- **Incidence in de Mos study**: 4x higher than the Sandroni study
- **Difference in incidence**: most likely due to case definitions and validation
- **Mean age**: 52.7 years in the de Mos study and 46 years in the Sandroni study

### Incidence and Prevalence

- **Both studies show**:
  - Women more than men
  - Upper limbs more than lower
  - Fracture and sprains are the most precipitating events
Barriers in Identifying CRPS

- Some argue that CRPS I does not exist as a neuropathic pain disorder
- The more rare it is believed to be, the less likely it is to be considered a relevant diagnosis
- CRPS incidence is dependent on how it is diagnosed
- No Gold Standard for diagnosis

What does this mean for us?

- CRPS should be in the differential diagnosis when the patient is:
  - Female
  - Has had a fracture/sprain
  - 46-71 years of age
  - Meets IASP criteria

IASP Criteria for Diagnosing CRPS

- Develops after an initiating noxious event (type 1) or after nerve injury (type 2)
- Spontaneous pain or allodynia/hyperalgesia that is not limited to the territory of a single peripheral nerve and is disproportionate to the inciting event
Definitions

- Allodynia—"A nonpainful stimulus is felt as painful in spite of the tissues appearing normal; common in many neuropathic conditions."

- Hyperalgesia—"An increased response to a stimulus that is normally painful."


IASP Criteria for Diagnosing CRPS

- There is or has been evidence of edema, skin blood flow abnormality or abnormal sudomotor activity in the region of the pain since the inciting event

- This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction
Signs and Symptoms

- **Pain**
  - Severe, continuous burning, a deep ache or both without involvement of a major nerve
  - All tactile sensation may be painful (allodynia)
  - Repetitive tactile stimulation may cause increasing pain, pain may continue after stimulation is stopped
  - Point-tender spots
  - Spontaneous, sharp jabs of pain
  - Pain aggravated by use and relieved by immobilization

- **Edema**
  - Diffuse edema is pitting or hard
  - Localized to painful and tender region
  - If edema is sharply demarcated on the surface of the skin along a line, it is almost proof that the patient has CRPS
Diagnostic Workup

- Plain radiograph or bone scan
  - Advanced cases may show bone atrophy
- Sympathetic block may be diagnostic

Treatment

- Sympathetic block
  - Nerve block to the affected extremity
  - As soon as possible in the course of the disease
- Regional block
- Ketamine
  - NMDA receptor antagonist
  - Thought to suppress hyperalgesia and central sensitization

- Anticonvulsants
- Tricyclic antidepressants
  - Blocks norepinephrine
- Oral local anesthetic agent
- NSAIDs
  - Inflammatory pain
Treatment

- Opioids
- Spinal cord stimulation
  - Alters local neurochemistry in dorsal horn suppressing hyperexcitability of neurons

- Clonidine patch (or in epidural infusion)
  - Centrally-acting alpha₂-adrenergic
  - Thought to block the sympathetic nervous system
  - May produce analgesia for pain that may be a result of circulating catecholamines

- Physical therapy/Occupational therapy
  - Assist with gentle, normal movement of limb
  - Promote fine motor function
  - Aggressive therapy may aggravate
Duration

- Varies from weeks, months or years followed by exacerbations

Untreated CRPS

CRPS Case Study

First Admission

- 55 yoa
- Past Medical History
  - Sleep apnea
  - Diverticulitis
  - Bilateral knee scope
  - Right hip arthroscopy
  - Right trigger finger release
- Home medications – tylenol, Advil, Temazepam 15mg q hs pm, OTC probiotics

First Admission

- R THA for OA
  - Parathesias in R leg immediately post-op
- POD #1 R Sciatic nerve palsy
- POD #2 R leg weakness sciatic vs plexus palsy
Post-op

- Pain consult
  - Weak R quad
  - Poor pain control, 3-5/0-10 sitting, 20/0-10 with PT, “fireball of pain”/spasming/burning pain
- Neurology Consult
  - R leg weakness, probably nerve stretch injury
- POD #3 R foot drop noted

Post-op

- Oxycodone 10mg q 8 hours
  - Oxycodone 10mg q 3 hours prn mild breakthrough pain
  - Oxycodone 20mg q 3 hours prn mod-severe breakthrough pain
- Gabapentin 300mg q 8 hours
- Valium 5mg q 6 hours
- Give Oxycodone 10mg and valium 5mg at 0630 for premedication for PT

Neurology Consult Note

- ASSESSMENT: Right leg weakness. This localizes to either the plexus or the sciatic nerve, although his reflexes at the knee are depressed as well which would go against this.
Post-op Day #3

- Last 24 hours:
  - Valium 5mg PO q 6 hours (2 doses = 10mg)
  - Oxycodone 10mg PO q 3 hours (2 doses = 20mg)
  - Oxycodone 20mg PO q 3 hours (1 dose = 20mg)
  - Dilaudid 1mg IV q 3 hours (last 1000 on 9/2) = 2mg = 27mg PO oxycodone
  - Gabapentin 300mg tid
- Slept well
- Pain 2/0-10 at rest; 10/0-10 with PT
- Pt and wife express satisfaction with pain management regimen, APS signed off

2nd admission

- APS meds adjusted
  - Clonazepam 0.5mg QD and 1mg q hs
  - Benadryl 25mg qhs
  - Oxycontin 30mg q 12 hours
  - Dilaudid 2-4mg q 4 pm BTP
  - Celebrex
  - Toradol 30mg IV x1
  - APS signed off

Admission for Sciatic Pain
2nd Admission (3 weeks post-op)

- Meds adjusted by APS:
  - Oxycodone 10mg q 4 hours scheduled
  - Oxycodone 20mg q 4 hours pm BTP
  - Toradol 15mg IV pm
  - Gabapentin increased to 600mg tid
  - Restoril for sleep
2nd Admission

- Pt up walking, R foot with 2+ edema
- Ultrasound negative for DVT
- NIVA study—non-invasive vascular assessment, looks at blood vessels to determine if normal blood flow or DVTs are present, usually arms, legs and neck.
  - MRI of spine
- Neurology consult suspects neuropathic pain 2/2 sciatic neuropathy, suspects his depression (no h/o depression) is causing him to be intolerable to pain and does not feel his symptoms represent CRPS

2nd Admission

- APS re-consulted, APS saw patient and recruited an anesthesiologist to exam patient for suspected CRPS
- Diagnosis made for CRPS II
- L1-2 tunneled epidural placed
  - Ropiv 0.125% with 5mcg/ml hydromorphone
    - 8ml/hour, 5ml q 15minutes PCEA, 28ml 1 hour lockout

Medication Adjustments

- Added/Continued or Changed
  - Acetaminophin 1gm q 8
  - Celebrex 200mg BID
  - Clonazepam changed to 1mg BID
  - Clonidine 0.1mg patch q 7 days to R LE
  - Gabapentin 600mg TID
  - Hydromorphone IV 1mg q 3 hour pm BTP not relieved with epidural infusion
  - Nortriptyline 25mg q hs

- Discontinued
  - Oxycodone
  - PO Hydromorphone
  - Valium
Day 1 of epidural

Day #1 & 2 Epidural

- Pain improved
- PT for desensitization (touch therapy)
- Increased pain
- Pt refusing physical therapy
  - Re-education on utilizing PCEA and the importance of physical therapy

Day #3 & 4

- Increased pain, edema and allodynia overnight
- Catheter bolused with 0.5% bupivicaine
- Catheter bolused again
- Infusion changed to 0.125% bupivicaine
- Pain and vasomotor symptoms are very labile and difficult to control
Day 3 of Epidural

- Improving, less edema, foot veins more visible
- Plan for a slow wean of epidural
- Rate decreased to 8ml/h with 6ml q 15 minutes
- Pt with urinary catheter

Epidural Day 5

- Doing well, edema resolving, R foot color similar to L foot, veins clearly visible
- Pt tolerating slow wean of epidural
  - Down to 3ml/hour 6ml PCEA q 15 minutes, pt has not utilized PCEA
  - Possible d/c Tuesday

Day 6 through 9

- Doing well, edema resolving, R foot color similar to L foot, veins clearly visible
- Pt tolerating slow wean of epidural
Close but no Cigar

Day 10
- Alloydnic pain returned
- Foot mottled, edematous
- Catheter bolused with 3ml 1.5% lido/epi and 3ml of 0.5% bupivacaine
- Rate increased to 5ml/ hour
- Plan for d/c aborted

Day 11 of Epidural
- Nortripyline continued at 50mg qhs
- Considered switching to Desipramine or Amitriptyline 2/2 reports of bothersome dry mouth and needing to use his glasses more often
- Denied double vision
- It was felt that the side effects would not be any less on Amitriptyline or Desipramine

Day 11 of Epidural
- Very labile vasomotor function
- R foot can turn from blue to red to near normal in a short period of time
- Edema worsens in dependent position and improves with elevation
- Epidural site without problem
- Epidural rate decreased to 4/6/16
- No further wean plan
Disappointing

- Catheter connector became disconnected overnight but was repaired by on call anesthesiologist
- Connector became dislodged again in the morning, pt was without epidural infusion x several hours
- Full return of symptoms despite 15 days of epidural therapy and neuropathic medications
- Severe burning foot pain, edema and foot very mottled
- Catheter re-bolused with good control of symptoms
- Infusion between 8 and 6ml/hour for the next few days

Ketamine

- Day 17 - 21
  - 100mg of Ketamine over about an 1 hour
  - Premedicated with 2mg of versed, then 1mg q 5 minutes prn agitation
- Had anxiety, hallucinations and residual nightmares with Ketamine despite versed
- Last dose had to be aborted at the 50mg 2/2 to these side effects
Day 22 of epidural

- C/O of point tenderness at epidural site, lack of appetite and energy. Neck stiffness in the AM and achy joints
- Epidural d/c’d, tip sent for culture
- Methadone started 5mg bid
- UA negative
- Urinary catheter d/c’d
- Keflex 500mg QID had been started 3 days earlier as prophylaxis

Now What

- Plan for lumbar sympathetic block to bridge
- Spinal cord stimulator trial
- Day after the epidural was d/c’d, pt required a lumbar sympathetic block
- Tylenol/Percocet stopped 2/2 to jaundice
  - Acute Hepatitis panel negative
  - Negative for cirrhosis and fatty liver

Neurostimulator

- Neurostimulator placed at Good Samaritan
- Returned to Saint Joseph with 10/0-10 pain
- Can feel stimulator at times down to ankle but not toes
- Program adjusted by tech
- Pt c/o that the controller is too big
- 2 days later full return of admitting symptoms
  - Edema, pallor and coldness
- Neurostimulator d/c’d
- L3-4 epidural placed
2nd Epidural
- Infusion Bupivacaine 0.125%, 10mcg hydromorphone and 2mcg clonidine
- Up walking, no pain, able to urinate
- Increased sleepiness and feeling out of it
  - Methadone stopped
  - Clonidine patch stopped
  - Clonidine in epidural infusion decreased to 1mcg/ml

2nd Epidural
- Increase in pain 5/0-10 and could not participate in PT, catheter bolused by anesthesiologist with 0.25% bupivacaine
- Severe abd/flank pain, pt thought it was his diverticulitis
- Increased foot pain
  - Bolused attempted through catheter by the anesthesiologist, intense back pain, epidural catheter d/c'd
  - Urgent MRI of lumbar spine is negative

Next Couple of Days
Hospital time 6 weeks and 4 days
- Current medication regimen:
  - Clonidine patch 0.1mg
  - Gabapentin 900mg tid
  - Nortriptyline 50mg q hs
  - Oxycodone 10mg qhs pm (0)
  - Dilaudid PCA 0.2mg/h with 0.3mg q 8” (12mg)
  - Dilaudid 1mg IV q 1 hour pm (5mg)
Ketamine

- 150mg in procedure room
  - With anesthesiologists
  - With propofol and midazolam
- Dilaudid PCA basal rate stopped
- Dilaudid PCA (1.2mg last 24 hours)
  - Foot looks good, he looks better but reports feeling frazzled
- R Lumbar sympathetic block 20ml of 0.25% bupivicaine under floro
  - Pt is dramatically better, no foot edema, and only slight burning pain
  - No IV pain medications

D/C to Home!

- No pain, full ambulation, no edema, color normal
- D/C to home with PT
  - f/u with Ortho in 4-6 weeks
  - Lumbar sympathetic blocks prn
  - Medications
    - Clonazepam 1 tab bid
    - Gabapentin 900mg tid
    - Nortriptyline 50mg qhs
    - Temazepam 15mg q hs pm sleeplessness

Summary

- 1st epidural 22 days
- 2nd epidural 6 days
- 450mg of ketamine by APS
- 150mg of ketamine by Anesthesiologists
- 2 lumbar sympathetic block
- Medications (multimodal)
  - Acetaminophen 1gm q 8
  - Celebrex 200mg BID
  - Clonazepam to 1mg BID
  - Clonidine 0.1mg patch q 7 days to R LE
  - Gabapentin 900mg TID
  - Nortriptyline 50mg q hs
- Methadone trial
- Minimized opioids
D/C’d to home or was he?

- Message on pain cell phone
- Wife called complaining that no one was following up
- Explained that his primary care physician would manage his medications
- Any interventions would be done in the pain clinic with an appointment
- Primary MD wanted him to go to ED, pt refused
- Admitted to ED for slurred speech, blurry vision, can’t walk a straight line

ED

- In ED, full work up for CVA, which was negative
- Medications adjusted
  - Clonazepam stopped
  - Nortriptyline decreased to 25mg q hs
  - Gabapentin decreased to 600mg tid
- Pt d/c’d to home

ED

- Admitted again to ED for burning pain in toe and foot
- Foot looks great, even dependent there was only minimal edema and slightly flushed compared to L
- R lumbar sympathetic block
- Meds at this time:
  - Gabapentin 600 tid
  - Nortriptyline 25mg q hs
  - Lopressor
- Had an appointment at Rock Creek for lumbar sympathetic block
- Suggested next medication regimen: keep gabapentin at current dosing, stop nortriptyline, add topiramate
  - Weekly lumbar sympathetic block
How is he doing now?

- No opioids
- Acupuncture, chiropractic
- Medical marijuana, mostly at night
- Orthotic brace, states this has been the most helpful
- Can drive and walk but not for very long
- Not working

References

Reference