A Complicated Case of CRPS after THA

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History

- Originally described in the American Civil war
- Reflex sympathetic dystrophy
  - based on the theory that sympathetic hyperactivity was involved in the pathophysiology.
  - S/S remote from inciting injury
- Causalgia
  - developed after injury to a major peripheral nerve

Terms

- Complex Regional Pain Syndrome (CRPS has been the preferred term since 1995 per IASP (International Association for the Study of Pain)

- Divided into 2 categories

- CRPS type I (reflex sympathetic dystrophy) occurs after minor injuries or fractures of a limb

- CRPS type II (causalgia) develops after injury to a major peripheral nerve

Pathophysiology

- Multifactorial, which may include:
  - 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 feed back 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- repetitive tactile stimulation may cause increasing pain, pain may continue after stimulation is stopped (finger tapping affected area)

Pathophysiology

- Peripheral sensitization
  - Tissue injury cause primary afferent fibers to release substance P and bradykinin that increase background firing of nociocepters, 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 s/s 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:
  - Its 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 s/s which may be linked to SNS activity in some cases

Pathophysiology

- SNS dysfunction
  - While sympotho-afferent coupling is linked to SNS activity it does not imply that excessive SNS outflow is responsible

Pathophysiology

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

Pathophysiology

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

Pathophysiology

- 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. 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 nondermatomal distribution of pain and sensory symptoms

Pathophysiology

- Genetics
  - Studies examining familial CRPS occurrence patterns indirectly support genetic contributions

- Pyschogentic 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

- 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

- Incidence about 5.5/100,000 people in one year at risk
- Prevalence about 2.1/100,000 people in one year
- Prevalence about 4/100,000 people in one year for CRPS II
- Female : male ratio 4:1 with median age at 46 years at onset
- Upper limbs affected twice as commonly as lower limbs

Incidence and Prevalence

- de Mos (2007)
  - Source population comprised 190,902 persons from 46 practices
  - Potential cases were identified using a broader list of synonyms and abbreviations for CRPS
  - This study determined a higher rate of prevalence

Incidence and Prevalence

- Incidence (in the Netherlands) 26.2 cases/100,000 people in one year
- 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

- Women more than men
- Upper limbs more than lower
- Fracture and sprains are the most precipitating events
  - Right side 47%
  - Left side 51%
  - Bilateral 2%
  - Involving multiple extremities 7%

Original IASP Criteria for Diagnosing CRPS

- The presence of an initiating noxious event or a cause of immobilization.

- Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event.

- Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain.

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

Revised diagnostic Criteria for CRPS

1. Clinical pain which is disproportionate to the inciting event

2. Must report at least one symptom in 3 of 4 following categories:

1) **Sensory abnormalities**

Spontaneous pain

Mechanical hyperalgesia

Thermal hyperalgesia

Deep somatic hyperalgesia

2)**Vascular abnormalities Vasodilation**

Vasoconstriction

Skin temperature asymmetries

Skin color changes

3)**Sudomoter/Edema**

edema and/or sweating changes

and/or sweating asymmetry

Revised Diagnostic Criteria for CRPS

4)**Motor, trophic changes**

Motor weakness

Tremor

Dystonia

Coordination deficits

Nail, hair changes

Skin atrophy

Joint stiffness

Soft tissue

Revised Diagnostic Criteria for CRPS

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

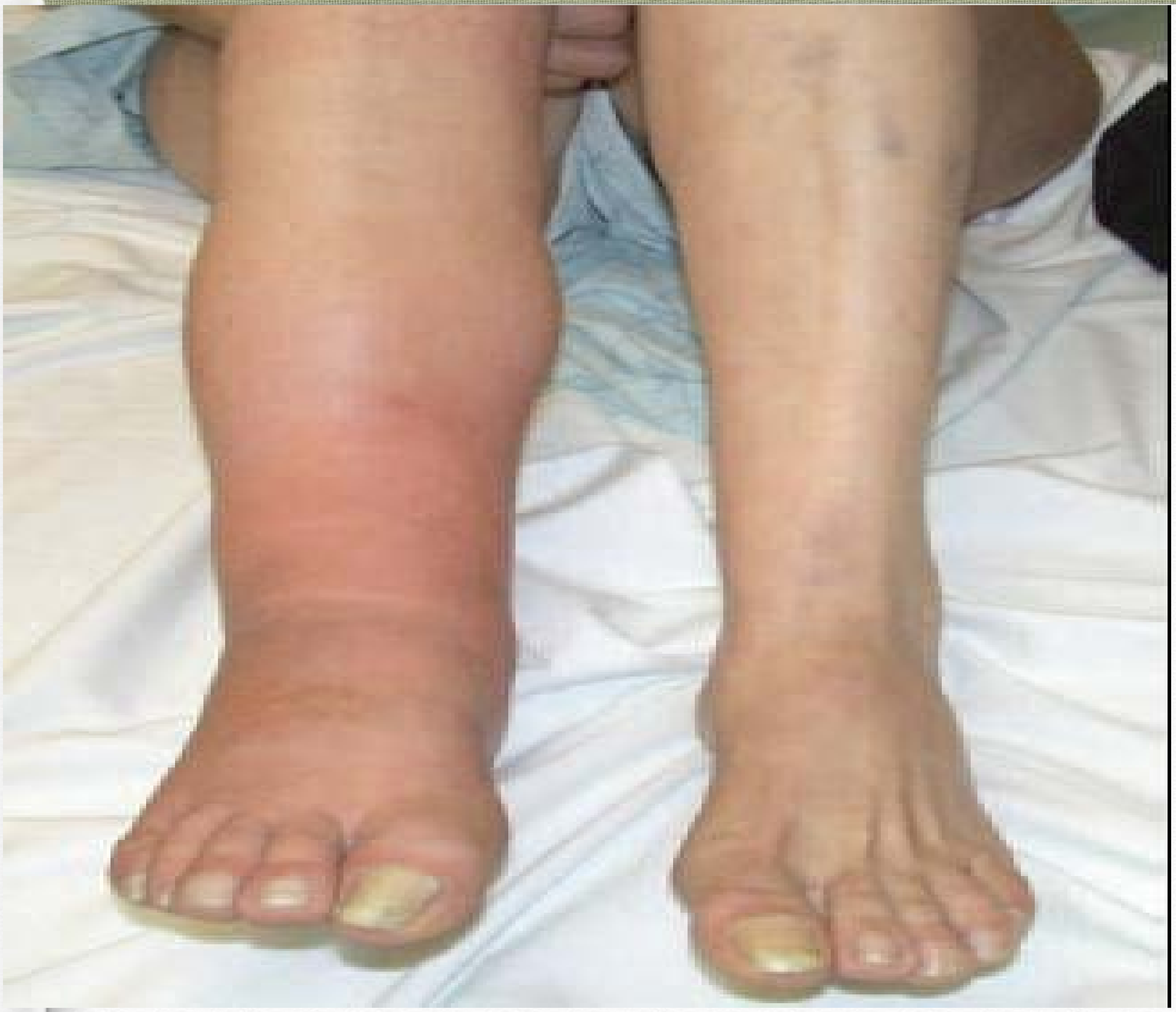
1) Sensory: evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)

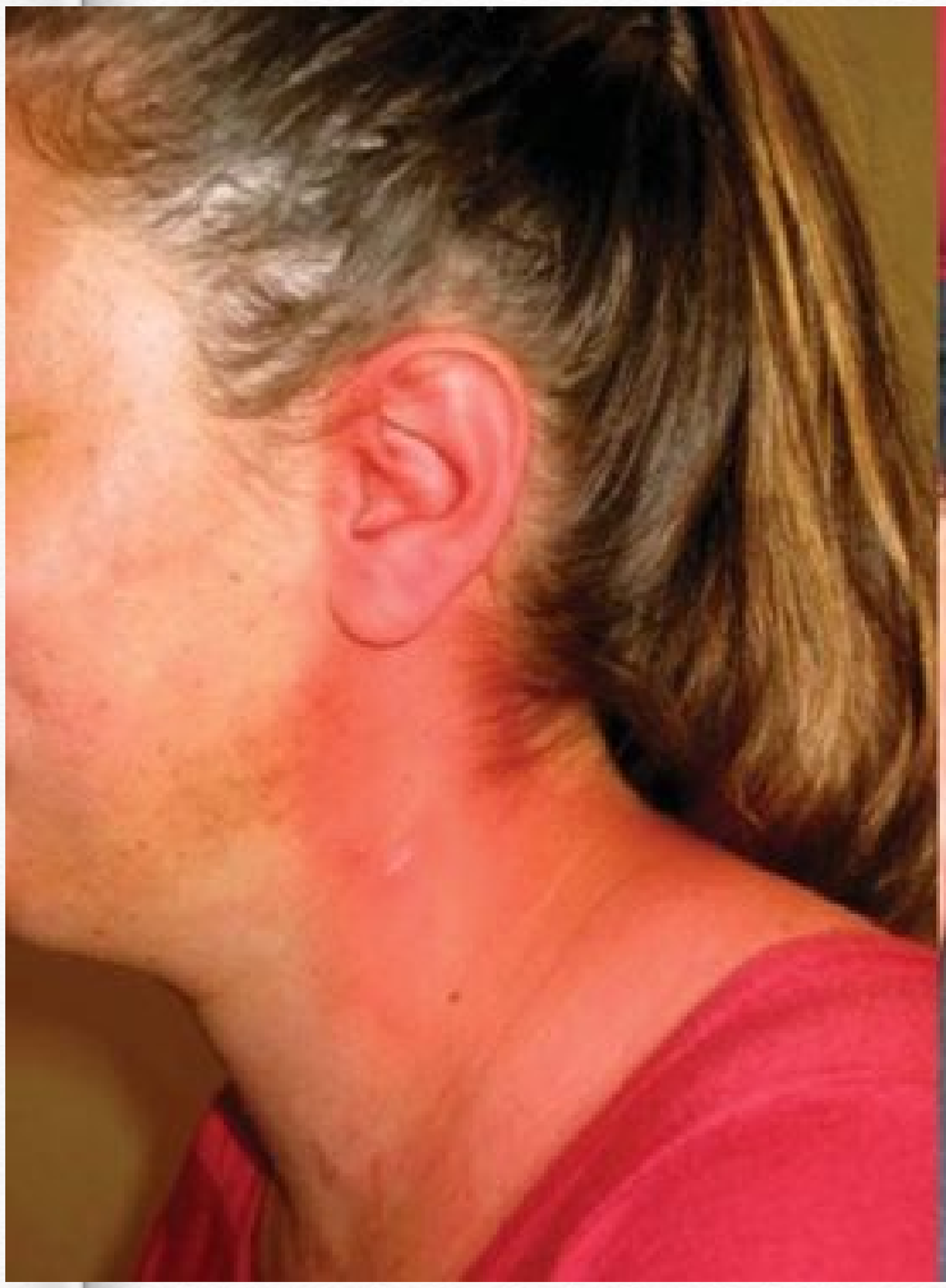
2) Vasomotor: evidence of temperature asymmetry and/or skin color changes and/or asymmetry

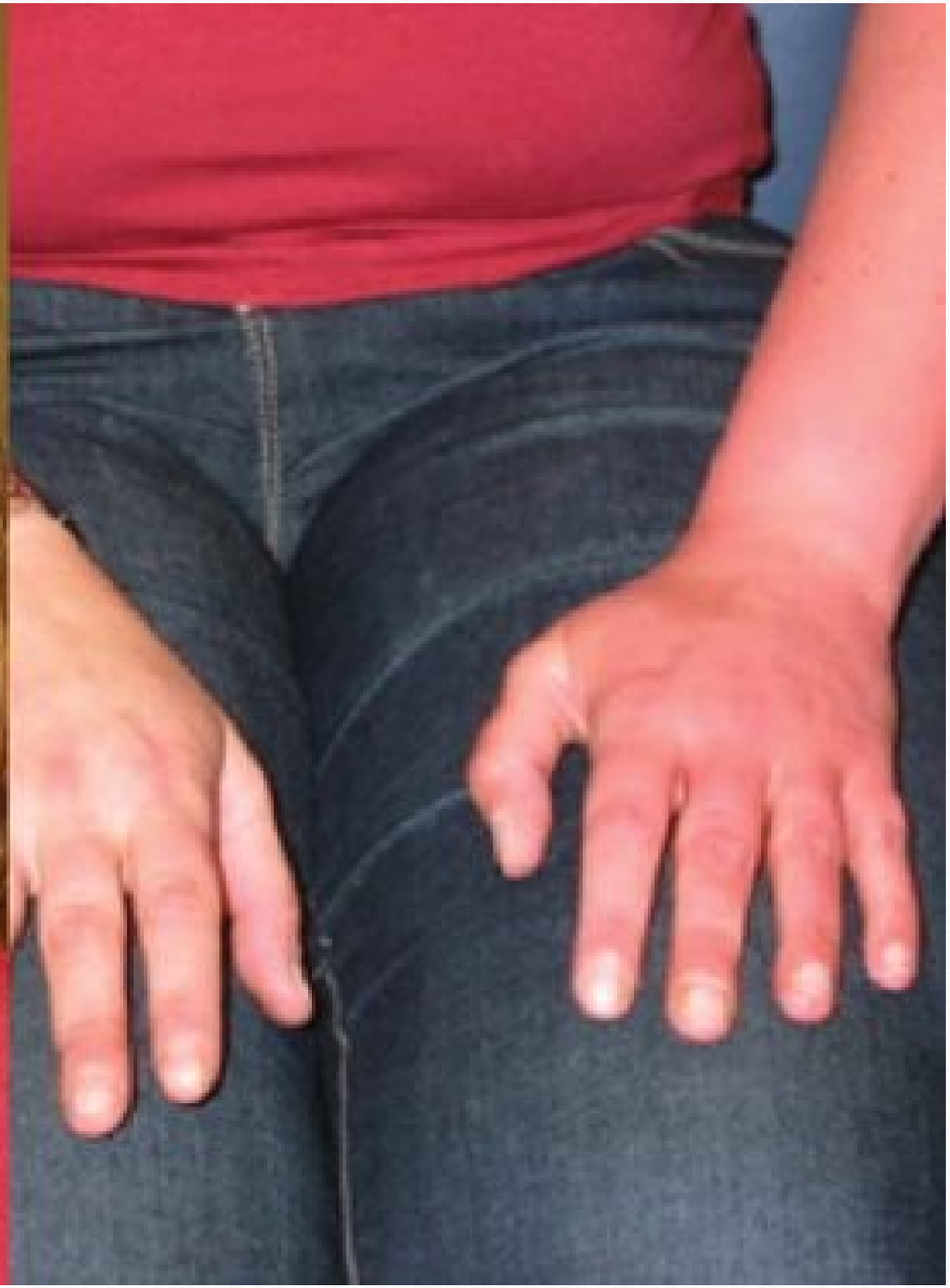
3) Sudomotor/edema: evidence of edema and/or sweating changes and/or sweating asymmetry

4) Motor/Trophic: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or tropic changes (hair, nail, skin)

4. There is no other diagnosis that better explains the signs and symptoms







Tests that aid in diagnosis

- Bone scintigraphy- looks for osseous changes common in CRPS
- Plain radiographs & MRI- looks for osseous changes. MRI has been proposed to be more reliable but has to prove their value in further studies
- Quantitative Sensory Testing (QST)- used to detect alterations in mechanical and thermal sensory presentation, not specific to CRPS
- Skin temperature measurements
- Skin biopsy- looking for changes in the innervation of the epidermis, dermis, including blood vessels, sweat glands and hair follicles

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
  - Spontaneous, sharp jabs of pain
  - Pain aggravated by use and relieved by immobilizationEdema
    - Diffuse edema is pitting or hard
    - Localized to painful and tender region
    - Edema

Treatment

- Early diagnosis and treatment
- Treatment should be focused on functional restoration
- Interdisciplinary pain management techniques emphasizing functional restoration
- Medications, injections, psychotherapy as needed to facilitate functional restoration and have a better change of full rehabilitation

Treatment

Reason for inability to begin or progress	Action
Mild-to-moderate pain	Simple analgesics and/or blocks
Excruciating, intractable pain	Opioids and/or blocks
Inflammation/swelling and edema	Steroids, systemic or targeted (acutely) or NSAIDs (chronically); immune modulators
Depression, anxiety, insomnia	Sedative, analgesic antidepressant/anxiolytics and/or psychotherapy
Significant allodynia/hyperalgesia	Anticonvulsants and/or other sodium channel blockers and/or NMDA receptor antagonists
Significant osteopenia, immobility, trophic changes	Calcitonin or bisphosphonates
Profound vasomotor disturbance	Calcium channel blockers, sympatholytics, and/or blocks

Treatment Interventional

- Sympathetic block
  - Nerve block to the affected extremity
  - As soon as possible in the course of the disease
- Regional block
- Epidural
- Spinal cord stimulation
  - Alters local neurochemistry in dorsal horn suppressing hyperexcitability of neurons

Treatment Medications

- Anticonvulsants
- Tricyclic antidepressants
  - Blocks norepinephrine
- NSAIDs
  - Inflammatory pain
- Opioid
- Clonidine
  - Centrally-acting alpha$_2$-adrenergic
- Infusions:
  - Ketamine
    - NMDA receptor antagonist
    - Thought to suppress hyperalgesia and central sensitization
  - Lidocaine
    - sodium channel blocker

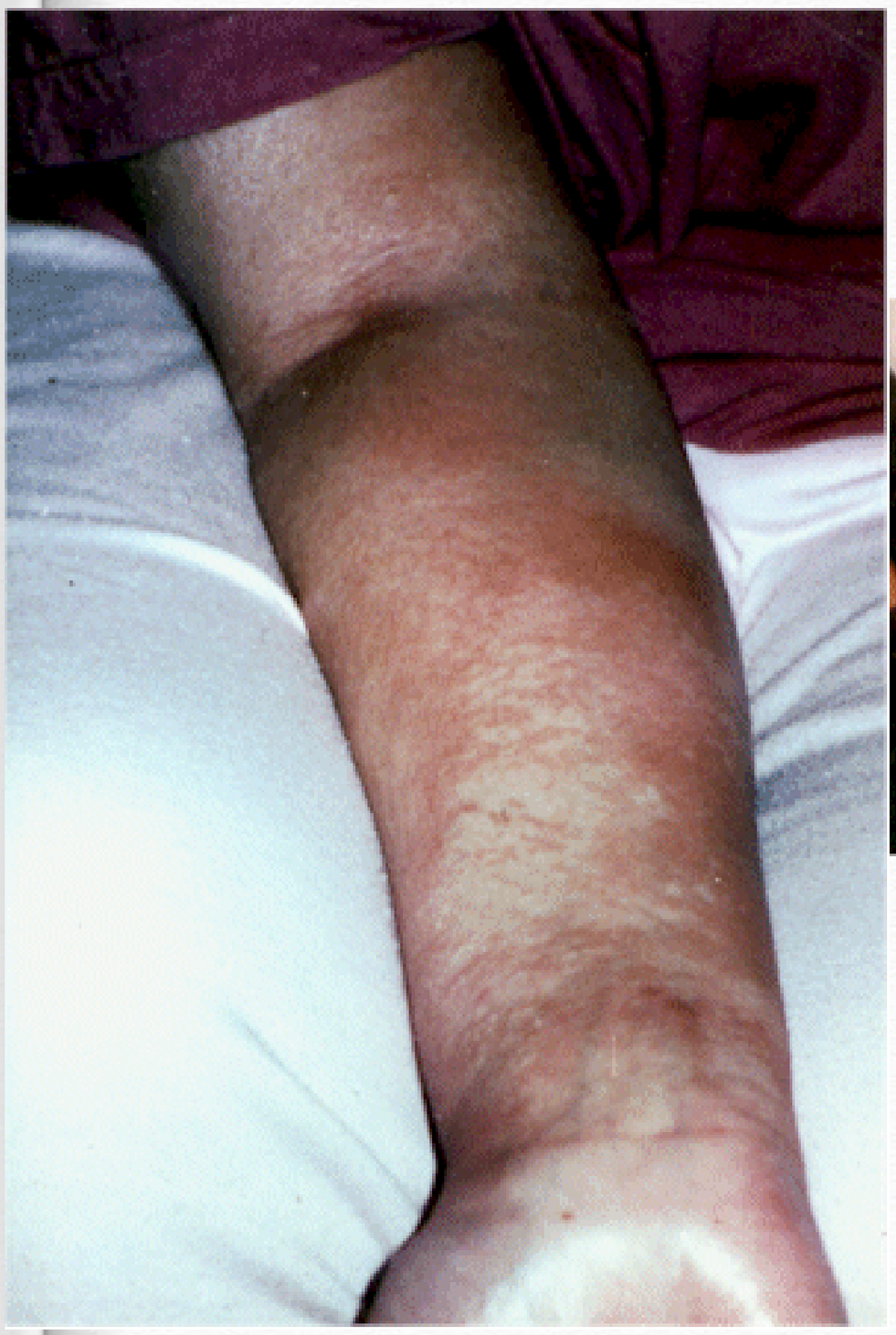
Treatment

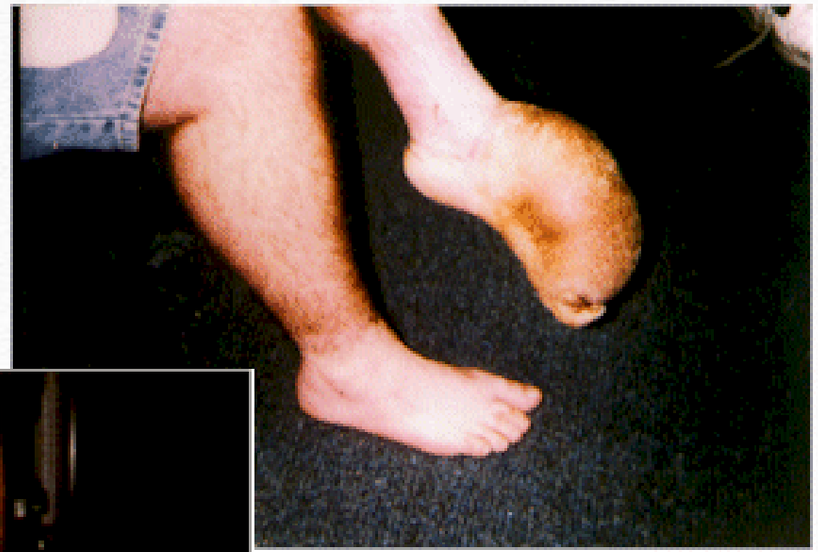
- Physical therapy/Occupational therapy
  - Assist with gentle, normal movement of limb
  - Promote fine motor function
  - Desensitization therapy
  - Aggressive therapy may aggravate
- Psychotherapy

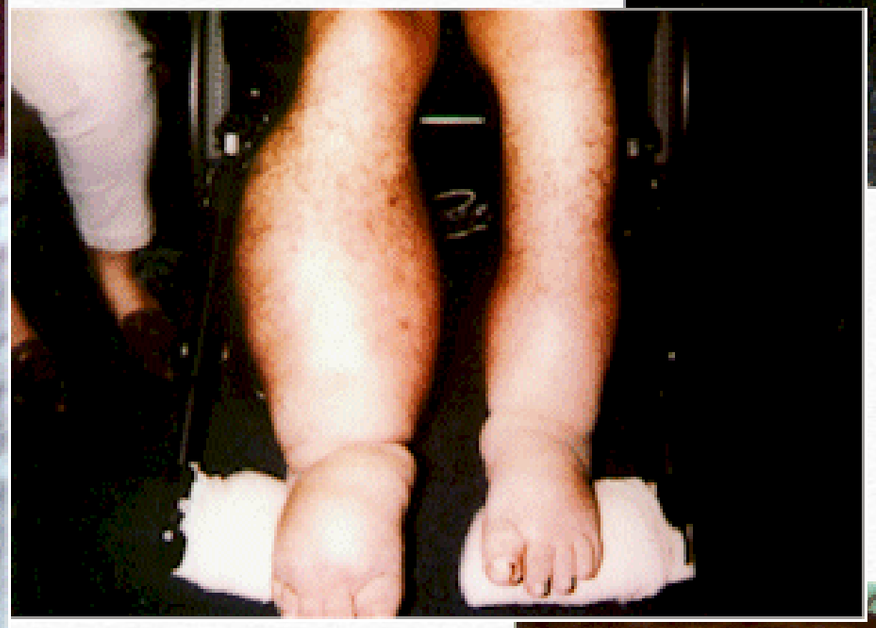
Duration

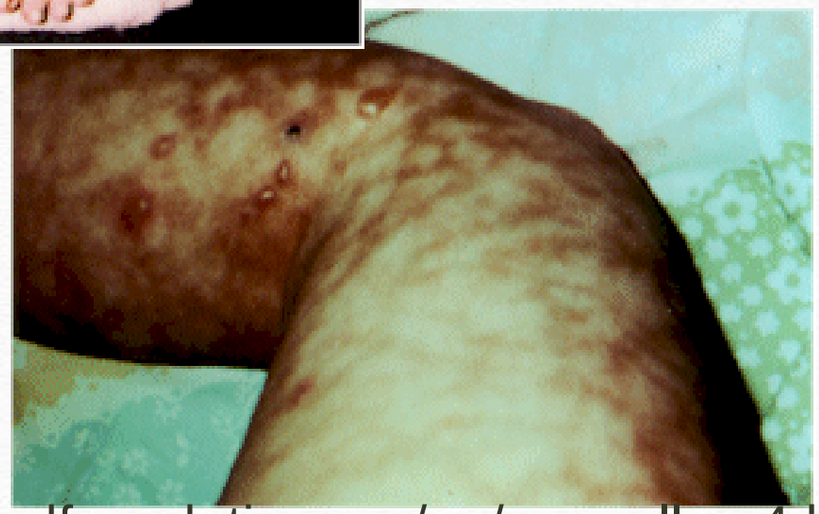
- Varies from weeks, months or years followed by exacerbations

Untreated CRPS









http://rsdfoundation.org/en/en_gallery4.html

Cast Study: First Admission

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

- Oxycontin 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 (2 doses = 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 prn 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 prn BTP
  - Toradol 15mg IV prn
  - Gabapentin increased to 600mg tid
  - Restoril for sleep

2nd Admission

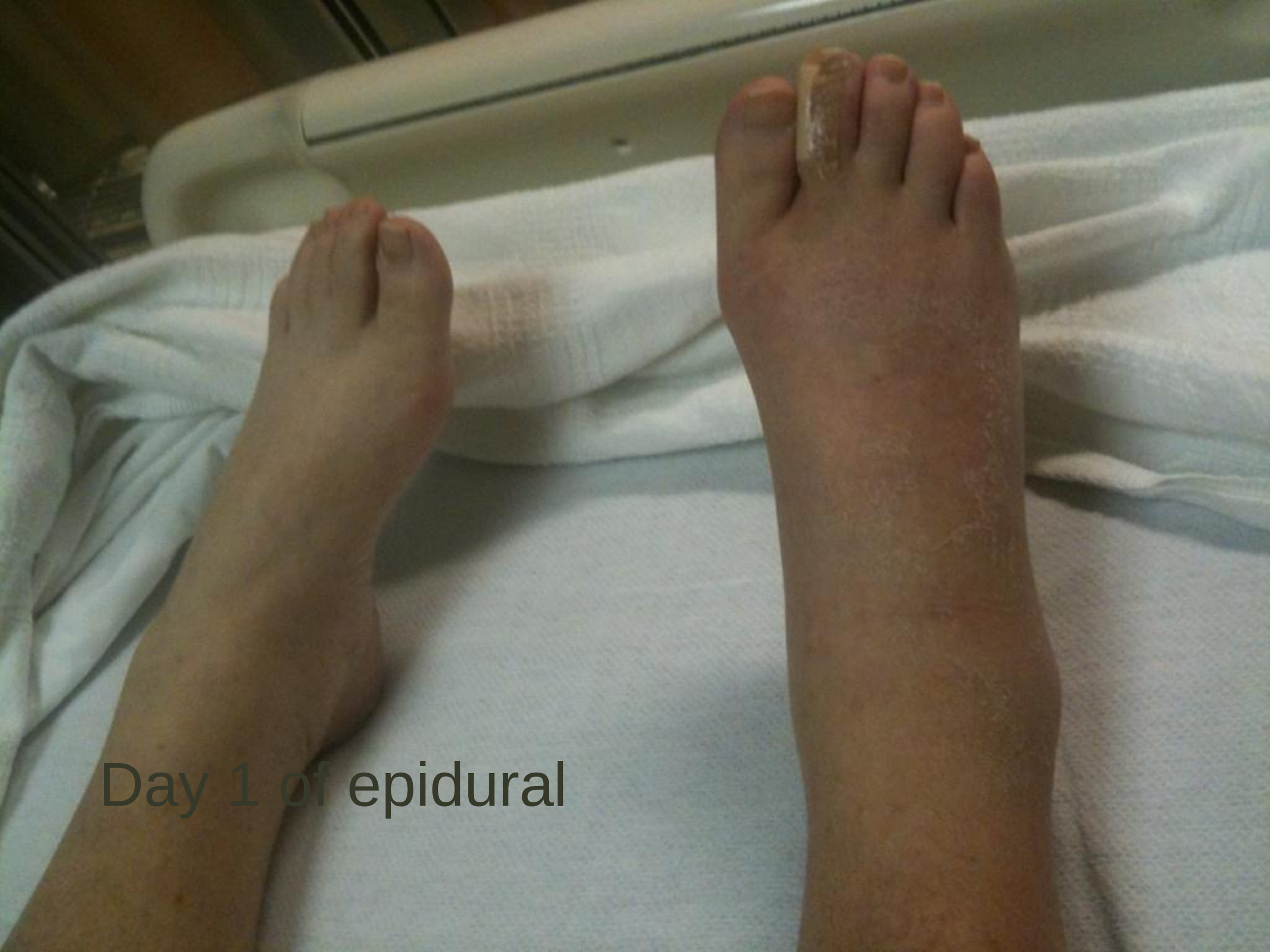
- Pt up walking, R foot with 2+ edema
- Ultrasound negative for DVT
- NIVA study negative– non-invasive vascular assessment, looks at blood vessels to determine if normal blood flow or DVTs are present, usually arms, legs and neck.
- MRI of spine
- Neurology consult suspects neuropathic pain 2/2 sciatic 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 boarded in pain management to exam patient for suspected CRPS
- Diagnosis made for CRPS II
- L1-2 tunneled epidural placed
  - Ropivacaine 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 q3 hour prn BTP not relieved with epidural infusion
  - Nortriptyline 25mg q hs
  - D/C'd oxycontin, hydromorphone and valium


Day 1 of epidural

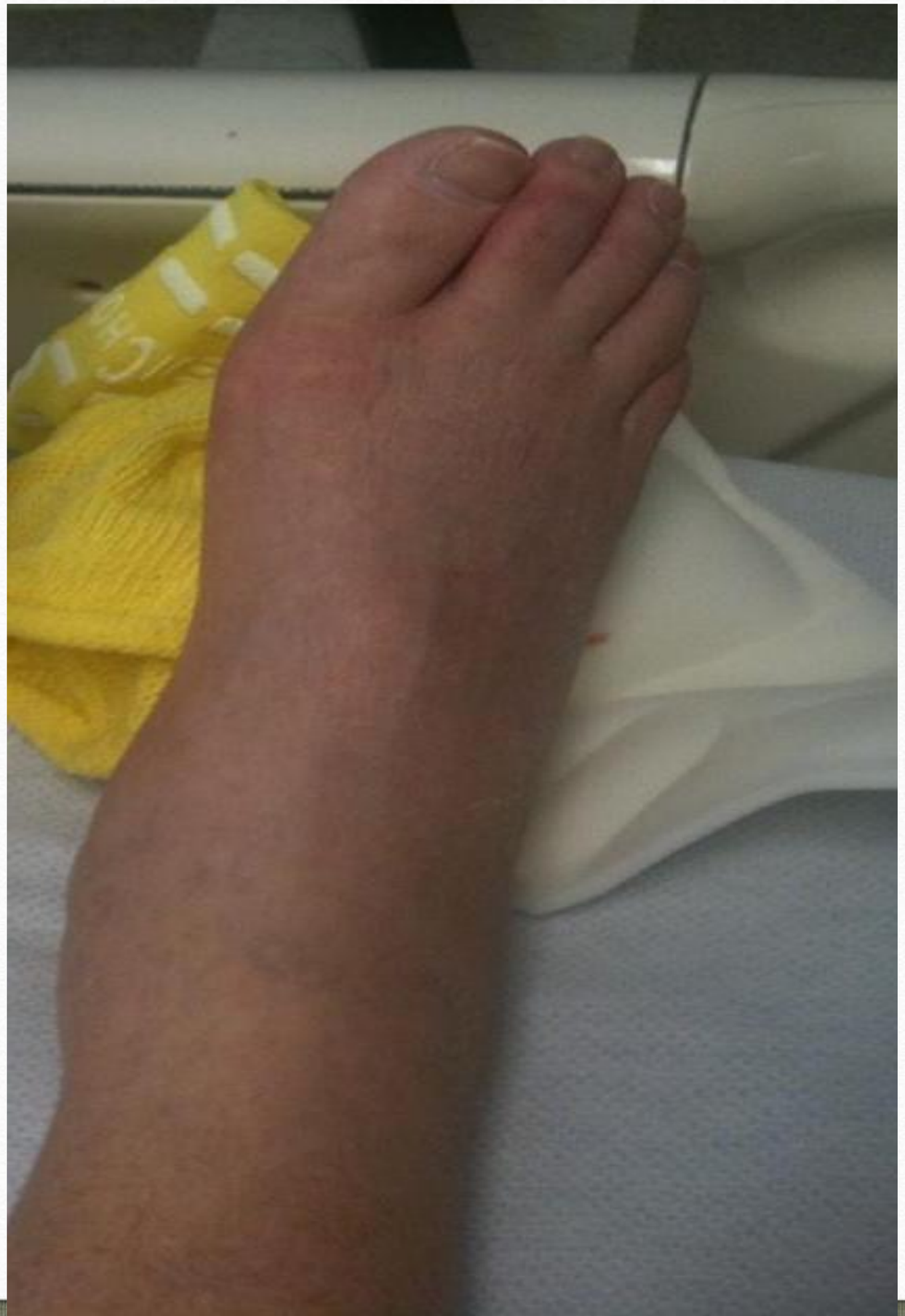
Day #1 & 2 Epidural

- Pain improved
- PT for desensitization (touch therapy)
- 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% bupivacaine
- Infusion changed to 0.125% bupivacaine
- Pain and vasomotor symptoms are very labile and difficult to control

Day 3 of Epidural



Epidural Day 5

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

Epidural

- Day 6 through 9
  - 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

Epidural continued

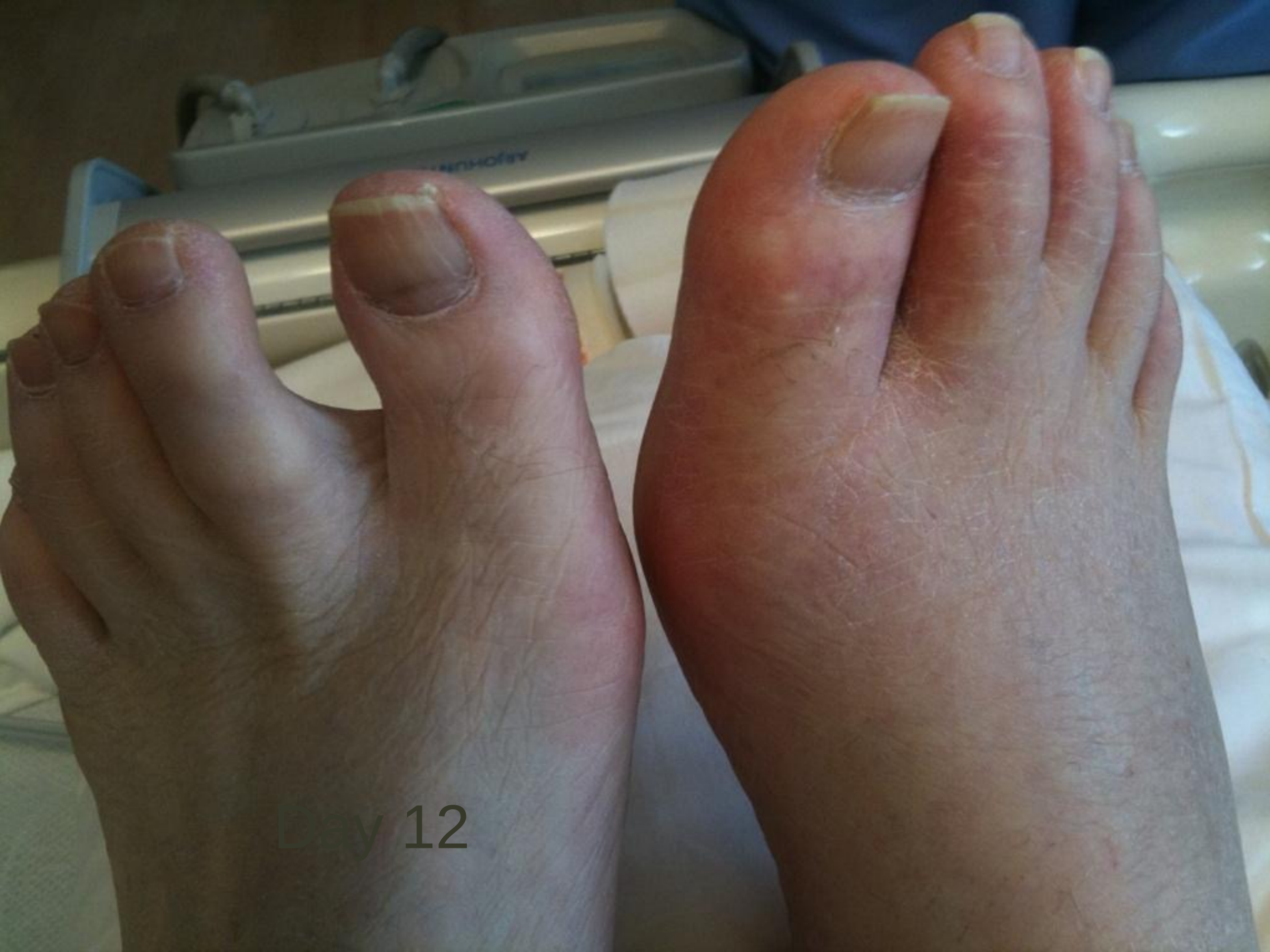
- Day 10
  - Alloydnic pain returned
  - Foot mottled, edematous
  - Catheter bolused with 3ml 1.5% lido/epi and 3ml of 0.5% bupivacaine
  - Rate increased to 5ml/ hour
- Plan for d/c aborted

Day 11 of Epidural

- Nortriptyline 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
- No further wean plan


Day 12

Epidural

- 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 prn (0)
  - Dilaudid PCA 0.2mg/h with 0.3mg q 8” (12mg)
  - Dilaudid 1mg IV q 1 hour prn (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% bupivacaine 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 prn sleeplessness

Summary

- 1st epidural 22 days
- 2nd epidural 6 days
- 450mg of ketamine by APS
- 150mg of ketamine by Anesthesiologists
- 2 lumbar sympathetic block
- Spinal cord stimulator
- Medications (multimodal)
  - Acetaminophin 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

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

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