Charcot Neuroarthropathy

Etiology

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Disclaimer

✓ No relevant financial relationships
✓ No conflicts of interest to disclose
Objectives

- Summarize and understand basic pathophysiology behind Charcot Neuroarthropathy (CN)

Definition

- Progressive, noninfectious, destructive inflammatory process of the foot and ankle (1)
- Jean-Martin Charcot
  - French Neurologist
  - Dr. Elliott has uncovered literature to dispute the original description
- Tabes Dorsalis (Tertiary syphilis)
- Long-standing diabetes (1)
Diabetes

- CDC 2017 Report:
  - 30.3 million Americans have diabetes (9.4%)
  - 70 million Americans are prediabetic

Advances in modern medical treatments → Prolonged lifespan → Diabetic-associated complications

Negative Impacts of CN

- Physical disability/limitations
- Financial burden
  - Individual
  - Health Care System
- Social stigma
Etiology

- Peripheral Neuropathy (PN)
  - Absence of protective sensation

Causes of PN

- **Diabetes**
- **Alcoholism**
- **Dietary (Vitamin deficiencies)**
- **Especially B1, B6, B12, E**
- **Infectious**
  - **Viral or Bacterial**
  - **Lyme disease, shingles, Epstein-Barr virus, hepatitis C, leprosy, syphilis, diphtheria, HIV**
- **Autoimmune**
  - **Sjogren's syndrome, lupus, rheumatoid arthritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, necrotizing vasculitis**
- **Hereditary**
  - **Charcot-Marie-Tooth disease**
- **Trauma**
  - **Motor vehicle accidents, falls or sports injuries**
  - **Iatrogenic (casts, OR positioning)**
- **Tumors**
  - **Benign or malignant**
  - **Can directly involve nerves or place pressure on nerves**
- **Other**
  - **Kidney disease, liver disease, connective tissue disorders and an underactive thyroid (hypothyroidism)**
- **Idiopathic**
How does Diabetes cause PN?

- Selectively damages cells whose glucose transport rate does not rapidly decline in response to hyperglycemia, leading to high glucose levels inside the cell (2)
  - Activates four major pathways
    - Polyol, Hexosamine, Protein Kinase C, Advanced Glycation End products (AGE)
    - Inhibits a key glycolytic enzyme
      - Glyceraldehyde-3 phosphate dehydrogenase (GAPDH)

Two Explanations for CN

- **Neurotraumatic**
  - Trauma in context of PN
    - Acute, subacute, cumulative/repetitive
    - Traumatic event activates a cascade of proinflammatory cytokines, TNF-α, interleukin-1β, interleukin-6 (3-5)
      - TNF-α upregulates the receptor activator of nuclear factor-κB (RANK) ligand, i.e. RANKL system
      - Intense osteoclast activity = excessive bone turnover
    - Decreased anti-inflammatory cytokines and antagonist to RANKL system – osteoprotegerin (3-5)
    - Bone breakdown ensues without regulation, leading to a collapse of the foot structure
Two Explanations for CN

- **Neurovascular**
  - Originally described by Jean-Martin Charcot (French Neurologist) in 1883
  - Hyperemia develops from overactive vaso-autonomic neuropathy (6)
  - Increased blood flow raises venous pressure and enhances fluid filtration through capillary leakage → Increased compartmental pressure and deep tissue ischemia → compromizes tendons and ligaments in the foot & ankle → joint instability → collapse (7)
  - Additionally, increased blood flow causes increased delivery of osteoclasts and monocytes resulting in greater bone resorption (8)
  - Patients with Charcot Foot demonstrate increased blood flow (macro) to the foot/ankle; patients with peripheral arterial disease (PAD) rarely develop Charcot neuroarthropathy (9-10)

Combination Theory

- CN is likely caused by a combination of both theories
- Continued weight-bearing without sufficient protection (guarding, offloading, activity restriction) leads to repetitive microtrauma and perpetuates increased proinflammatory cytokines, magnifying the intensity of a Charcot event, preventing proper bone remodeling and eventual loss of structural integrity of the bones & joints of the foot (i.e. fracture, subluxation/dislocation)
Charcot Foot

Ultimately...
References

Clinical Presentation and Classification of Charcot Neuroarthropathy

Andrew D. Elliott, DPM, JD
September 2018

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Charcot Neuroarthropathy:

- Originally described in 1703 by an English physician, Sir William Musgrave, secondary to a venereal disease.
- Jean-Martin Charcot, a French Neurologist, in 1868 described a neuroarthopathy in the foot related to Tabes Dorsalis (from neurosyphilis).
- Not until 1936 was the condition described in diabetics by Dr. William Rely Jordan.

Charcot Neuroarthropathy: Fun Facts

- Seen in patients with the following conditions:
  - Alcoholism
  - Leprosy
  - Tabes dorsalis
  - Myelomeningocele
  - Congenital insensitivity to pain
  - Solid Organ Transplant
  - Diabetic Neuropathy


CN within diabetics:
- Incidence: 0.1% - 5.0%
- Prevalence: 0.08% - 8.5%
- 29% of diabetics had radiographic changes consistent with CN
- 80% of cases occurring in patients with DM > 15 yrs
- Mean age of onset: 50.3 yrs
- Men = Women
- 5yr mortality: 28.3%


Type I
- Presents in the 50th decade (40s)
- 20-24yr ave duration with the disease

Type II
- Presents in the 60th decade (50s)
- 5-9yr ave duration with the disease


- Type I presents in the 50th decade (40s), 20-24yr ave duration with the disease.
- Type II presents in the 60th decade (50s), 5-9yr ave duration with the disease.

Charcot Neuroarthropathy (CN):
- Acute CN can look like lots of things...
- Gout
- Cellulitis/osteomyelitis
- Trauma
- Stress Fractures
- Deep Vein Thrombosis

Yes, but what does CN look like?

- Acute CN can look like lots of things...

- Gout
- Cellulitis/osteomyelitis
- Trauma
- Stress Fractures
- Deep Vein Thrombosis
Clinical Picture of Acute CN

Is it cellulitis? (Necrotizing fasciitis rarely)

What about trauma? (Didn’t Dr. Simonson say something about that?)

Very few remember an inciting event but of those that did there was a 5 week delay from trauma to presentation.


Clinical Picture of Chronic CN

Stable or Unstable deformities (luxation or dislocation at multiple joints of foot/ankle)


But is it painful? Maybe… 50% had pain on presentation


What about trauma? (Didn’t Dr. Simonson say something about that?)

Very few remember an inciting event but of those that did there was a 5 week delay from trauma to presentation.

Where does CN occur?

As Drs. Brodsky, Sanders and Frykberg taught us: the midfoot is the most common area for occurrence.

How to Classify CN?

Brodsky’s anatomic classification system can be useful to discuss treatment options; however, it doesn’t include any staging.

<table>
<thead>
<tr>
<th>Type</th>
<th>Location</th>
<th>Involved joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Midfoot</td>
<td>Tarsometatarsal, navicularcuneiform</td>
</tr>
<tr>
<td>2</td>
<td>Hindfoot</td>
<td>Subtalar, talonavicular, calcaneocuboid</td>
</tr>
<tr>
<td>3A</td>
<td>Ankle</td>
<td>Tibiotalar</td>
</tr>
<tr>
<td>3B</td>
<td>Calcaneus</td>
<td>Tuberosity fracture</td>
</tr>
<tr>
<td>4</td>
<td>Multiple regions</td>
<td>Sequential, concurrent</td>
</tr>
<tr>
<td>5</td>
<td>Forefoot</td>
<td>Metatarsophalangeal</td>
</tr>
</tbody>
</table>
However...

<table>
<thead>
<tr>
<th>Stage</th>
<th>Radiographic findings</th>
<th>Clinical findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (normal)</td>
<td>Normal radiographs</td>
<td>Swelling, erythema, warmth</td>
<td>Plantar abrasion, serial radiographs to monitor progression</td>
</tr>
<tr>
<td>I (acute)</td>
<td>Absence of warm, decreased erythema and warmth</td>
<td>Absence of warm, absence of swelling</td>
<td>Plantigrade foot: custom inlay shoes with rigid shank and rocker bottom sole</td>
</tr>
<tr>
<td>II (reduction)</td>
<td>Consolidation of deformity, joint arthrosis, fibrous ankyloses, rounding and smoothing of bone fragments</td>
<td>Absence of warm, absence of swelling, absence of erythema, stable joint ± fixed deformity</td>
<td>Nonplantigrade foot or ulceration: debridement, exostectomy, deformity correction, or fusion with internal fixation</td>
</tr>
<tr>
<td>III (reconstruction)</td>
<td>Absence of warm, absence of swelling, absence of erythema, stable joint ± fixed deformity</td>
<td>Plantigrade foot: custom inlay shoes with rigid shank and rocker bottom sole. Nonplantigrade foot or ulceration: debridement, exostectomy, deformity correction, or fusion with internal fixation</td>
<td></td>
</tr>
</tbody>
</table>

Because it ignores the most clinically relevant stage, in 1990, Shibata et al. proposed a stage 0 based primarily on clinical and scintigraphic signs without obvious radiographic findings.


Let's try MRI...

Chantelau and Richters' MRI based system can be used for diagnosis, initiation and duration of treatment.

Immediate offloading and immobilization in the acute phase of CN resolves the inflammation and stops the acute bone and joint damage thus preventing full blown arthropathy.

Schon Midfoot Classification

Severity of Deformity based on lateral X-rays

A: Mild: collapse not to level of the plantar surface
B: Moderate: collapse to the level of the plantar surface
C: Severe: collapsed beneath the level of the plantar foot (Rocker Bottom)


Medial Column Classification

Sella and Barrette's system is based on x-rays, clinical findings and bone scans:
- Stage 0 Localized heat and swelling; x-ray normal
- Stage 1 Stage early bone involvement on radiographs
- Stage 2 Joint subluxation
- Stage 3 Joint dislocation and collapse
- Stage 4 Healing and sclerosis

Rogers and Bevilacqua considered the complications associated with CN which may be prognostic for amputations. Used clinical judgement although at the time was a best guess.


In Conclusion

- If you have a red, hot swollen foot in a long standing diabetic no obvious explanation, get an MRI

- Eichenholtz is still a fairly common staging system

- Other newer staging systems are also in use that provide better, more predictive information
THANK YOU

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Charcot Neuroarthropathy

IMAGING

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SEPTEMBER 2018

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Objectives

- Summarize and understand imaging considerations for Charcot Neuroarthropathy (CN)

Diagnosis

- Diagnosis of CN is primarily clinical (1-3)
- A clinical suspicion for acute CN should be followed by ordering appropriate diagnostic imaging
- Provides details to establish a definitive diagnosis and guide treatment
Venous Duplex Ultrasonography

- Performed when deep vein thrombosis (DVT) is suspected
- Results should be normal in acute CN (4)
- DVT
  - Unilateral edema, erythema, calor and pain

Plain Radiographs (X-rays)

- Initial imaging of choice
- Weightbearing (WB)
  - Unless patient is not able to stand
  - Better assess for subtle joint abnormalities
- Bilateral feet
  - Unless patient only has one foot
  - Allows comparison with unaffected side
- Accuracy of differentiating osteomyelitis from Charcot is only about 50-60% (1)
- Findings may be absent/negative within first 2-3 weeks of acute event (1,2) or even longer (4)
Plain Radiographs (X-rays)

Stable findings

Loss of joint congruency
Plain Radiographs (X-rays)

Stable joints

Loss of joint congruency

Plain Radiographs (X-rays)

WT BEARING
Plain Radiographs (X-rays)

- Findings most accurate:
  - Demineralization
  - Periosteal reaction
  - Cortical destruction
- Useful in ruling out other pathology (fractures, arthritis, etc.)
- Serve as a baseline for future studies, especially in at risk patients

Computed tomography (CT)

- More sensitive than plain film radiographs
- With contrast, can aid in detecting abscess formation
- Cannot determine early bone marrow edema or microfractures
  - Found in the acute phase of CN
  - Therefore is not recommended for diagnosis (2,3)
Nuclear Imaging

- Well established for detecting bone infections
- Can seem complicated if you don’t order these scans with regularity
- 3-phase bone scintigraphy (1)
  - Highly sensitive for osteomyelitis (80-100%)
  - Not specific
  - Trauma, arthritis, recent surgery or CN will result in high uptake
  - Negative bone scan excludes only infection

Nuclear Imaging

- Labeled leukocyte scans have better specificity than 3-phase alone (1-3)
  - $^{99}$Technetium methylene diphosphonate ($^{99}$Tc MDP) labels hydroxyapatite, which is used to measure bone turnover
    - Bone turnover is high in Charcot, trauma and infection, so this scan alone cannot differentiate between Charcot and infection
Nuclear Imaging

- Labeled leukocyte scans have better specificity than 3-phase alone (1-3)
  - $^{111}$Indium labeled leukocytes localize in neutrophil-mediated inflammatory processes, such as bacterial infections in bone – should not appear in the absence of infection (1-3)
  - $^{99}$Tc MDP & $^{111}$Indium in combination for the diagnosis of osteomyelitis (1)
    - 50% sensitive
    - 100% specific
    - 81% accurate

Nuclear Imaging

- Labeled leukocyte scans have better specificity than 3-phase alone (1-3)
  - $^{99}$Tc sulfa colloid scans image areas of reticuloendothelial cells, found in the liver, spleen and bone marrow
    - Known as “bone marrow imaging”
    - No uptake in areas of bone infection
  - Using $^{99}$Tc sulfa colloid & $^{111}$Indium together can improve the accuracy in differentiating between infection and inflammation seen in acute Charcot (1-3)
Magnetic resonance imaging (MRI)

- Generally supported as superior to nuclear imaging tests in aiding diagnosis (1)
- Can effectively detect soft tissue edema, joint effusion and bone marrow changes in the early/acute phase
  - Detects abnormalities earlier than plain film radiographs

- Helpful in ruling out abscess, sinus tracts and osteomyelitis
  - Osteomyelitis - focal involvement of a single bone or joint
  - Charcot arthropathy - involves several joints/bones (1,5)
- More sensitive, but less specific than combined $^{99}$Tc SC & $^{111}$Indium bone scan (2)
- Limitations
  - Recent surgery
  - Retained hardware
  - Pacemaker, aneurysm clips or renal insufficiency preventing IV contrast
Magnetic resonance imaging (MRI)

- **Osteomyelitis**
  - Hot red foot with ulcer
  - Forefoot: MTP’s IP’s
  - Hindfoot: calcaneus
  - X-ray normal first weeks
  - MRI marrow edema in forefoot and hindfoot near ulcer

- **Active Charcot**
  - Hot red foot - no ulcer
  - Midfoot subarticular
  - X-ray normal first weeks
  - MRI marrow edema in midfoot subchondral

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**PET Scans**

- Shows promise in differentiating CN from infection, but these techniques are not widely available, and clinical usefulness is yet to be determined (1,3)
Take Home Points

- X-rays are a MUST, but may not be enough
- Don’t use CT imaging
- If using bone scan/nuclear imaging, use combination of $^{99}$Tc sulfa colloid & $^{111}$Indium
- **MRI with contrast is your best bet, unless CN & infection both present**
- PET Scans?

References

Thanks!

- Retinopathy leading to vision loss
- Increased risk of stroke
- 2-4x times higher heart disease deaths
- 44% of new cases of kidney failure
- >60% of all non-traumatic lower limb amputations
DISCLAIMER

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Treatment Options

• Conservative Treatment
• Pharmacological Treatment
• Surgical Treatment

How do we know how long to treat?
• Publications have suggested anywhere from 2-6 mo of NWB in a TCC
• Difference of less than 2° between the two feet
• Gradual return to WB to tolerance

Conservative Treatment

✓ Acute tx focus:
  ✓ Stabilizing the unstable externally
  ✓ Allow the inflammation to subside
  ✓ Allow the Fractures to heal
  ✓ Plantigrade foot that can be protected in a custom/rocker bottom shoe

Better to start CN treatment earlier rather than later:
24 patients with Eichenholtz Stage 0
  11 tx’d within 1mo of onset of s/s with 3mo TCC
  13 tx’d ave 3mo after onset of s/s 5mo TCC

All 13 of the delayed treatment group advanced to flatfoot/rockerbottom rigid deformities

But in the early group only 1 did


How important is NWB?

Although the expert consensus remains NWB immobilization in a TCC, literature exists that suggests that continued WB while immobilized does not hinder the resolution of acute Charcot with a stable, plantigrade foot.


Pinzur MS, Lio T, Posner M. Treatment of Eichenholtz Stage I Charcot foot arthropathy with a weightbearing total contact cast. Foot Ankle Int 2006; 27: 3249.


In a study by du Souza et al Patients were initially instructed to be NWB. However, the authors found that patients often did not comply with this instruction.

1) A lack of proprioception and inability to determine how much weight was being placed on the foot due to peripheral neuropathy,
2) Poor eyesight secondary to diabetic retinopathy, and
3) Poor strength and coordination which made the use of ambulation assistive devices difficult.

The authors found that despite the patients being WB more often than not, only one progressed to deformity of the foot during the treatment period. Thus, they allowed all subsequent patients to be WB as tolerated.


But does it work?

Small study of patients with Eichenholtz Stage 1 midfoot Charcot. The authors found that TCC immobilization provided effective resolution with maintenance of a stable, plantigrade foot in 75% of cases at 32mo, concluding that TCC immobilization remains the mainstay of treatment for midfoot Charcot.

This has been replicated in several other studies.


Recurrence? Yes...

Some studies have shown as high as 23% within 27mo

Noncompliance and obesity (>30kg/m²) were the two main predisposing factors.

### Bracing Instead?

- **Charcot Restraint Orthotic Walker (CROW boot)**
- **Patellar tendon bearing brace**
- **Removable walking boot**

**Immobilization** times with these devices are longer compared to those of non-removable devices as patients may remove the device and ambulate without them.

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### Pharmacologic Answers?

**Bisphosphonates** are drugs that

- No serious adverse events
- A more rapid reduction in skin temperature was noted however, this reduction was not sustained over time.
- Pain reduction was not consistently reported.
- Two studies reported longer immobilization times
- The overall conclusion was that the use of bisphosphonates is not supported.

- Zoledronic acid

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Pharmacologic Answers?

A randomized controlled trial for intranasal calcitonin as adjunct to conservative tx of CN looked at 32 pts over 6mo.

✓ Markers for bone turnover were measured at 3 and 6mo.
✓ Significantly greater reduction in ICTP and BALP was noted at 3mo.
✓ Reduction in BALP was not seen at 6mo.
✓ Daily nasal calcitonin may be an effective adjunctive treatment modality.


Bone stimulator?

Hanft et al. study on 31 pts with Stage 1 CN who were followed for an average of 23.3 weeks:

- Tx’d with a TCC or TCC and application of a combined magnetic field bone growth stimulator for 30 min daily.
- Bone stimulator statistically significant reduction with a mean time to osseous consolidation occurring in the study Group 12 wks before the control Group.
- Use of a combined magnetic field bone growth stimulator may be an effective adjunctive modality in the treatment of acute CN.

Surgical Treatment

We got options:
- Exostectomy and soft tissue coverage
- Screw/Staple Compression Stabilization
- Multiple Plate & Screw Stabilization
- Plantar Plate Stabilization
- Locking Plate and Screw Stabilization
- Multiple Screw Stabilization
- External Fixation Alone
- Percutaneous Stabilization
- Mini-Open Joint Preparation
- Ring External Fixation

Grim Statistics

Systematic Literature Review (2011)
- Results: 111 manuscripts reviewed in entirety
  - 67: Case Report or Retrospective case Series
  - 29: Other [Brace Therapy; TCC; Gait Analysis; Etc.]
  - 16: QOL/Demographic Studies
- Surgical Tx: 389 Feet; 2.4 year F/U; NWB 3.3 Months
  - Recurrent Ulceration: 15/267 (5.7%)
  - Deep Infection: 32/264 (12.1%)
  - Hardware Failure/Non-unions: 64/264 (24.2%)
  - Re-operation: 67/310 (21.8%)
  - Trans-tibial Amputation: 29/298 (9.8%)
- Mortality: 330/1138 patients (29%) @ 5yr. F/U
- QOL: ↓ Physical Functioning & General Health; Similar effect to TTA
“Non-weightbearing was prescribed and a physical therapist provided instructions during the 1 to 3 day hospitalization until the patient demonstrated the ability to walk for short distances with a walker or crutches and transfer effectively. However, compliance with non-weightbearing instructions was noted to be poor even during hospitalization.”


Patient Factors that Effect Surgical Outcome

- Intelligence + Cognitive Skills
- Motivation
- Family + Social support network
- Expectations
- ETOH ± TOB
- Compliance

Try to stay off of your foot as much as you can. Your foot cannot look, touch, lean, rest, glance, graze, hover, or taunt the ground and the ground is anything in the entire world your foot could come in contact with.

“A Mere Flesh Wound!”

LIGER!
THANK YOU

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