Pain Management in Vasculitis

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June, 2017
Pain in Vasculitis – Where?

- **Neuropathy**
  - EGPA, GPA, MPA, PAN, Cryo
- **Nose / Sinus / Ear**
  - GPA, EGPA
- **Eye**
  - GPA, Behcet’s
- **Chest**
  - Takayasu’s (coronary arteries)
  - Pleuritis (lining of lungs/heart), especially GPA?
  - Pulmonary embolism (blood clot in lungs), especially GPA
- **Abdomen**
  - Directly: Takayasu’s, IgA vasculitis (HSP), PAN, others
  - Indirectly: side effects of treatment....
Pain in Vasculitis – Where?

- **Joint**
  - Directly: all, in different ways
  - Indirectly: all, due to side effects of treatment

- **Muscle**
  - Directly, vasculitis of muscle: EGPA, GPA, MPA, PAN, Cryo
  - Directly, “flu-like” symptoms: all
  - Directly, poor blood flow to hands and feet: Takayasu’s, GCA (large-vessel vasculitis)
  - Indirectly: all (Fibromyalgia)

- **Other “soft tissues”**
  - Directly, poor blood flow to regions of skin, fingers/toes: EGPA, GPA, MPA, PAN, Cryo, HSP, skin-limited

- **Headache**
  - Directly, vasculitis: GCA, CNS
  - Directly, “flu-like” symptoms: all
  - Indirectly: all, due to side effects of treatment
Pain in Vasculitis – Why?

- Due to active vasculitis?
- Due to permanent damage from vasculitis?
- Due to medication side effects?
- Unrelated to vasculitis??
Pain in Vasculitis – Why?

• Due to active vasculitis?
  – If so: immune-suppressive drugs!

• Due to permanent damage from vasculitis?
  – The focus of this talk

• Due to medication side effects?
  – Reversible or permanent?
  – If reversible, switch medications

• Unrelated to vasculitis??
  – If so, identify and treat as such
Tangent on Medications

• Reversible
  – Abdominal: methotrexate, azathioprine, mycophenolate, leflunomide, colchicine
  – Headache: “any medication”?  
  – Joint/muscle pain: mycophenolate, zoledronic acid, “any”?  
  – Always think about medication as the cause of a new symptom if the timing fits

• Long-term or permanent damage
  – Fractures, osteonecrosis, scoliosis, tendon/muscle tears from prednisone
  – Pain from fracture or tendon injury usually improves
Nerve ending in tissue
Inflammation

Other “noxious stimuli”
Complex interactions with other parts of the brain!

“Descending” pathways that *usually* feed back to reduce signaling of pain
Classification of Pain

• Nociceptive and Non-nociceptive
  – Nociceptive: Somatic and Visceral
  – Non-nociceptive: Neuropathic, various classification schemes

• Peripheral and Central
  – Peripheral: Inflammatory and Non-inflammatory

• Acute and chronic
Classification of pain

Pain

Pain classified by duration
- Acute
- Chronic

Pain classified by nature
- Nociceptive
  - Somatic
  - Visceral
- Non-nociceptive
  - Neuropathic
  - Sympathetic
Primary nociceptive
(For example)
- Osteoarthritis
- Visceral pain
- Headache
- Ischemic pain
- Cancer pain (without nerve injury)
- Back pain (without nerve injury)

Pain including both nociceptive and neuropathic component
- Chronic back pain (nerve lesion/dysfunction + nociceptive activation from ligaments, joints, muscles, tendons)
- Cancer pain (with nerve infiltration)
- CRPS I (without nerve injury)

Primary neuropathic
(For example)
Peripheral
- Back pain (due to nerve injury / dysfunction)
- PHN
- Trigeminal neuralgia
- HIV
- CRPS II
- Phantom pain

Central
- Post stroke
- Multiple sclerosis
- Spinal cord injury

Injured / irritated somatic or visceral structure
Nociceptive and neuropathic components
Injury of the neural structure
<table>
<thead>
<tr>
<th>Acute Pain</th>
<th>Chronic Pain</th>
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</thead>
<tbody>
<tr>
<td>...is caused by external or internal injury or damage.</td>
<td>...is uncoupled from the causative event.</td>
</tr>
<tr>
<td>...has an intensity correlates with the triggering stimulus.</td>
<td>...has an intensity that no longer correlates with the triggering stimulus.</td>
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<tr>
<td>...can be clearly located.</td>
<td>...becomes a disease in its own right.</td>
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<tr>
<td>...has distinct warning and protective functions.</td>
<td>...has lost its warning and protective functions.</td>
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<tr>
<td></td>
<td>...is a special therapeutic challenge.</td>
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</tbody>
</table>
Depression

Anxiety

Disturbed sleep

Limited social function

Limited work function

Reduced mobility

REduced QUALITY OF LIFE

Grunenthal – Change Pain
Sites of dysfunction in chronic pain

- Nerve ending in tissue
- Somatosensory cortex
- Thalamus
- Amygdala
- Insular cortex
- Prefrontal cortex
- Anterior cingulate cortex
- Nucleus accumbens
- PAG
- Locus coeruleus
- RVM
- Midbrain
- Pons
- Medulla oblongata
- Ascending transmission
- Descending modulation
- Primary afferent neuron
- Spinal cord/spinal nucleus of the trigeminal complex
Chronic Pain in Vasculitis

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Chronic Pain in Vasculitis
Re-organized

• Neuropathy
• Nose / Sinus
• Joint / Muscle “mechanical”
• Fibromyalgia
• Inadequate blood flow
Chronic Pain in Vasculitis

Re-re-organized

- Inadequate blood flow
- Nose / Sinus
- Joint / Muscle “mechanical”
- Neuropathy
- Fibromyalgia

Usually “frequent acute”

Nociceptive

Neuropathic
Tangent on Ischemic Pain

- Ischemia = poor blood flow to tissues
- Large arteries (TAK, GCA)
  - Pain only with use = a form of acute pain
  - Often doesn’t resolve with treatment of vasculitis
  - Angioplasty/stent, surgery
- Small arteries and microscopic vessels
  - Ulceration, swelling, blue fingertips
  - Tissue usually dies or heals: death of some tissue and replacement by new tissue, or relief of ischemia by treatment of vasculitis
## Nociceptive vs. Neuropathic: why it matters

<table>
<thead>
<tr>
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<th>Nociceptive (NC) component</th>
<th>Neuropathic (NP) component</th>
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<tbody>
<tr>
<td>Non-opioids (NSAIDs)</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Weak Opioids</td>
<td>+</td>
<td>○</td>
</tr>
<tr>
<td>Strong Opioids</td>
<td>+</td>
<td>○</td>
</tr>
<tr>
<td>Co-analgesics (Antidepressants/Anticonvulsants)</td>
<td>○</td>
<td>+</td>
</tr>
</tbody>
</table>

- **+** Effective
- **○** Partially efficient
- **-** No NP-mechanism-related action

Modified from Davis et al. 2007 [1]
What is Fibromyalgia?

- Chronic widespread pain without evidence of tissue injury
- Thought to represent chronic malfunction of pain pathways
- Possible to have both a physical reason for pain and also fibromyalgia – which makes the pain more severe
- Medications for neuropathic pain are helpful
- Medications for nociceptive pain are not, except to treat a physically identifiable source
More about Fibromyalgia

• Highly associated with poor sleep
• Common association with depression, PTSD
• Associated “somatic” symptoms
  – Irritable bowel
  – Bladder pain = “interstitial cystitis”
  – Chronic fatigue
Approaches to Pain Management

• **Pharmacologic (Medications)**
  – FDA-approved
  – Experimental, anecdotal, “alternative”

• **Non-pharmacologic**
  – Physical
  – Psychological

• “Multi-modal” or “multi-disciplinary” approach is currently recommended
Medications for Pain Relief
(supported by scientific evidence)

• Acetaminophen (Tylenol)
• Non-steroidal anti-inflammatory drugs (NSAIDs)
  – Ibuprofen (Motrin, Advil), naproxen (Aleve), many others
• Weak opioids
  – Tramadol
• Strong opioids
  – Oxycodone (Percocet), hydrocodone (Vicodin), morphine, hydromorphone (Dilaudid), others
• Anti-depressants and anti-convulsants
  – Gabapentin (Neurontin), pregabalin (Lyrica), duloxetine (Cymbalta), amitriptyline, nortriptyline
Acetaminophen

• Weak pain relief for nociceptive pain, such as arthritis or headache
• Safest unless you have liver disease
• Affects levels of warfarin (Coumadin)
NSAIDs

• Better pain relief than acetaminophen for nociceptive pain
• Also anti-inflammatory, more helpful in other rheumatic diseases than in vasculitis
• Risky in patients with kidney disease
• Increases risk of peptic ulcer disease (a lot)
• Increases risk of heart attack (somewhat)
• Unhelpful for neuropathic pain, not very helpful for chronic pain
Opioids

- For severe, acute pain, better than NSAIDs because dose can be increased with monitoring
- Risk of overdose (reduces breathing rate)
- Risk of abuse
- If used chronically, often stops working (tolerance), then withdrawal symptoms if drug is stopped
- Not very helpful for neuropathic pain, nor for chronic pain
Anti-depressants and anti-convulsants

• Drugs of choice for neuropathic pain
• Drugs of choice for fibromyalgia
• Not helpful for nociceptive pain unless there is a central/neuropathic component due to development of chronic pain
• Still only modestly effective for most patients
• Safe, but wide range of side effects, because these drugs act in the brain....
Surveys in Painful Conditions

- FDA-approved drug for pain relief

- Surprisingly effective
- 38 Fibromyalgia Treatments
- 30 Arthritis Treatments
- 35 Treatments for Neuropathy

= FDA-approved drug for pain relief
Unproven Medications

• Marijuana
• Low dose naltrexone
• Search on-line and you will soon know more than I do
  – On-line statements, vitamin stores, and herbalists are not subject to high-quality scientific review
• There is a very good reason why we need rigorous scientific study of medications, especially when used for pain...
Mind over Matter

15-20% improvement with placebo, typical of pain management studies!
Non-pharmacologic approaches for treating chronic pain

• Physical
  – TENS
  – Physical therapy, Chiropractic
  – Acupuncture
  – Tai chi, Yoga, Aquatic therapy, other exercise... or rest
  – Diet change

• Psychological
  – Mindfulness / meditation
  – Cognitive-behavioral therapy
  – Group therapy

• When tested scientifically, these perform about the same as medications for chronic pain
Surveys in Painful Conditions

= Non-pharmacologic approach to pain relief
Combining approaches

• Multi-modal therapy works better than single approaches...
• ... but not a lot better, no synergy

• The key message is that different approaches work (or don’t) for different people – try something and then move on if necessary
A Mixed Message

• Be optimistic!
  – The placebo effect is powerful and has real neurochemistry behind it

• Be skeptical!
  – Don’t spend a lot of money or put yourself at risk through approaches that haven’t been tested scientifically

• Only keep doing something if it works for you personally!
Thanks