Pain and Sensory Symptoms: A case based approach

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Objectives

* Identify types of pain and sensory symptoms typical to patients with MS
* Review pharmacological and non-pharmacological methods of managing pain
* Identify factors that contribute to pain response
Why Does it Matter?

* Pain prevalence reports vary from 29-86% of MS patients\(^1,2\)
* More than 50% MS patients find pain to be a problem, and for 10-20% it is a significant problem\(^3\)
* Pain is estimated to comprise nearly 30% of all symptomatic treatment\(^4\)
* Pain can interfere substantially with the ability of patients with MS to work, sleep, maintain relationships and enjoy life\(^5\)

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Pain in MS

* Central Neuropathic Pain: Direct consequence of a demyelinating lesion in the central nervous system
  - Lancing, pins and needles, burning, electric shock.
  - Commonly associated with allodynia (painful response to non-painful stimuli) and/or hyperalgesia (increased response to painful stimuli)

* Non-neuropathic Pain: Indirect consequence of the disability associated with MS

Classifications of MS related pain

* Intermittent Central Neuropathic Pain
* Continuous Central Neuropathic Pain
  * Musculoskeletal Pain
  * Mixed Neuropathic and Non-neuropathic pain

Case Study: Norma

- 56-year-old female
- Diagnosis of RRMS at age 34 with progression since age 48.
- Presents with minute long episodes of excruciating left jaw pain present for 3 weeks. It is painful to eat, talk, brush her teeth.
- Evaluated by the dentist, no cause of pain identified.
Interrnt Central Neuropathic Pain

* Neuropathic pain that occurs spontaneously or is paroxysmal
* Described as shooting, stabbing, shock-like, lancing, crushing or searing
* More intense than continuous central neuropathic pain
* Examples: Trigeminal Neuralgia, Lhermitte’s sign


Trigeminal Neuralgia

* Incidence of TN in MS is roughly 20 times the prevalence of the general population
* Prevalence in patients with MS ranges 2-6%2,3
* Described as a paroxysmal sharp, lancing pain lasting seconds to minutes affecting one or more branches of the trigeminal nerve2
* Triggered by facial movement/stimulation talking, chewing, breeze

**Trigeminal Neuralgia**

- First line treatment consists of anti-epileptic drugs (AED)
- Poor tolerability of medications and/or severity of pain necessitates early consideration for neurosurgical consult
- Interventional treatment options:
  - Percutaneous retrogasserian glycerol rhizotomy
  - Radiofrequency rhizotomy
  - Microvascular decompression (reserved for non-responders)


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**Guiding Principles for Treating Pain**

- Educate patients regarding off label uses of medications
- Start low, go slow
- Lower doses of a combination of medications may result in better toleration than high dose of a single agent
- All AEDs and antidepressants have the potential to increase the risk of suicidal thoughts and behaviors for patients taking them for any reason
- Consistently assess for benefit and wean appropriately
Anticonvulsants

* Carbamazepine (Tegretol)
  - Indications: AED, TN
  - Side Effects: drowsiness, dizziness, nausea, unsteadiness
  - Black Box Warning: SJS, TEN, Aplastic Anemia, SI
  - Monitoring: CBC and CMP at baseline and periodically
  - Start 100 mg bid. Max dosage 1200 mg/day
  - Reduces plasma concentrations of oral contraceptives

* Oxcarbazepine (Trileptal)
  - Indications: AED
  - Side Effects: drowsiness, dizziness, nausea, unsteadiness
  - Monitoring: hyponatremia
  - Caution with concurrent meds known to decrease Na levels
  - Start 150 mg bid, increase every 3-7 days. Max dosage 2400 mg/d
  - Reduces plasma concentrations of oral contraceptives

* Gabapentin (Neurontin)
  - Indications: AED and post herpetic neuralgia (PHN)
  - Side Effects: somnolence, weight gain, dizziness, ataxia, peripheral edema
  - Caution in renal impairment
  - ~30% prescriptions for fibromyalgia or chronic neuropathic pain
  - Initial: 100-300 mg tid, max dosage 3600 mg/day

* Pregabalin (Lyrica)
  - FDA indications: AED, neuropathic pain associated with diabetes, fibromyalgia, PHN, and GAD
  - Similar SE profile to gabapentin
  - Initial: 50 mg bid, max dosage 600 mg/d

Anticonvulsants

* Topiramate (Topamax)
  - Indications: Migraine Prophylaxis, AED
  - Side Effects: weight loss, somnolence, psychomotor slowing, paresthesias
  - Rare: acute myopia and secondary angle closure glaucoma
  - Caution: history of renal calculi, renal or hepatic impairment
  - Monitoring: metabolic acidosis
  - Start 25 mg q hs, can increase by 25 mg weekly. Max dosage 400 mg daily

Norma Continued

* MRI brain with and without contrast revealed enhancing pontine lesion
* IVSM 1000 mg x 3 days given
* Pain reduced from a 10/10 on VAS Pain scale to 5/10
* Pain reported to be severe enough to merit further treatment
* Initiated Carbamazepine 200 mg twice daily
* Depending on benefit and toleration at follow up appointment in 4 weeks, will consider neurosurgery referral.
Other types of Intermittent Neuropathic Nerve Pain

Painful Tonic Spams

* Paroxysmal abrupt onset attacks of abnormal posture of either arm or leg, typically lasting less than 2 minutes

* Estimated to occur in 11% MS patients

* Correlates with MRI lesions in the basal ganglia, internal capsule, cerebral peduncle, medulla, and spinal cord

* Not always associated with pain

* Anecdotal reports of benefit seen with AEDs, baclofen, benzodiazepines

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Lhermitte’s Sign

- Transient, short-lasting sensation related to neck movement, felt in the back of the neck, lower back or in other parts of the body
- Associated with MRI lesions of the cervical spine\(^1,2\)
- Tends to occur during exacerbations
- 25% patients never reported the symptom\(^1\)
- Symptomatic treatment is not necessary

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Case Study: Kate

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Case Study: Kate

- 32 year old female
- Diagnosis of RRMS 2008
- Initial symptoms consisted of numbness from the waist down
- Residual paresthesias to both feet rated as a 2/10 on the VAS pain scale

Continuous Central Neuropathic Pain

- Correlates with a CNS lesion/spinothalamic dysfunction
- Characterized by abnormal sensations including burning, tingling, aching, itching, band-like, throbbing
- Central neuropathic pain occurs in nearly 50% MS patients
- Most common type of pain associated with MS is dysesthetic extremity pain

Dysesthetic Extremity Pain

* Typically bilateral
  - Affects the legs and feet more often than upper extremities
  - Usually worse at night
  - Can be exacerbated by physical activity
* Symptoms may not be bothersome enough to merit medication
* Often managed with AEDs and/or certain antidepressants

Back to Kate

* Kate presents to the office with a significant increase in burning pain to both legs and feet for the past 6 weeks. (VAS 7/10)
* Neurological exam reveals no changes. She has reduced vibratory sensation and altered temperature sensation to both feet, but these findings are stable.
* No recent infections, and no symptoms of urinary tract infection.
* BDI Fast Screen Score is 11 (scores >4 are suggestive of depression).
* Kate's boyfriend of the past 4 years has broken up with her. She is sleeping poorly, and is stressed at work.
Depression and Pain

- Pain is associated with depression, anxiety, fatigue.\(^1\)
- Pain is exacerbated by sleep disturbance and spasticity
- Negative thoughts and catastrophizing pain enhance the intensity of pain \(^2\)
- Pain influences psychological aspects of quality of life resulting in poorer mental health and increased social handicap \(^1\)
- **Comprehensive management recommended over single-system approach** \(^1\)


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Tricyclic Antidepressants

- **Indications:** Depression
- Common side effects include weight gain, sedation, dry mouth, constipation, urinary retention
- **Contraindications:** heart block, BPH, use of MAOIs

- **Amitriptyline**
  - Initial 10-25 mg q hs, may increase up to 150 mg/d
  - Typically most effective, but also has most side effects. Carries potential for cardiac conduction changes, especially with higher doses
  - Nortriptyline
  - Desipramine
SNRI
(Selective Norepinephrine Reuptake Inhibitors)

* Venlafaxine
  - Indications: MDD (major depressive disorder)
  - CI: use of MAOi
  - Side effects: nausea, agitation, dry mouth, sweating, may increase blood pressure
  - Start 37.5 mg each morning. Increase by 37.5-75 mg per week. Max dosage 450 mg/d
  - Inhibits NE reuptake at dosages >150 mg/d. Weakly blocks dopamine reuptake at very high doses (above 350 mg/d)

SNRI cont’d

* Duloxetine
  - Indications: MDD, GAD (generalized anxiety disorder), PDPN (painful diabetic peripheral neuropathy), fibromyalgia, chronic OA pain, chronic low back pain
  - Balanced inhibitor of NE and 5-HT reuptake
  - Common side effects: nausea, dry mouth, somnolence, decreased appetite
  - Start 30 mg daily x 7 days then increase to 60 mg daily. Max dosage of 120 mg/day
  - Isolated cases of liver failure have been reported, most cases in patients with history of liver injury, including alcohol abuse
SNRI cont’d

* Milnacipran
  - Indications: management of fibromyalgia
  - MOA: NE and 5-HT reuptake inhibition (3:1 NE to 5-HT)
  - Side effects: nausea, headache, constipation, dizziness, insomnia, increased heart rate and blood pressure
  - Dosing: Day 1: 12.5 MG. Day 2-3: 12.5 mg bid. Day 4-7: 25 mg bid. After day 7: 50 mg bid

Kate: Treatment Plan

* Obtain mental health history.
  - History of mild depression, treated with sertraline many years ago
* Discuss management of stressors with Kate
  - Counseling
  - Sleep Hygiene
* Offer medical management with SNRI
* Follow up in 6 weeks to assess response
Case Study: Pete

* 48-year-old male
* Diagnosis of PPMS at age 42
* Presents with worsening gait and low back pain
* Reports low back pain as 6/10, worsening to 8/10 with activity
Musculoskeletal Pain

* MS predisposes patients to secondary musculoskeletal pain by causing weakness, muscle spasms, spasticity and reduced mobility
* Prevalence ranges from 10-16%
* MS treatments can cause myalgias, osteoporosis resulting in compression fractures, AVN
* Low back pain can be associated with scoliosis, degenerative joint disease
* Back pain can be central in origin as well


Musculoskeletal Pain

* Management consists of identifying underlying issue
* Physical Therapy for assessment and management of safety, gait, positioning, seating and effective use of mobility aids
* Medication management to include NSAIDS, acetaminophen, muscle relaxers
Patients More Likely to Experience Pain¹...

* Older
* Longer disease duration
* Greater disease severity
* Men and women are equally likely to experience pain, but women tend to have greater severity of pain
* Progressive forms of MS
* Co-morbid depression and mental health impairment


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Exercise

Chronic pain >>>> kinesiophobia >>>> deconditioning>>>>>pain when attempt activity>>>>>more rest

Breaking this cycle is critical for rehabilitation to take place

Exercise is another way for patients to be active participants in their own care

Correlates of Reduced Functioning

- Catastrophizing cognitions
- Guarding and resting as coping techniques
- Belief that one is disabled by pain, that others should be solicitous when one experiences pain, and that pain is an indication of physical damage
- Solicitous environmental responses to pain behaviors

Measures to address Reduced Functioning

- Increase the use of coping strategies such as task persistence, acceptance of disability, behavioral activities, exercise, ignoring pain, and coping self-statements
- Increase the belief that the patient can control pain and its effects
- Help the patient seek and obtain more general (non-pain contingent) social support

Other Measures

Chronic Pain Rehabilitation Program
* Stretching for spasticity
* Massage
* Distraction
* Acupressure and Acupuncture
* Cooling
* Guided imagery

Pete: Assessment

* Pete denies radicular pain
* Observation of gait reveals left LE circumduction and mild foot drop
* Palpation of low back reveals muscle spasm with trigger points to the lumbar paraspinals
* Pete has a sedentary lifestyle and denies regular exercise or stretching
Pete: Plan

* Referral to physical therapy to address abnormal gait and lower extremity weakness
* Referral to orthotist for assistive device evaluation (AFO, E-stim device)
* Stress importance of home exercise plan once PT has concluded
* May need to consider anti-spasmotic medications if therapy alone doesn’t address low back pain

Mixed Neuropathic and Non neuropathic Pain

* Headache
  - More common in patients with MS than in general population
* Muscle Spasms/Spasticity
A few words on Opioids...

Opioid Therapy

- Opiates have minimal effect in central MS pain and are not recommended
- In 2007, opioids were associated with more deaths than heroin and cocaine combined
- Approximately 1/3 of chronic pain patients may not use prescribed opioids as prescribed or may abuse them
- Opioids have become the most commonly prescribed drug category in the US

REMS

* Risk Evaluation and Mitigation Strategy
* In 2012, The US Food and Drug Administration (FDA) directed makers of all ER/LA opioids to provide free continuing education (CE) to educate prescribers and patients.
  - Ensure that benefits outweigh risks
  - Introduces new safety measures to reduce risks and improve safe use of ER/LA opioids while continuing to provide access to these medications for patients.

http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm363722.htm

Best Practices for use of Opioids

* Opioid treatment agreement
* Screen for prior or current substance abuse/misuse (alcohol, illicit drugs, heavy tobacco use)
* Screen for depression
* Prudent use of random urine drug screening (diversion/non-prescribed drugs)
* Do not use concomitant sedative-hypnotics or benzos
* Track pain and function to recognize tolerance and track effectiveness

Best Practices for use of Opioids¹

* Track daily morphine equivalent dosing (MED) using online dosing calculator
* Seek help if MED reaches 80-120 mg and pain and function have not substantially improved
* Use the state Prescription Drug Monitoring Program to monitor all sources of controlled substances.


Conclusion

* Pain and sensory symptoms comprise significant amount of symptomatic treatment
* Multiple modalities exist to assist in the management of pain
* A comprehensive approach is recommended over single-system approach
Thank you!

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