Post-herpetic Neuralgia

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Overview

• Herpes Zoster
  – Epidemiology, clin. presentation
• Post-herpetic neuralgia (PHN)
  – Definition, epidemiology, clin. presentation, risk factors
• Management of chronic PHN
  – Prevention, pharmacological & non-pharmacological
• Key points

Herpes Zoster/Shingles

• Results from activation of varicella zoster virus (VZV) latent in the DRG
  – Cell-mediated immunity prevents viral replication
  – Replication followed by transmission down nerve axons to skin -> local infection resulting in blister formation
  – Also travels centrally to meninges & spinal cord

Pathophysiology

• Primary inflammation from reactivation leads to widespread neural damage
• Idea of different subtypes (clinical and neurophysiological mechanisms)
  – Variable sensory changes and nature of pain
• Novel agents being developed target specific receptors & ion channels a/w neuropathic pain (TRPV1, TPRM8, Nav1.8, Nav1.9, CB1, CB2)

Epidemiology of HZ

• Annual Incidence: 1.3-4.1 per 1000 pop
• Higher in elderly >80 yr: 10.1 per 1000 person-years (5x incidence cf <50 yr)
  – Decline in cell-mediated immunity
• Common condition: 20-30% lifetime risk in developed countries
• Immunocompromised patients: 8-10%

Clinical Presentation of HZ

• Clin. Diagnosis
  – Typical unilateral vesicular rash in dermatomal pattern (usually single, 20% adjacent)
  – Pain may precede rash (prodromal; also pruritus/dysesthesia)
  – Tender, sharp, stabbing, shooting, & throbbing
  – Allodynia is common, can be severe, and distressing affecting daily activities
• Distribution:
  – Thoracic nerves, V1 division of trigeminal nerve
Clinical Presentation of HZ

- Viral swabs for immunofluorescence or culture
- Beware HZ ophthalmicus (10-20% of cases)
  - Vision loss, early eye referral
- Differential Diag:
  - Zosteriform herpes simplex, contact dermatitis, impetigo, candidiasis, drug eruptions, autoimmune blistering diseases, and insect bites
- Complications: PHN most common
  - Disseminated HZ & neurologic complications occur mainly in immunocompromised pts (encephalitis, meningitis, myelitis, cranial & peripheral nerve palsies, GBS)

Post-herpetic neuralgia

- Definition:
  - No agreed criteria
  - Clinically meaningful pain (≥3/10) 3 or 4 months after onset of HZ rash
- Pain in PHN
  - Constant background pain, often burning
  - Paroxysmal shooting pain
  - Alodynia (painful hypersensitivity), usually light touch
    - 90% pts, often most distressing symptom, last to disappear

PHN

- Most common complication of HZ
  - Annual incidence 40 per 100,000 person-years
  - Prevalence in gen. pop. unknown; estimate based on GP records ~ 0.7 per 1000 pop
- Incidence higher in elderly
  - 18% in >75 yr @ 1/12
  - 11% in 65-74 yr
  - 4% in 45-54 yr

Most cases of PHN improve with time but a small minority become chronic

- Estimates of clinically significant PHN pain range from 5-7% at 3/12 -> 3-5% at 6/12 -> 2-4% at 12/12
- Prospective study of acute HZ pts (>50 yr)
  - 16% had pain @ 6/12, 10% @ 4 yrs
  - but severe pain only in 2% @ 6/12, 0.7% @ 4 yrs

- Chronic PHN commonly a/w psychiatric morbidity
  - Poor sleep, low mood, social isolation
  - Significant disability

Risk Factors for PHN

- ↑ Age (>60 yrs)
- Pain >5/10
  - Independently predicted PHN but specificity poor
- Extent of rash/inflammation, female gender, ophthalmic location not shown to predict risk
Management of chronic PHN

• Remember biopsychosocial model of pain
  – Assess -> multimodal multidisciplinary treatment plan
  – Pharmacological measures to decrease pain should be combined with efforts to address any psychological or social issues

• Can be difficult and frustrating for both pt & dr
  – Set realistic expectations regarding likely effects on treatment

Management of chronic PHN

• RCTs indicate that TCAs, gabapentinoids, opioids, tramadol, topical lidocaine, and topical capsaicin may result in significant pain relief for some patients
  – Response varies in individual patients
  – Adverse effects may outweigh benefits of meds
  – Repeat reviews to optimise treatment
    • 3A(s): Analgesia, Adverse effects, Addiction

Prevention of PHN

• Prevent VZV infection
  – Paediatric vaccination at 18/12 or 10-13 yrs

• Prevent VZV reactivation
  – Adult vaccination at 60 yrs & above (high titre)

• Acute HZ management
  – Standard pain mgmt to reduce severity/duration of pain

• Corticosteroids do not prevent PHN
  – Cochrane Review (2010)

Role of Antivirals in HZ/PHN

• Acyclovir/famciclovir/valaciclovir are recommended by experts to maximize the resolution of symptoms including pain
  – Within 72 hours after onset of rash

• Cochrane review (2009) concludes there is no evidence that antiviral treatment prevents PHN

Pharmacological management

• Drugs supported by strong evidence
  – TCA, gabapentinoids, opioids, tramadol, topical lidocaine or capsaicin

• Drugs supported by some evidence
  – Sodium valproate, corticosteroids
  – IV lignocaine

• Combination therapy provides synergism
  – Expert opinion although no RCTs
  – Gabapentinoids/TCAs + opioids/tramadol
### Tricyclic antidepressants
- Nortriptyline, Amitriptyline, Desipramine
- **Dose**
  - Start 10-25 mg on, titrate wkly up to 75-150 mg
- **SE**
  - Sedation, dry mouth, blurred vision, weight gain, urinary retention, constipation, sexual dysfunction
- **CI/caution**
  - Cardiac disease, glaucoma, suicide risk, seizure disorder, concomitant tramadol, SSRI, SNRI

### Gabapentinoids
- Gabapentin, Pregabalin
- **Dose**
  - G: 100-300 mg on/bd, titrate up to 1800-2400 mg/d
  - P: 75 mg on/bd, titrate up to 300-600 mg/d
- **SE**
  - Sedation, dizziness, ataxia, peripheral oedema, weight gain, blurred vision
- **CI/caution**
  - ↓ dose in renal impairment,
  - Advantages
  - Improved sleep, no clin. sig. drug interactions, relatively safe

### Topical lidocaine
- **Dose**
  - Start 1-2 5% patch, titrate up to 3 patches 12h
- **SE**
  - Local erythema, rash, blisters
- **CI/caution**
  - Known hypersensitivity to amide LA, caution in pts receiving class 1 antiarrhythmics (mexiletine, tocainide)

### Treatment Algorithm

#### 1st line drugs
- TCA, gabapentinoids
- * consider combination therapy in severe pain

#### 2nd line drugs (also used as 1st line)
- Opioids, tramadol
- Topical lidocaine

#### 3rd line options
- Sodium valproate, corticosteroids
- IV lignocaine

### Non-pharm management
- **Physical measures**
  - Firm garment, physical desensitisation
- **Psychological interventions**
  - Reduced QOL -> poor mood & functioning
  - Partial pain relief with drugs
  - CBT shown in chronic pain states to possibly reduce pain severity and improve QOL and function by improving pain management skills
Non-pharm management

- Interventional strategies
  - Sympathetic nerve blocks controversial as studies poor quality & marginal long-term analgesic effects
  - Spinal cord/peripheral nerve stimulation: used in chronic neuropathic pain, case series have shown efficacy but long-term benefit uncertain
  - No evidence or uncertain: epidural steroids, intrathecal morphine, DREZ, neurectomy, DBS, cordotomy

Key points

- PHN is the most common complication of HZ
  - Often difficult to treat and may lead to significant psychosocial consequences and disability
- The best treatment for PHN remains prevention
  - Role of GPs paramount
  - National paediatric vaccination program + adult vacc.
- Pharmacological management may involve TCAs, gabapentinoids, opioids & topical agents
  - Careful titration and monitoring required

Key points

- Goal of management is to increase activity and function
  - Best achieved by combining both pharmacological & nonpharmacological strategies
  - Poor response to treatment should prompt early referral to a pain medicine specialist

THE END