Diabetic Peripheral Neuropathy
The Forgotten Complication

Presented by

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Neuropathy from Toe to Head
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The Peripheral Nervous System
What is Peripheral Neuropathy

• Neuropathy: Any disease or process which damages the nerves
• The nervous system is divided into two parts:
  – Central Nervous System: Brain and Spinal Cord
  – Peripheral Nervous System: The nerves after they leave the spinal cord on the way to skin and muscle

Nerves are like telephone wires

Normal Nerve

Abnormal Nerve
Individual axons within the nerve

Normal Nerve

Nerve showing focal myelin stripping

Courtesy Alan Pestronk, MD

Neuropathic Symptoms

- Loss of sensation
- Pain: burning, stabbing, tingling
- Weakness
- Balance difficulties
Neuropathic Symptoms

- Imperative to be protective of your feet with loss of feeling
- More than 40,000 amputations per year are related to neuropathy
- Feet need to be cleaned daily
- Toe nails need to be cut weekly
- Always inspect feet
- Podiatry exams

Common Causes of Neuropathy

- Idiopathic---50%
- Diabetes
- Vitamin B12 def.
- Toxic Exposures
  - Chemotherapy
- Alcohol
- Hereditary
- Infections
  - HIV, Syphilis, Lyme

- Autoimmune disease
  - Our own immune system attacks our nerves
  - Often assoc with abnormal antibodies
  - IgG or IgM
Evaluation of Peripheral Neuropathy

- Confirm that it is a peripheral neuropathy
  - Mimics: Vascular insufficiency
  - Spinal Stenosis
  - Focal Podiatric Causes: tarsal tunnel, neuroma, plantar fasciitis
- Is the disease process demyelinating or axonal
  - EMG/NCVs
  - Blood tests to look for common causes
- Is there evidence that abnormal antibodies in the blood are directly attacking the nerve
  - Specific blood tests
- How progressive and disabling is the neuropathy
  - Consider muscle and nerve biopsy

Demyelinated vs Normal Nerve

![Graph showing CMAP and DL for Acute GBS and Recovery](image)

- Acute GBS: CMAP = 0.5 mV, DL = 12.9 ms
- Recovery: CMAP = 7.0 mV, DL = 4.9 ms
Legs Symptoms

- Walking versus resting
  - Many other things cause leg pain
  - Radiculopathy/ Stenosis
    - Often asymmetric
  - Vascular Claudication
    - Improves with rest period
  - Restless Leg Syndrome
  - Periodic Limb Movements
    - Treat with Parkinson’s meds

Sexual Symptoms

- Can affect the nerves that control normal sexual function.
- Males can experience difficulty with erection or sexual climax.
- Women can experience difficulty with achieving orgasm and vaginal dryness
- Libido is generally not affected
- May respond to ED drugs
  - Men and women
**Bladder Symptoms**

- Urinary incontinence is not a common problem
  - Can lead to loss of sensation which leads to overflow incontinence
  - Many other causes of urinary incontinence
    - Prostate in men
    - Muscle weakness in women
    - Diagnose the problem
      - Urologist
      - Urodynamic testing
    - Therapy
      - Anticholinergics
      - Rarely need catheterization

**Gastrointestinal Symptoms**

- Autonomic nervous system controls the peristalsis in the gut
- Gastric stasis (lack of motility) can occur causing severe symptoms
  - Many other causes for abdominal pain
    - GI evaluation
    - Radiographic and Laboratory evaluation
  - Severe pain or vomiting after eating
  - Weight loss
    - Smaller more frequent meals
    - Pro-motility drugs
- Lower intestinal problems are less common
  - Incontinence of bowels is very uncommon
Cardiac Symptoms

- Impaired control of heart-rate and blood pressure
  - Lightheadedness
  - Syncope
  - Fatigue
  - Palpitations

Cardiac Symptoms

- Evaluation often involves autonomic testing
- Tilt-table test
- Treatment
  - Increase baseline blood pressure
    - Stop anti-hypertensives
    - Increase fluid, salt, and caffeine intake
    - Keep Head of Bed elevated at night
    - Compression stockings
    - Drugs to increase blood pressure
Swallowing Problems

- Swallowing involves a complex interplay of sensing the movement of food in the mouth and coordinating muscle movement.

- Dysphagia
  - Choking
  - Weight Loss
  - Requires evaluation by GI or ST
    • Numerous causes for dysphagia

Causes of Dysphagia

- Head an Neck Surgery 36%
- Stroke 29%
- Closed Head Injury 7%
- Spinal Cord Injury 6%
- Neuromuscular Disease 6%
- Vocal Cord Problem 4%
- Zenker’s Diverticulum 2%
- Anxiety 2-5%
Emotional Side Effects

• Depression/ Anxiety
  – As many as 30% of chronic PN pts develop depression
  – Treatment options
    • Cognitive behavioral therapy/ Counseling
    • Exercise
    • Medications
      • SNRI- Cymbalta
      • SSRI
      • TCA

Sleep Dysfunction

• Very high percentage of patients have sleep problems associated with their neuropathy
  – Restless legs syndrome
  – Pain
  – Disrupted sleep architecture
  – Other causes of sleep problem
    • Sleep apnea
    • Insomnia
    • Need for sleep study to decide on therapy
Treatment of Painful Neuropathies

- Antiepileptic Medications
  - Gabapentin (Neurontin)
  - PreGabalain (Lyrica)
- Antidepressants
  - Duloxetine (Cymbalta)
  - Tricyclics: amitriptyline, nortriptiline
- Nutritional Supplements
  - Alpha Lipoic Acid
  - Acetyl L-carnitine
  - Metanx
- Chronic Pain Medications
  - Long acting opioids

PROTOCOLS FOR DIAGNOSIS AND MANAGEMENT OF NON-PAINFUL DIABETIC NEUROPATHY

ALLEN MARK JACOBS, DPM, FACAFS, FAPWCA, FASPS
DIABETIC NEUROPATHY

- MOST COMMON PERIPHERAL NEUROPATHY
- PATHOLOGIC BASIS REMAINS UNCLEAR
- NO UNEQUIVOCALLY EFFECTIVE THERAPY
- THERAPEUTIC GOALS:
  - INTERDICT SYMPTOMATOLOGY
  - PREVENT NERVE DEGENERATION
  - ENHANCE NERVE REGENERATION

YASUDA H., TERADA M., MAEDA K., ET AL. PROG NEUROBIOL 69 (4) 2003

RISK FACTORS FOR INFECTION

- INADEQUATE CONTROL 93%
- NEUROPATHY 88%
- PAD 74%
- SMOKING 56%
- HX PRIOR ULCERATION 28%
- PENETRATING INJURY 20%
- POOR FOOTWEAR 15%
- CHARCOT’S JOINT DISEASE 11%

OZKARA A, DELIBASI T, SELCOKI Y, ARKAN MF CENTRAL EUROPE JOUR OF MED 2008
### Symptoms and Signs of Diabetic Peripheral Neuropathy

#### Symptoms

**Small Fiber**
- Numbness or loss of feeling (asleep or "bunched up sock under toes" sensation)
- Prickling/Tingling
- Aching Pain
- Burning Pain
- Lancinating Pain
- Allodynia
- Defective Thermal Sensation
- Decreased Sweating

#### Signs

**Large Fiber**
- Diminished vibratory perception
- Decreased knee and ankle reflexes
- Reduced protective sensation such as pressure, hot and cold, pain
- Diminished ability to sense position of toes and feet
- Pain is deep, aching or cramping

### DIABETIC NEUROPATHY

- **66% PATIENTS WITH DM**
- **80% DPN**
- **50% SYMPTOMATIC**
- **10-20% ANTINOCICEPTIVE TX**

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RISK OF AMPUTATION

- **NEUROPATHY**
- ALTERED BIOMECHANICS
- INCREASED PLANTAR PRESSURE
- OSSEOUS DEFORMITY
- PAD
- PRIOR HISTORY OF ULCER OR AMPUTATION
- SEVERE TOENAIL PATHOLOGY

THE DIABETIC FOOT

SIMPLE, EVERYDAY PROBLEM

VASCULAR DISEASE
IMMUNOPATHY
DEFORMITY

SENSORY NEUROPATHY
MOTOR NEUROPATHY
AUTONOMIC
NEUROPATHY
NEUROPATHIC ULCERATION

DIABETES

PERIPHERAL NEUROPATHY

FOOT ULCER

NO INFECTION

CELLULITIS

OSTEOMYELITIS

AMPUTATION

DIABETIC FOOT ULCERS

• COMMON COMPLICATION OF DIABETES
• ANNUAL INCIDENCE 1% to 4%1-2
• LIFETIME RISK 15% to 25%3-4
• ~15% OF ULCERS RESULT IN AMPUTATION3,5
• ~85% OF AMPUTATIONS IN DIABETES PRECEEDED BY ULCERATION6-7
• PERIPHERAL NEUROPATHY A MAJOR FACTOR1-7

CAN AMPUTATIONS BE PREVENTED

- FROM 1998-2008 DM INCREASED FROM 5.4-17.1 MILLION
- BETWEEN 1996-2008 AMPUTATION RATES HAVE DECREASED 8.6%/YEAR
- AGE ADJUSTED AMPUTATION RATES DECREASED FROM 11.2/1000 IN 1996 TO 3.9/1000 IN 2008
- AMPUTATION RATES IN DM 8X GREATER
- NO CHANGE IN AMPUTATION RATE IN NON-DM

LI Y. DIABETES CARE 35 2012
“NON-PAINFUL” NEUROPATHY

- AUTONOMIC
  - NEUROPATHIC EDEMA
  - SUDOMOTOR ABNORMALITIES
  - VASOMOTOR ABNORMALITIES
  - CHARCOT’S JOINT DISEASE
- MOTOR
  - DIMINISHED ACHILLES’ REFLEX
  - ABNORMAL MUSCLE CONTRACTILE PROPERTIES
  - INTRINSIC MINUS FOOT
- SENSORY
  - ANESTHESIA

PROXIMAL MOTOR NEUROPATHY

- KNEE INSTABILITY
- DIFFICULTY STANDING
- DIFFICULTY WALKING
- DIFFICULTY WITH STAIRS, STEPS
- PAIN
ATROPHY OF THE FOOT MUSCLES IN DIABETES MELLITUS

• SMALL MUSCLE ATROPHY NOT INFREQUENTLY OCCURS PRIOR TO THE CLINICAL DETECTION OF NEUROPATHY
• ATROPHY IS COMMON
• STRONG ASSOCIATION BETWEEN DPN AND MUSCLE ATROPHY

GREENMAN R, KHAODHIAR L, LIMA C, DINH T, GIURINI J DIABETES CARE 28 (6) 2005

MOTOR NEUROPATHY: MANIFESTATIONS

• EARLY
  – LOSS OF ANKLE REFLEX
  – DEFORMITY OF TOES
• LATE
  – INABILITY TO STAND ON HEELS
  – ATROPHY OF FOOT MUSCLES
  – INSTABILITY, FALLS
MOTOR NEUROPATHY

HAMMERTOES ➔ ANTERIOR FAT PAD DISPLACEMENT

HAMMERTOES ➔ INCREASED PLANTAR PRESSURE

ULCERATED CALLUS
AUTONOMIC NEUROPATHY

- 30% patients with diabetes 1 or 2
- Silent myocardial infarction
- Postural hypotension
- Resting tachycardia
- Neurogenic bladder
- Intermittent diarrhea
- Hypoglycemic unawareness
- Sudomotor abnormalities
- Vasomotor abnormalities
- Neurogenic edema
- 53% vs 15% 5 year mortality

EWING DJ, CAMPBELL IW, CLARKE BF. QUAR. J. OF MED 49, 193: 1980
HUBEAX, K., DEFFIEUX, X., RAIBAUT, P ET AL. PELVI-PERINEOLOGIE 3 (3) 2008

AUTONOMIC NEUROPATHY

- Vasomotor abnormalities
- Sudomotor abnormalities
- Neuropathic edema
- Charcot’s joint disease
- Vascular calcification
PEDAL CONSEQUENCES OF AUTONOMIC DENERVATION

- INCREASED BLOOD FLOW
- RIGID, CALCIFIED ARTERIES
- SWEATING DIMINISHED OR ABSENT
- EDEMA

PODIATRIC CARE

- REGULAR VISITS
  - FOOT EXAMINATIONS
    - RISK FACTORS
    - NEUROPATHY, PAD, DEFORMITY
    - DETECTION OF PREULCERATIVE LESIONS
  - PROPHYLACTIC FOOT CARE
    - DEBRIDEMENT CALLUSES, NAILS
    - TREATMENT OF ONYCHOMYCOSIS, TINEA PEDIS
  - AGGRESSIVE MANAGEMENT OF LESIONS
    - DEBRIDEMENT
    - OFF-LOADING
    - WOUND CARE
  - RISK ASSESSMENT
  - RISK FACTOR INTERVENTION
Clinical Case Outcome I

INITIAL 6 MONTH STUDY

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SUMMARY

• NON-PAINFUL NEUROPATHY RESULTS IN SIGNIFICANT MORBIDITY

• RISK EVALUATION OF THE DIABETIC FOOT SHOULD INCLUDE;
  – MOTOR NEUROPATHY EVALUATION
  – AUTONOMIC NEUROPATHY EVALUATION
  – EVALUATION FOR SENSORY LOSS

Q & A