Signs of Neuromuscular Disorders that MUST NOT be Missed

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NEUROMUSCULAR DISEASE
RUSSELL N. DeJONG, M.D.
(1906-1990)

THE NEUROLOGIC EXAMINATION

Incorporating the Fundamentals of Neuroanatomy and Neurophysiology

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WITH 368 ILLUSTRATIONS

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“Not only is neurology closely linked to internal medicine, and not only do serious nervous system manifestations and complications accompany systemic disease, but these nervous system manifestations may be the first evidence of disease elsewhere in the body.”

- Russell N. DeJong, M.D.
“YET TODAY I CONSIDER MYSELF THE LUCKIEST MAN ON THE FACE OF THE EARTH.” July 4, 1939
MOTOR NEURON DISEASE

Slowly Progressive Motor Symptoms
   Usually Distal in Hands or Legs
Atrophy
Fasciculations: multifocal spontaneous muscle fiber twitches that do not move the limb.
Cramping
Bulbar Symptoms: dysarthria, dysphagia, drooling
Amyotrophic Lateral Sclerosis: must have clinical signs of both UMN and LMN dysfunction.
MND “mimics.”
AMYOTROPHIC LATERAL SCLEROSIS

UMN SIGNS:
spasticity
hyperactive reflexes
Babinski’s sign
(dementia)
(pseudobulbar affect)

LMN SIGNS:
fasciculations
atrophy
cramping
ALS MIMICS

Syringomyelia
Adult Onset Spinal Muscular Atrophy (SMA IV)
Progressive Muscular Atrophy
Juvenile Segmental Spinal Muscular Atrophy (Hirayama Disease)
Scapuloperoneal Spinal Muscular Atrophy (Davidenkow Disease)
X-Linked Spinobulbar Muscular Atrophy (Kennedy’s Disease)
Multifocal Motor Neuropathy with Conduction Block
Chronic Inflammatory Demyelinating Polyradiculoneuropathy
Neuralgic Amyotrophy (Parsonage-Turner Syndrome)
Inclusion Body Myositis
Cramp Fasciculation Syndrome
Benign Fasciculations
MOTOR NEURON DISEASE
MOTOR NEURON DISEASE
PROTOTYPIC NEUROPATHY

CHRONIC (8 WEEKS to YEARS)
SYMMETRIC and LENGTH DEPENDENT
SENSORY-PREDOMINANT SYMPTOMS

PARESTHESIAS +/- NUMBNESS

NO or MINIMAL WEAKNESS
SENSORY DEFINITIONS

NEGATIVE SYMPTOMS
Numb: lost sensation
Balance
  • Unsteadiness
  • Gait dysfunction
  • Frequent Falls

POSITIVE SYMPTOMS
Paresthesias: abnormal sensations in the absence of stimulation (burning, prickly, tingling, cold, “asleep”, etc.).
Dysestheisia: abnormal sensation in response to stimulation.
Allodynia: pain following stimulation that is not painful.
Hyperalgesia: increased pain evoked by a noxious stimulus.
PROTOTYPIC NEUROPATHY

Distal Sensory Deficits to Temperature, Vibration, Pin and/or Position Sense. Minimal Atrophy and Weakness of Distal Muscles. Hypoactive or Reduced Ankle Reflexes. Romberg’s Sign May or May Not be Present.
The Diagnostic Yield of a Standardized Approach to Idiopathic Sensory-Predominant Neuropathy

A. Gordon Smith, MD; J. Robinson St FASTING

Background: Peripheral neuropathy is a common problem that often provokes a lengthy and expensive diagnostic evaluation. A rational, evidence-based diagnostic approach to peripheral neuropathy is desirable. Prior studies have focused on patients presenting to a tertiary referral center with a diagnosis of unclassified neuropathy. However, most patients with peripheral neuropathy have primarily sensory symptoms. This study focuses on patients with sensory predominant neuropathy. The goal was to develop a focused diagnostic algorithm that can be easily applied in a general medical setting.

Methods: Patients referred with predominantly sensory symptoms and no previously defined cause were included and evaluated using a standardized approach.

Results: Among 138 patients, 25% had at least 1 first-degree relative with symptoms suggestive of neuropathy. Among laboratory studies, a 2-hour oral glucose tolerance test had the highest diagnostic yield (31%) and was more sensitive than other measures of glucose metabolism. Vitamin B12 deficiency was identified in 7 patients. Results of serum protein electrophoresis, immunofixation, and antimicrobial antibody testing were abnormal in less than 5% of patients, and these rates are similar to those found in the general population. Using this approach, only 31% of patients completing the recommended evaluation were found to have an idiopathic neuropathy.

Conclusions: Patterns with sensory-predominant neuropathy should be tested for glucose tolerance and vitamin B12 concentration. The significance of abnormalities of serum protein electrophoresis and antimicrobial antibodies is uncertain. Other tests should be performed only when the clinical scenario suggests it. Patients with atypical features may benefit from referral to a peripheral neuropathy center.

Arch Intern Med. 2004;164:1021-1025

Peripheral Neuropathy is one of the most common neurologic disorders encountered in general medical practice. Population-based estimates suggest that at least 2% to 7% of individuals may have neuropathy. 1 Although peripheral neuropathy is common, its evaluation frequently provokes feelings of diagnostic nihilism. Patients often undergo an extensive and expensive evaluation that frequently fails to reveal a definitive cause, and up to 30% of patients are left with a diagnosis of idiopathic neuropathy. 2 Several investigations have demonstrated an improved diagnostic yield with thorough evaluation of peripheral neuropathy and several rational diagnostic algorithms have been suggested. 3 These algorithms are largely based on identification of atypical features such as prominent weakness, asymmetry, proximal involvement, or autonomic failure, and accurate diagnosis often requires experience and expertise in peripheral nerve disease. Development of an algorithm that can be easily used in the primary care setting is desirable to minimize unnecessary laboratory testing and increase diagnostic yield.

Methods:

Patients presenting to our tertiary referral center with possible sensory peripheral neuropathy between July 2002 and July 2003 were eligible for the study. A thorough neurologic history of each patient was taken, with focus...
DIAGNOSTIC YIELD

138 patients with sensory symptoms:
- Paresthesias of the feet
- Numbness of the feet
- Painful feet

Clinical examination consistent with neuropathy:
- Distal sensory changes
- Absent or reduced ankle reflexes
- No significant weakness
DIAGONSTIC YIELD-POSITIVE RESULTS

2 hour OGTT: 61%
HbA1c: 26%
Fasting glucose: 11%
SPEP/Immunofixation: 3%
ANA: 3%
Vitamin B12: 2%
ESR: 0%
Folate: 0%
TSH: 0%
LABORATORY EVALUATION of PROTOTYPIC NEUROPATHY

ORAL GLUCOSE TOLERANCE TEST
- DIABETES
- IMPAIRED GLUCOSE TOLERANCE
- MORE SENSITIVE THAN HbA1C OR FASTING BLOOD GLUCOSE

B12: METHYLMALONIC ACID +/- HOMOCYSTEINE if B12 LEVEL LOW NORMAL

SPEP with IEF: ASSOCIATION WITH DEMYELINATING NEUROPATHIES ESTABLISHED but NOT CLEAR FOR THE MORE COMMON AXONAL SENSORY-PREDOMINANT NEUROPATHIES.

LIPID PROFILE: METABOLIC SYNDROME NOW CONSIDERED RISK FACTOR for NEUROPATHY.
MYASTHENIA GRAVIS

Fluctuating Symptoms

Ptosis
Diplopia
Facial Weakness
Dysarthria
Dysphagia
Dyspnea
Arm and/or Leg Weakness

Examination Attempts to Provoke these Symptoms with Repetitive or Sustained Activity.
MYASTHENIA GRAVIS
MYASTHENIA GRAVIS
MYASTHENIA GRAVIS

Acetylcholine Receptor Antibody
Striated Muscle Antibody
  Positive Predictive Value for Thymoma when AChR-Ab and Str-Ab present:
    50% when diagnosed before 40 years of age
    < 9% after 40 years

TSH

MuSK Antibody?
  Females with prominent bulbar symptoms

Trial of Mestinon 30 to 60 mg tid

Tensilon Test?
MYOSITIS

Progressive Proximal > Distal Muscle Weakness
CK Levels can Range from Normal to Very High
Pain and Tenderness May or May Not be Present
Sensation Usually Normal Unless Coincidental Neuropathy
Reflexes Usually Normal
  may be reduced if muscles very weak
Other Systemic Signs Frequently May Be Present
  skin
  joint
  cardiac
  pulmonary
  gastrointestinal
1. Symmetric proximal muscle weakness (hip, shoulder, neck flexors), progressive over weeks to months.
3. Heliotropic eyelid/periorbital rash, Gottron’s sign, erythematosis dermatitis over face, neck, joints:
   - Definite PM—4 of the first criteria
   - Definite DM—3 of 4 with rash
   - Probable PM—3 of the first 4
   - Probable DM—2 of the 4 with rash
   - Possible PM—2 of the first 4
   - Possible DM—1 of the 4 with rash
4. Elevation of serum muscle enzyme
5. Electromyography evidence of myopathy: fibrillation, positive sharp waves, myopathic motor unit potentials
DERMATOMYOSITIS v POLYMYOSITIS
MYOSITIS DIFFERENTIAL DIAGNOSIS

Polymyositis
Dermatomyositis
Inclusion Body Myositis
Necrotizing Myositis

Drugs
Connective Tissue Disease
Paraneoplastic
Immune Mediated Necrotizing Myopathy
# Toxic Myopathy

<table>
<thead>
<tr>
<th>Inflammatory Myopathy</th>
<th>Rhabdomyolysis &amp; High CK ± Chronic myopathy</th>
<th>Painful myopathy ± Rhabdomyolysis</th>
<th>Myalgia ± Myopathy</th>
<th>Cramps</th>
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<tbody>
<tr>
<td><strong>Definite</strong></td>
<td>Alcohol, (\varepsilon)-Amino Caproic Acid, Amphetamines, Anti-Psychotics, Loxapine, Quetiapine, Cocaine, Cyclosporine, Hypokalemia, Isoniazid, Lipid lowering agents, Fibrates, Bezafibrate, Clofibrate, Gemfibrozil, Statins, Lovastatin, Simvastatin, Pravastatin, Fluvastatin, Atorvastatin, Cervistatin, Red yeast rice, Lithium, Mibefradil, Neuroleptic-Malignant, Propofol, Zidovudine</td>
<td>Colchicine, Emetine, Germanium, Hypervitaminosis E, Taxanes, Zidovudine</td>
<td>All-Trans-Retinoic Acid, Azathioprine, Bryostatin 1, Captopril, Ciguatoxin, Corticosteroids, Withdrawal, Cytotoxics, Danazol, Enalapril, Gemcitabine, Gold, Interferon (\alpha)-2a, Interferon (\alpha)-2b, Isotretinoin, Ketorolac, Labelatal, Methotrexate, Metolazone, Mycophenolate mofetil, Paclitaxel, Retinoids, Rifampin, Spanish toxic oil, Suxamethonium (Succinylcholine), Tyrosine kinase inhibitors, Vinca alkaloids, Zimeldine</td>
<td>Albuterol, Anti-Cholinesterase, Bergamot (bergapten), Caffeine, Clofibrate, Cyclosporine, Diuretics, Labetalol, Lithium, Nifedipine, Terbutaline, Tetanus, Theophylline, Vitamin A</td>
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<tr>
<td><strong>Possible</strong></td>
<td>Cimetidine, Interferon-(\alpha), Ipecac, Levodopa, Levodopa, Penicillin, Phenytoin, Propylthiouracil, Proton pump inhibitors, Sulfonamide</td>
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*Source: neuromuscular.wustl.edu*
NECROTIZING MYOSITIS v POLYMYOSITIS
INCLUSION BODY MYOSITIS
INCLUSION BODY MYOSITIS
INCLUSION BODY MYOSITIS v POLYMYOSITIS
INCLUSION BODY MYOSITIS