TWO CASES OF WEAKNESS

Huntsville Rounds February 7, 2018
By: Nancy Bozek
The Planning Committee for this event has done the following in the interest of Mitigating Potential Bias:

- All PPC members and speakers have signed a COI form.
- All speakers have been emailed the certification/accreditation requirements for their presentation.
- Each presentation will be reviewed by the Academic Coordinator prior to its delivery. The coordinator will be looking for any signs of bias including use of brand names and logos of pharmaceutical companies.
- If bias is detected the PPC would review it and the speaker would be notified so that the bias can be corrected before the presentation is given. If the bias cannot be corrected or removed the session would be cancelled.
- If a bias is detected by a planning committee member during the presentation they would question the speaker about it.
- All biases would be reviewed at the next PPC meeting.
OBJECTIVES

After attending this session participants will be able to:

- Describe the approach to weakness
- Discuss causes of gait and balance disorders in older adults
- Present two interesting cases and their diagnosis
CONFLICTS OF INTEREST

I have no personal or financial conflicts to disclose
What percentage of people over the age of 65 have difficulty walking 3 city blocks or climbing 1 flight of stairs?

a) 10%
b) 20%
c) 30%
d) 40%
Approach to the adult patient with the complaint of weakness

Objective muscle weakness

Yes

Generalized
- Cachexia
- Myasthenia gravis (worse with exertion)
- Periodic paralysis

Localized

Asymmetric
- Regional neurologic disorders
- Cerebrovascular or spinal cord disease
- Demyelinating disorders
- Compression neuropathy
- Mononeuropathy/mönoneuritis multiplex
- Disuse atrophy
- Myasthenia gravis

Symmetric

Specific pattern
- Muscular dystrophy
- Hereditary neuropathy
- Myasthenia gravis

Proximal
- Myopathy
- Duchenne muscular dystrophy
- Myasthenia gravis

Distal
- Peripheral neuropathy
- Motor neuron disease
- Myasthenia gravis

No

Cardiopulmonary disease
- Anemia
- Chronic infection
- Malignancy
- Depression
- Deconditioning
- Arthritis
- Fibromyalgia
CLUES TO MUSCLE WEAKNESS

• Complain of inability to perform tasks such as stairs, getting out of tub
• Rarely have pain
• Muscle tenderness occurs with infectious myopathies
MEDICAL CONDITIONS AND RISK FACTORS FOR GAIT AND BALANCE DISORDERS

- Psych
  - Depression
  - Fear of falling
  - Sleep disorders
  - Substance abuse

- Cardiac
  - Arrhythmias
  - CHF
  - Coronary artery disease
  - Orthostatic hypotension
  - Peripheral arterial disease
  - Thromboembolic disease
MEDICAL CONDITIONS AND RISK FACTORS FOR GAIT AND BALANCE DISORDERS CONTINUED

• Infectious and metabolic
  • Diabetes
  • Hepatic encephalopathy
  • HIV associated neuropathy
  • Hyper/hypo thyroidism
  • Obesity
  • Tertiary syphilis
  • Uremeia
  • Vit B12 deficiency

• MSK disorders
  • Cervical spondylosis
  • Gout
  • Lumbar spinal stenosis
  • Muscle atrophy
  • Osteoarthritis
  • Osteoporosis
  • Podiatric conditions
MEDICAL CONDITIONS AND RISK FACTORS FOR GAIT AND BALANCE DISORDERS CONTINUED

- Neurologic disorders
  - Cerebellar dysfunction
  - Delirium
  - Dementia
  - Multiple sclerosis
  - Myelopathy
  - Normal pressure hydrocephalus
  - Parkinson's disease
  - Stroke
  - Vestibular disorders

- Sensory disorders
  - Hearing impairment
  - Peripheral neuropathy
  - Visual impairment

- OTHER
  - Acute illness
  - Recent surgery
  - Some medications
The “get up and go test” involves standing up from a chair, walking forward 3 meters, turning around and walking back to the chair then turning to be seated.

For an average 70 year old it should take:

a) 8 seconds
b) 9 seconds
c) 11 seconds
A meta-analysis of 12,800 adults over the age of 60 did not show a difference in scores between fallers and non-fallers who were living independently (J Am Geriatr Soc 2013).

In the AFP article it was reported to be 87% sensitive and 87% specific for identifying older adults who are prone to falls.

They used <10 seconds as normal, 14 seconds or more is abnormal and associated with an increased risk of falls.
GROUP EXERCISE, HOME EXERCISE AND TAI CHI REDUCE THE RISK OF FALLING AND THE RATE OF FALLING

TRUE OR FALSE
MR BW AGE 74

- Presented age 68 in 2013 with weakness in both feet, said his feet were “flopping” when he walked
- 2 years prior was able to run
- 5 yr history of L arm problems with a weak fist- not better with physio
- Progression gait issues over 2 years
- Trouble with stairs, had to “pull himself up”
- No proximal limb issues – able to raise arms over head
- Had a fall with no warning or LOC
PAST HISTORY

- Macular degeneration
- Sarcoidosis which has never required treatment
- Squamous cell on rt face treated by resection and radiation 2009
EXAMINATION

• Power 4/5 lower limbs
• Reflexes 1+ bilaterally
• Sensation was normal with pinprick but decreased with vibration
• Co-ordination was normal
• “steppage gait”
• Unable to heel or toe walk
• Distal Weakness > proximal
VIDEO OF STEPPAGE GAIT
FOR 300 POINTS...

Your next step should be?
• DDX
  • Myopathy – poly or inclusion body
  • Motor neuron disease
  • Polyradiculopathy

• Investigations
  • MRI head- (mild to moderate atrophy)
    cervical and lumbar- normal
  • EMG- changes in keeping with myopathy
  • CK 574
  • ESR 25
  • ANA, RF, lyme serology, west nile- neg
  • Muscle biopsy 2013 of rt quad- inclusion body myositis cannot R/O polymyositis
<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Site of lesion</th>
<th>Site of lesion</th>
<th>Site of lesion</th>
<th>Site of lesion</th>
<th>Site of lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper motor neuron</td>
<td>Leukodystrophies</td>
<td>Spinal muscular atrophy</td>
<td>Peroneal muscular atrophy</td>
<td>Myasthenia gravis</td>
<td>Muscular dystrophies</td>
</tr>
<tr>
<td>Anterior horn cell</td>
<td>Vasculitis</td>
<td>Amyotrophic lateral sclerosis</td>
<td>Guillain-Barre</td>
<td>Myasthenia gravis</td>
<td>Polymyositis</td>
</tr>
<tr>
<td>Peripheral nerve</td>
<td>Brain abscess</td>
<td>Poliomyelitis</td>
<td>Leprosy</td>
<td>Botulism</td>
<td>HIV</td>
</tr>
<tr>
<td>NM junction</td>
<td>Brain tumor</td>
<td>Paraneoplastic syndrome</td>
<td>Myeloma/amyloid</td>
<td>Eaton-Lambert syndrome</td>
<td>Malignancy-associated myositis</td>
</tr>
<tr>
<td>Muscle</td>
<td>Radiation</td>
<td>Lead</td>
<td>Lead</td>
<td>Organophosphate poisoning</td>
<td>Steroid</td>
</tr>
<tr>
<td></td>
<td>Vitamin B12 deficiency</td>
<td>Diabetes</td>
<td>---</td>
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<td>Hypothyroid</td>
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<td></td>
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<td></td>
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<td>Hypoglycemia</td>
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</tbody>
</table>
• Muscle weakness
  • Proximal > distal
  • Fatigue
  • Difficulty with getting out of tub/chair, going up stairs
  • Difficulty with overhead tasks
  • May affect respiratory muscles
  • Bulbar weakness — speech, swallowing, oculomotor, facial
MR BW UPDATE

• Treated for 4-6 mo with 60 mg prednisone in case it was polymyositis
• No clinical change so therapy stopped, CK dropped to 46
• Current meds: lyrica 150 mg bid and fentanyl 12.5 mg q 3 d
• Indwelling foley for neurogenic bladder
• Spends most of his time in his reclining chair, only able to do transfers but is still at home with his wife
## Major causes of myopathy

<table>
<thead>
<tr>
<th>Inflammatory</th>
<th>Drugs and toxins</th>
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<tbody>
<tr>
<td>Polymyositis</td>
<td>Illicit drugs - cocaine, heroin</td>
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<tr>
<td>Dermatomyositis</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Inclusion body myositis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Juvenile dermatomyositis</td>
<td>Other - colchicine, antimalarial drugs, HMG-CoA</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>reductase inhibitors, penicillamine, zidovudine</td>
</tr>
<tr>
<td>Overlap syndromes - lupus, scleroderma,</td>
<td></td>
</tr>
<tr>
<td>rheumatoid arthritis, Sjögren's syndrome</td>
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<td>Rheumatoid arthritis, Sjögren's syndrome</td>
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<tr>
<td><strong>Endocrine disorders</strong></td>
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<tr>
<td>Hypothyroidism</td>
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<tr>
<td>Cushing's syndrome (or exogenous steroid</td>
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<tr>
<td>administration)</td>
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<td></td>
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<tr>
<td><strong>Electrolyte disorders</strong></td>
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<tr>
<td>Hypokalemia</td>
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<tr>
<td>Hypophosphatemia</td>
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<tr>
<td>Hypocalcemia</td>
<td></td>
</tr>
<tr>
<td>Hypernatremia or hyponatremia</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic myopathies</strong></td>
<td></td>
</tr>
<tr>
<td>Disorders of carbohydrate, lipid, and</td>
<td></td>
</tr>
<tr>
<td>purine metabolism</td>
<td></td>
</tr>
</tbody>
</table>

### Infections
- Viral - influenza, para influenza, Coxsackie, HIV, cytomegalovirus, echovirus, adenovirus, Epstein-Barr virus
- Bacterial - pyomyositis, lyme myositis
- Fungal
- Parasitic - trichinosis, toxoplasmosis

### Rhabdomyolysis
- Crush trauma
- Seizures
- Alcohol abuse, including hyperkinetic state with delirium tremens
- Exertion, especially with environmental heat illness
- Vascular surgery
- Malignant hyperthermia

### Inherited myopathies
- Acid maltase deficiency
- Muscular dystrophy

HIV: human immunodeficiency virus.
Power of 3/5 means

a) The patient is able to move the limb with gravity eliminated
b) The patient is able to move the limb against gravity
c) The patient is able to move against resistance a little
INCLUSION BODY MYOSITIS

- Most common inflammatory myopathy in people over 50 yrs
- 7.9 cases per million
- Starts insidiously
- May be asymmetric
- Earlier features: involvement of distal muscles, atrophy of forearms and quadriceps, frequent falls due to quadriceps muscle weakness, mild facial muscle weakness
- Dysphagia occurs in 50%
- Inflammation is perivascular
- May get camptocormia
AND FOR 500 POINTS...

What is camptocormia?

a) Head drop
b) Weakness of the voice when doing a camp cheer
c) Bending forward of the spine
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Dermatomyositis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pattern of muscle weakness</strong></td>
<td>Subacute onset of proximal symmetric weakness with characteristic skin rash in patients of any age</td>
</tr>
<tr>
<td><strong>Creatine kinase level</strong></td>
<td>High, up to 50 times the upper limit of normal; can at times be normal</td>
</tr>
<tr>
<td><strong>Electromyography</strong></td>
<td>Myopathic units (active and chronic)</td>
</tr>
<tr>
<td><strong>Muscle biopsy</strong></td>
<td>Perivascular, perimysial, and interfascicular inflammation; necrotic fibers in &quot;wedge-like&quot; infarcts; perifascicular atrophy; reduced capillaries†</td>
</tr>
<tr>
<td><strong>Autoantibodies</strong></td>
<td>Anti-MDA-5, anti-Mi-2, anti-TIF-1 and anti-NXP-2 (implicated in cancer-associated dermatomyositis)</td>
</tr>
<tr>
<td><strong>Magnetic resonance imaging</strong></td>
<td>May show active inflammation, could guide biopsy site</td>
</tr>
</tbody>
</table>

* Drug-induced myopathies (e.g., penicillamine, statins, or antiretrovirals), inflammatory dystrophies (such as those due to mutations in the genes encoding dysferlin, calpain, or anoctamin); Becker's muscular dystrophy; facioscapulohumeral muscular dystrophy; or myofibrillar myopathies), inclusion-body myositis, necrotizing autoimmune myositis, metabolic myopathies, and fasciitis or fibromyalgia need to be ruled out.
† Similar pathologic changes in the perifascicular, perimysial, and interfascicular areas (to a lesser degree of severity) can be seen in overlap myositis (without skin lesions) or the antisynthetase syndrome.
‡ Metabolic muscle diseases presenting as myoglobinuria and toxic or drug-induced myopathies need to be ruled out.
§ In clinicl included myositis, when patients have the typical inclusion-body myositis phenotype, vacuoles are absent; such patients are erroneously thought to have polymyositis because of polymyositis-like inflammation; ragged-red fibers or cytochrome oxidase-negative fibers are frequently present and are helpful in diagnosis.
¶ TDP43 and p62 deposits, detected with the use of immunostaining, have been proposed as tissue biomarkers.
LMN

- Flaccid
- Hypotonic
- Hyporeflexic
- Denervation
  Atrophy
- Babinski -ve
- Less muscle contraction
- Less muscle tone
- Less muscle reflexes
- Less muscle innervation
- Toes point down

UMN

- More
- Spastic
- Hypertonic
- Hyperreflexic
- More
- Disuse Atrophy
- More
- Toes point up
- Babinski +ve
Upper motor neuron impairment can occur with the common acute stroke syndromes, space occupying lesions of the central nervous system, and lesions of the spinal cord. Spinal cord lesions can be related to trauma, infection, tumor, vascular anomalies, hypertrophic degenerative skeletal changes, demyelinating diseases, and congenital leukodystrophies.

Lesions of the Upper Motor Neurons

Diagnosis can be made with MRI of the brain and spinal cord.
• Weakness due to involvement of the anterior horns cells is seen in motor neuron disease, (ALS) familial spinal atrophy, lead poisoning, and poliomyelitis, West Nile and other virus infections
AND FOR 200 PTS…

What is Gowers Sign?
LESIONS OF THE PERIPHERAL NERVOUS SYSTEM

- Symmetric polyneuropathy may be a sequela of diabetes mellitus or a variety of toxic or metabolic insults, as well as heritable disorders.
- Mononeuropathy may be the result of nerve compression (i.e. carpal tunnel syndrome)
- Mononeuropathy multiplex (i.e. asymmetric polyneuropathy) occurs in diabetes mellitus or one of the vasculitic syndromes such as polyarteritis nodosa
MYOPATHIES

- inflammatory disorders, endocrinopathies, metabolic myopathies, drugs and toxins, infections, and the various causes of rhabdomyolysis
- muscular dystrophies - age is clue
- Medication, alcohol, or substance-abuse may be a clue to drug-induced myopathy
- Endocrinopathy, such as thyroid dysfunction (hypo or hyperthyroidism) or Cushing's syndrome
- Inflammatory myopathy should be suspected if there is symmetric proximal muscle weakness
CASE 2: MRS NS

Age 73
June 2013 having issues with L knee pain, had a cortisone shot with some relief

Xray showed only mild OA

Aug 2013 – ongoing pain, still feels like L leg is going to give out

Sept 2013 – saw Dr. Smyth, he felt that the pain was related to hip OA

She had a L hip replacement

May 2014- L knee slowly improving but it gave out and she fell – no injury

Next 2 yrs, mult visits for urine incontinence, memory concerns and not fully recovering from her L hip surgery
HISTORY CON’T

• Aug 2016 – fear of falling, feels like she is going backward, fell into frig
• Using walking poles, trouble getting out of the tub
• Sept 2016- “can’t get feet to move right when gets out of bed”
• Using rollator at times or walking poles
• Trouble rolling over in bed
• Gait slow and shuffling, no rest tremor
FINALLY....
• Freq falls – 4 a month
• Dragging rt foot
• Trouble getting up out of a chair
• No speech or swallowing issues
• No tremor cogwheeling or bradykinesia
• Spastic lower extremity
• Weakness 4+/5 in hip and knee flexors
• Increased reflexes, bilat babinski
• Positive hoffman sign
• Spastic gait
AND FOR 500 POINTS…

What is a Hoffman sign?
VIDEO OF HOFFMAN SIGN
INVESTIGATIONS

• MRI cervical – no myelopathy
• EMG (Dr. Lapp) – widespread motor unit remodeling, consistent with a motor neuron disease
• B12, West Nile, Lyme, lead mercury levels all normal
• Discussed possibility of Amyotrophic lateral sclerosis (ALS) and referred to Sunnybrook clinic
ALS CLINIC

- Repeated EMG several times
- Not definitive initially
- Still considered possible thoracolumbar polyradiculopathy
- Initially felt it was possible upper motor neuron dominant ALS or PLS
- Now 6 months later, they feel more conclusively that it is ALS
- She did a trial of riluzole which is felt to decrease glutamate release but stopped it due to side effects
ACCORDING TO COCHRANE...

Riluzole increases survival in ALS by

a) 3 month
b) 6 months
c) 1 year
• In December they noted a more obvious tremor which she told me she has made them aware of for the last year
• She was sent to another neurologist at Sunnybrook and started on Levodopa
• Now she is on Levocarbidopa (100/25) tid
• She is able to cross her L leg over her right when sitting and roll over in bed for the first time in months
TEAM INVOLVEMENT

- Palliative care
- SLP – voice recorder
- PT/OT
- Nursing via CCAC
AND FOR 300 POINTS…

Who was Lou Gehrig?
WHAT IS ALS?

• Progressive paralytic disorder characterized by degeneration of motor neurons in the brain and spinal cord
• Typically death occurs in 3-5 yrs from respiratory paralysis
• Diagnosis is primarily clinical in conjunction with EMG to confirm denervation and lab tests to rule out reversible disorders that resemble ALS
Failure leads to muscle spasticity and stiffness.

When affected they show excessive electrical irritability (fasciculations) then later get atrophy.

1/3 of cases are bulbar at onset with difficulty chewing, speaking, or swallowing.
WHAT IS PLS (PRIMARY LATERAL SCLEROSIS)?

- Selective involvement of corticospinal and corticopontine motor neurons
- Very little lower motor neuron dysfunction
EPIDEMIOLOGY

- 3-5 cases per 100,000
- 10% of cases are familial
- In sporadic ALS males: females is 2:1
- Most frequent neurodegenerative disorder of midlife
- Onset mid-late 50's
- Earlier onset is indicative of familial ALS
- Time from onset of symptoms to diagnosis is 12 months
FRONTOTEMPORAL DEMENTIA

• 15-20% of ALS patients have progressive cognitive decline with behavioral changes
• This correlates with autopsy findings of degeneration of the frontal and temporal lobes
CONCEPTS IN PATHOGENESIS

• 3 Cellular and molecular events lead to motor neuron degeneration:
  • Protein homeostasis
  • RNA homeostasis and trafficking
  • Cytoskeletal dynamics
HOW DOES RILUZOLE WORK?

• Suppresses excessive motor neuron firing
SYMPTOM MANAGEMENT

• NG feeds
• Prevention of aspiration by controlling salivary secretions and use of cough assist devices
• Provision of ventilatory support such as bi pap
AND LAST QUESTION FOR 200 POINTS…

What environmental risk has been shown to correlate most with non familial ALS?

a) smoking
b) military service
c) exposure to heavy metals
d) occupational exposure to electromagnetic fields
REFERENCES

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- INFLAMMATORY MUSCLE DISEASE NEJM 2015;372:1734-1747
- INTERVENTIONS FOR PREVENTING FALLS IN OLDER PEOPLE LIVING IN THE COMMUNITY – COCHRANE REVIEW