HEADACHES, MOTOR DISORDERS, AND AMYOTROPHIES

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I have no relevant financial or nonfinancial relationships in the products or services described, reviewed, evaluated or compared in this presentation.
28-year-old female has a throbbing, one-sided headache three times a month. It occurs suddenly, persists for 2 days. This is what type of headache?

• A. Migraine with aura
• B. Migraine without aura
• C. Tension-type headache
• D. Cluster headache
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- C. Tension-type headache
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• Answer: Cluster Headache (D)
Migraines

- Unilateral, intermittent, throbbing
- Lasts 4 hours-3days
- Light sensitive/sound sensitive
- Associated with prodrome
- Aura- scintillating scotomas
- Triggers
- Acephalic- abnormal transient transient dysfunction No pain
Headaches, Motor Disorders, Amyotrophies

• General Classification of Headaches
  • Migraine
  • Tension
  • Cluster
  • Coital
  • Post-Traumatic
  • Temporal Arteritis
  • Pseudotumor Cerebri
  • Thalamic
Headaches, Motor Disorders, Amyotrophies

- **Treatment**
  - Acute
    - Serotonin agonists (Triptans)
    - NSAIDS
    - Ergotamine
    - Dopamine antagonists
    - Narcotics- rarely recommended
    - DHE IV- severe
  - Chronic- Botulinum Toxin A
Headaches, Motor Disorders, Amyotrophies

Prophylactic

- Beta blockers
- Tricyclic Antidepressants
- Divalproex
- Topiramate
Cluster Headaches

Occur daily for weeks then stop
Ice pick like
Associated with REM or early AM
“Worst Pain” known
Pain peaks in 5-10 min then throbs 2 hours
Ipsilateral Horner’s syndrome
Male
Drinkers and Smokers
Tall and THIN and Hazel eye color
Headaches, Motor Disorders, Amyotrophies

Treatment

- 5-HT1 Receptor agonists
- Triptans/Ergot Alkaloids
- Oxygen 8-10 L/min
- Lidocaine intranasal drops
- Corticosteroids
- Prophylactic = Calcium Channel Blockers
Headaches, Motor Disorders, Amyotrophies

- **Tension**
  - Chronic muscle contraction
  - Can have vascular component
  - Daily
  - Bilateral
  - Tight band feeling
  - Non throbbing
Headaches, Motor Disorders, Amyotrophies

Treatment
- NSAIDS
- Muscle Relaxants
- Tricyclics
- Beta Blockers
Headaches, Motor Disorders, Amyotrophies

• Other Headaches:

Coital
  • Benign  TX: Propanolol / Indomethacin

Post-Traumatic
  • Vascular  TX: same as migraine

Temporal Arteritis
  • >55 yr old
  • Sudden onset
  • Temporal artery tenderness
  • Elevated ESR- usually >60 Tx: Biopsy/Steroids

Pseudotumor Cerebri
  • Obese premenopausal women
  • Diplopia/headache visual field loss papilledema
  • CSF=>250 mm H2O  Tx: Diuretic/Steroids

Thalamic
  • Severe/debilitating after infarct usually has hemianesthesia
Headaches, Motor Disorders, Amyotrophies

**Motor Disorders:**
- Parkinsons Disease
- Progressive Supranuclear Palsy
- Huntingtons Chorea
- Essential Tremors
- Tardive Dyskinesia
- Neuroleptic Malignant Syndrome
- Tic Douloureux
- Giles de la Tourette
- Torticollis
- Meige Syndrome
- Creutzfeldt-Jakob disease
Parkinson's Disease

Clinical Diagnosis solely
Decrease dopamine producing cells in the substantia nigra

Signs/Symptoms:
- Resting Tremor
- Rigidity
- Retarded movement
- Loss of postural reflexes
Table 1. Common Presentations of Parkinson's Disease.

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Parkinsonism</th>
<th>Differential Diagnosis</th>
<th>Distinguishing Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor</td>
<td>Asymmetric rest tremor</td>
<td>Essential and other tremors</td>
<td>Symmetric postural and action tremor</td>
</tr>
<tr>
<td>Clumsy or weak limb</td>
<td>Bradykinesia</td>
<td>Carpal tunnel syndrome, radiculopathies, and stroke</td>
<td>Altered reflexes, sensation, and strength</td>
</tr>
<tr>
<td>Stiff or uncomfortable limb</td>
<td>Rigidity</td>
<td>Musculoskeletal syndromes</td>
<td>Pain and limitation of movement</td>
</tr>
<tr>
<td>Gait disorder</td>
<td>Asymmetric slowness, shuffling, reduced arm swing, minimal or no imbalance</td>
<td>Multiple ischemic lesions in the brain, hydrocephalus, and musculoskeletal disorders</td>
<td>Symmetric shuffling, retained arm swing, wide-based gait, prominent imbalance, limited movement at knee and hip</td>
</tr>
</tbody>
</table>
Headaches, Motor Disorders, Amyotrophies

• Treatment

• Increase the Dopamine
  Decrease the Acetylcholine
  Dopaminergic is most sucessful
  levodopa/carbidopa (Sinemet® or Atamet®)
  Anticholinergics-Artane
  Parlodel/Eldepryl/Mirapex/
  Ropinirole (Requip, Requip XL)
  Rasagiline (Azilect)
  Apomorphine (Apokyn)
  Amantadine
  Toicapone-COMT
  Entacapone-COMT

Deep Brain Stimulation
Surgery-Palliodotomy
Table 2. Initial Therapy for Symptoms in Parkinson’s Disease.*

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Example</th>
<th>Initial Dose</th>
<th>Final Dose</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line dopaminergic agents</strong></td>
<td><strong>Carbidopa plus levodopa</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate release (Sinemet)</td>
<td>25 mg carbidopa, 100 mg levodopa</td>
<td>1/2 tablet three times daily</td>
<td>1 to 2 tablets three times daily</td>
<td>At initiation: anorexia, nausea, vomiting, dizziness, hypotension (a 1:4 ratio of carbidopa:levodopa reduces gastrointestinal symptoms), long-term therapy: motor fluctuations, dyskinesias, confusion, hallucinations</td>
</tr>
<tr>
<td>Controlled release (Sinemet-CR)</td>
<td>25 mg carbidopa, 100 mg levodopa</td>
<td>1 tablet three times daily</td>
<td>—</td>
<td>Same as for immediate-release preparations</td>
</tr>
<tr>
<td></td>
<td>50 mg carbidopa, 200 mg levodopa</td>
<td>1/2 tablet three times daily</td>
<td>1 tablet three times daily</td>
<td></td>
</tr>
<tr>
<td>Carbidopa plus levodopa plus entacapone (Stalevo)</td>
<td>12.5 mg carbidopa, 50 mg levodopa, 200 mg entacapone</td>
<td>1 tablet three times daily</td>
<td>—</td>
<td>Same as with preparations above, plus diarrhea</td>
</tr>
<tr>
<td></td>
<td>25 mg carbidopa, 100 mg levodopa, 200 mg entacapone</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.5 mg carbidopa, 150 mg levodopa, 200 mg entacapone</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td><strong>Dopamine agonists</strong></td>
<td></td>
<td></td>
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<tr>
<td>Nonergot</td>
<td>Pramipexole (Mirapex)</td>
<td>0.125 mg three times daily</td>
<td>0.5–1.5 mg three times daily</td>
<td>Nausea, vomiting, hypotension, ankle edema, excessive daytime sleepiness, compulsive behavior, confusion, and hallucinations</td>
</tr>
<tr>
<td>Ropinirole (Requip)</td>
<td>0.25 mg three times daily</td>
<td>3–8 mg three times daily</td>
<td>—</td>
<td>Same as for pramipexole</td>
</tr>
<tr>
<td>Ergot</td>
<td>Pergolide (Permax)</td>
<td>0.05 mg three times daily</td>
<td>1 mg three times daily</td>
<td>Same as for nonergot drugs plus retroperitoneal, pulmonary, and cardiac fibrosis</td>
</tr>
<tr>
<td><strong>Second-line alternatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticholinergic agents</td>
<td>Trihexyphenidyl (Artane)</td>
<td>1 mg three times daily</td>
<td>2 mg three times daily</td>
<td>Impaired memory, confusion, constipation, blurred vision, urinary retention, xerostomia, and angle-closure glaucoma</td>
</tr>
<tr>
<td></td>
<td>Benztrapine (Cogentin)</td>
<td>0.5 mg twice daily</td>
<td>1 mg twice daily</td>
<td>Same as for trihexyphenidyl</td>
</tr>
<tr>
<td>Selective MAO-B inhibitors</td>
<td>Selegiline (Eldepryl)</td>
<td>5 mg daily</td>
<td>5 mg twice daily</td>
<td>Insomnia, nausea, anorexia, hallucinations, potential for interactions with SSRIs and meperidine</td>
</tr>
<tr>
<td>NMDA antagonist</td>
<td>Amantadine (Symmetrel)</td>
<td>100 mg twice daily</td>
<td>100 mg twice daily</td>
<td>Dizziness, insomnia, nervousness, livedo reticularis, hallucinations, confusion</td>
</tr>
</tbody>
</table>

* All antiparkinsonian drugs are started at low doses and increased slowly to reduce adverse effects. Likewise, slow withdrawal of these drugs after long-term treatment is prudent to avoid a marked worsening of parkinsonism or even the neuroleptic malignant syndrome (discussed by Keyser and Rodnitzky®). MAO-B denotes monoamine oxidase B, SSRI selective serotonin-reuptake inhibitor, and NMDA N-methyl-D-aspartate.
Progressive Supranuclear Palsy
Similar to Parkinson's
Erect Posture
Hyperextension Neck
No tremor
Vertical Ophthalmoplegia - can't look up or down
Over 2 yrs unable to walk
No treatment
Headaches, Motor Disorders, Amyotrophies

Huntingtons Chorea

Inherited
Autosomal Dominant
Hemiballismus
Facial twitching
Rigidity/Dystonia

Lab:

- H-D Gene
- Decreased GABA
- CT/MRI= Bulge of Caudate Nucleus/ enlarged ventricles

Treatment:

- Tetrabenazine
- Amantadine or Riluzole
Benign Tremor (Essential)

Not to be confused with Normal tremor

7 Hz

Autosomal Dominant

Treatment

  - Beta Blockers
  - Primidone
Tardive Dyskinesia

Effect of Long term antipsychotics
Involves Lips, tongue, face, and neck
Can affect limbs

Treatment

Exchanging the dopamine antagonist antipsychotic
Neuroleptic Malignant Syndrome

Response to antipsychotics
Dopamine Receptor Blockade
Fever - can be as high as 106
Rigidity
Increased CPK
Altered mental status

Treatment:
- Remove drugs
- Supportive therapy
- Dantrolene/Bromocriptine/Amantadine
Headaches, Motor Disorders, Amyotrophies

Tic Douloureux

Hemifacial spasm
Pain
Trigeminal neuralgia
80% have basilar artery affecting the facial n.
Treatment: Carbamazepine/Surgery
Headaches, Motor Disorders, Amyotrophies

Other:

- Giles de la Tourette- Neuroleptics- Risperdal/Geodon
- Torticollis- Botulinum toxin
- Meige Syndrome:
  Bilateral blepharospasm with lip/mouth involvement
- Creutzfeldt-Jakob disease
  Myoclonus with dementia/brain biopsy/no tx
  Sudden onset
Seizures

Excessive abnormal discharges of electrical activity in CNS

Epilepsy is a syndrome of recurrent episodes of seizure activity

Two Types:
- Partial-
- Generalized-
Partial Seizures

Also known as “Focal or Local Seizures”
Seizure activity occurs in a specific area
Sensory Phenomena
Autonomic manifestations
Psychic manifestations
Headaches, Motor Disorders, Amyotrophies

Generalized Seizures

Absence:
- Sudden
- Brief motor activity
- Blank Stare
- Unconsciousness

Myoclonic:
- Sudden
- Uncontrollable
- Jerking of single or multiple muscle groups
- Unconsciousness
- Confusion postictally
Headaches, Motor Disorders, Amyotrophies

Tonic Clonic Seizure - *Grand Mal*

May or May not have an Aura

Sudden loss of consciousness

Tonic Phase-

- abrupt increase in muscle tone and contraction

Clonic Phase-

- Rhythmic muscular contraction and relaxation
Headaches, Motor Disorders, Amyotrophies

Status Epilepticus
  Continuous seizures

Complex Partial Seizure
  Purposeless repetitive activities
  Evolves to secondary generalized
### Table 1. Principal Types of Seizures.

<table>
<thead>
<tr>
<th>Type of Seizure</th>
<th>Clinical Features</th>
<th>Electroencephalographic Features*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple partial seizures (focal)</td>
<td>Signs and symptoms may be motor, sensory, autonomic, or psychic, depending on the location of the electrical discharge; consciousness is not impaired</td>
<td>Focal slowing or sharp-wave activity, or both</td>
</tr>
<tr>
<td>Complex partial seizures (temporal lobe or psychomotor)</td>
<td>Seizure may begin with no warning or with motor, sensory, autonomic, or psychic signs or symptoms; consciousness is impaired; automatisms (automatic acts of which the patient has no recollection) may occur; seizure is often followed by a period of confusion</td>
<td>Focal slowing or sharp-wave activity, or both</td>
</tr>
<tr>
<td>Secondarily generalized partial seizures (tonic–clonic, or grand mal)</td>
<td>Seizures may begin with motor, sensory, autonomic, or psychic signs or symptoms; consciousness is lost, with tonic increase in muscle tone; subsequent rhythmic (clonic) jerks subside slowly; patient is comatose after seizure and recovers slowly; tongue biting or incontinence, or both, may occur</td>
<td>Focal slowing or sharp-wave activity, or both</td>
</tr>
<tr>
<td>Generalized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence seizures (petit mal)</td>
<td>Seizure begins rapidly, with a brief period of unresponsiveness (average, 10 seconds) and rapid recovery; there may be increased or decreased muscle tone, automatisms, or mild clonic movements. Seizure can be precipitated by hyperventilation; age at first seizure, 3–20 yr</td>
<td>Spike–wave pattern (3 Hz)</td>
</tr>
<tr>
<td>Primarily generalized tonic–clonic seizures (grand mal)</td>
<td>Loss of consciousness occurs without warning or is preceded by myoclonic jerks; clinical features are similar to those of a secondarily generalized partial seizure</td>
<td>Spike–wave pattern (3–5 Hz)</td>
</tr>
</tbody>
</table>

*The electroencephalographic features listed are those observed on routine electroencephalography during which a seizure does not occur.*
Headaches, Motor Disorders, Amyotrophies

MYOPATHIES
- Hereditary/Congenital
- Metabolic
- Inflammatory
- Toxic
Headaches, Motor Disorders, Amyotrophies

**Work up for Myopathy**

- CK with isoenzymes
- Electrolytes, calcium, magnesium
- Serum myoglobin
- Serum creatinine and BUN
- Urinalysis:  
  Myoglobinuria is indicated by positive urinalysis with few RBCs on microscopic evaluation.
- Complete blood count
- Erythrocyte sedimentation rate
- Thyroid function tests
- Liver Functions
- EMG-NCV
- Age appropriate cancer screening
- Specific Genetic testing- Cadisil, MELAS, etc
<table>
<thead>
<tr>
<th></th>
<th>McArdle Disease (glycogenosis V)</th>
<th>CPT Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic defect</td>
<td>Glycogen storage</td>
<td>Lipid storage</td>
</tr>
<tr>
<td>Exercise</td>
<td>Usually cramps with short strenuous exercise</td>
<td>Usually myalgia and tenderness (without cramps) with prolonged exercise, worse with fasting</td>
</tr>
<tr>
<td>Second-wind phenomenon</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Recurrent myoglobinuria</td>
<td>Less frequent (50% of patients)</td>
<td>Common</td>
</tr>
<tr>
<td>CK at rest</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>Ischemic forearm exercise test</td>
<td>Absence of normal increase in lactate level</td>
<td>Normal</td>
</tr>
<tr>
<td>Muscle biopsy</td>
<td>Usually shows glycogen accumulation</td>
<td>May be normal</td>
</tr>
<tr>
<td>Gene location</td>
<td>Band 11q13</td>
<td>Band 1p32 (CPT II)</td>
</tr>
</tbody>
</table>
Headaches, Motor Disorders, Amyotrophies

**Duchenne Muscular Dystrophy**

- X linked
- Progressive weakness
- Begins at 2 until young adult
- Weakness: proximal > distal
- Elevated CPK

**Treatment**
- Exondys 51 – (eteplirsen)
- Deflazacort
Myotonic Dystrophy

Inherited neuromuscular disorder
Autosomal dominant

Symptoms-
Weakness
Sleep apnea
Cardiac conduction defects
Mitral valve prolapse
Testicular atrophy
Headaches, Motor Disorders, Amyotrophies

Mitochondrial

Mitochondrial myopathy (MELAS)
Inherited maternal
Defect of the mitochondria
Lactic acidosis
Muscle weakness/ptosis/neurological
Cardiomyopathy - arrhythmias
Liver/Kidney problems
Stroke before 40
Red ragged fibers on biopsy
Headaches, Motor Disorders, Amyotrophies

Metabolic

Addison disease, particularly when fluid and electrolyte problems are present
Cushing disease
Hypothyroidism (CK may be mildly elevated)
Hyperthyroidism (CK may be normal)
Hyperparathyroidism
Conn Syndrome
Periodic Paralysis:
Normokalemic paralysis causes the **most severe and prolonged** attacks.
Patients usually feel well between attacks, but some have myotonia or residual weakness after repeated episodes. Acute hypokalemic periodic paralysis may be primary (i.e., familial) or secondary to excessive renal or GI losses or endocrinopathy.

Intracellular shift of potassium depolarizes the cell membrane rendering it inexcitable and no muscle contraction can occur.

**Familial periodic paralysis** usually occurs in Caucasian males, is autosomal dominant, and may last as long as 36 hours.

Attacks usually **occur at night or in early morning** upon awakening and can be precipitated by a diet high in carbohydrates, rest following exercise, or glucose and insulin given intravenously.
Headaches, Motor Disorders, Amyotrophies

**Inflammatory**
- Dermatomyositis / Polymyositis
  - Proximal muscle weakness
  - EMG- myopathic changes consistent with inflammation
  - MRI- shows inflammatory component
- **Responds to glucocorticoids**
- Inclusion Body Myositis
  - Does NOT respond to steroids
  - BX shows vacuolar inclusions with eosinophils
Headaches, Motor Disorders, Amyotrophies

Infections

Spiroctete
  Lyme

Bacterial
  Staphylococcal, Tuberculosis, Clostridium

Viral
  HIV, Influenza, EBV, CMV, Coxsackie, Adenovirus
Headaches, Motor Disorders, Amyotrophies

Toxic

Ingestion of chemicals or pharmaceuticals:
ETOH
Statins/Fenofibrates
Steroids
AZT
Cocaine
Diuretics
Amiodarone
Colchicine
Headaches, Motor Disorders, Amyotrophies

Myasthenia Gravis

Autoimmune- motor end plate disorder
Associated with thymomas
Diplopia and ptosis is common
Symptoms worsen as day progresses

Diagnosis:
- Anti-Acetylcholine receptor antibodies
- **Tensilon test** (while ptosis present)

Treatment:
- Anti-cholinesterase agents (mestinon)/ thymectomy
- In crisis- Plasma exchange/IVIG
Headaches, Motor Disorders, Amyotrophies

**Lambert-Eaton**

Associated with Oat cell carcinoma

Autoimmune

Presynaptic peripheral nerves antibodies that causes acetylcholine release to decrease

Proximal muscle weakness

Dry mouth

Hypo-reflexia- esp lower extremities

Treatment: Anti-cholinesterase agents