MID

Lecture 5

Pathology Mind Maps

Neurodegenerative Disorders-2

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This file contains the lecture material presented through mind maps to make the information clearer, more organized, and easier to follow. It is designed to simplify studying and make revision more effective.

We truly hope you find it beneficial.
If it helps you in any way, please remember us in your prayers.

Best of luck in your studies💙!

Parkinson Disease (PD)

رَبِّ اشْرَحْ لِي صَدْرِي وَيَسِّرْ لِي أَمْرِي وَاحْلُلْ عُقْدَةً مِّن لِّسَانِي يَفْقَهُوا قَوْلِي

Involving the basal ganglia → movement disorders
-Hypokinesia (PARKINSON DISEASE)
-Hyperkinesia (HUNTINGTON DISEASE)

Definition:

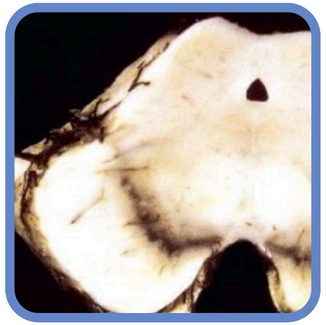
- A hypokinetic movement disorder that is caused by loss of dopaminergic neurons from the substantia nigra.
- Dopaminergic neurons project from substantia nigra to the striatum, involved in motor control.
- **Parkinsonism is a clinical syndrome:** tremor, rigidity, bradykinesia, and instability due to damage of dopaminergic neurons.
- Can be induced by drugs such as dopamine antagonists or toxins that selectively injure dopaminergic neurons.

Pathogenesis:

- **Protein** accumulation and aggregation , **mitochondrial** abnormalitie and **neuronal** loss in the substantia nigra.
- Clue and diagnostic feature: **Lewy body** (neuronal inclusions containing α-synuclein, a protein involved in synaptic transmission)
- Defects in autophagy and lysosomal degradation → Abnormal protein and organelle clearance.
- Most cases sporadic, some are autosomal dominant (mutation of α-synuclein gene)

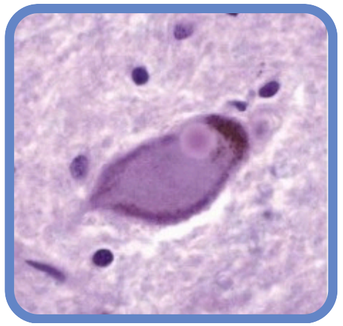
Morphology:

- Pallor of the substantia nigra and locus ceruleus
- Loss of the pigmented (catecholaminergic) neurons in these regions with gliosis.
- Lewy bodies in neurons (cytoplasmic, eosinophilic, round to elongated inclusions)
- Lewy neurites: dystrophic neurites that also contain aggregated α- synuclein
- **With progression involvement of medulla, pons, amygdala, and the cerebral cortex**

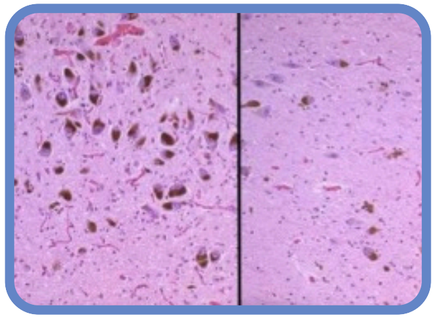


Normal substantia nigra

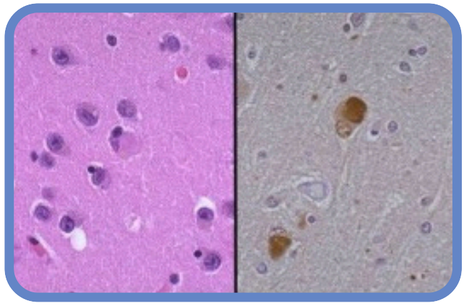
Depigmented substantia nigra in idiopathic Parkinson disease



Lewy body in a neuron from the substantia nigra stains pink



Left: normal
Right: loss of pigmented neurons in SN



Immunostaining to highlight Lewy bodies.
Contain alpha synuclein and ubiquitin.

Clinical Features:

- Characteristic symptoms: **tremor, bradykinesia and rigidity.**
- Tremor described as pill-rolling, occur at rest.
- Progresses over 10 to 15 years.
- Eventually: severe motor slowing or near immobility.
- **Death due to aspiration pneumonia or trauma from falls caused by postural instability.**
- When dementia develops within 1 year of onset of motor symptoms: Lewy body dementia (LBD).

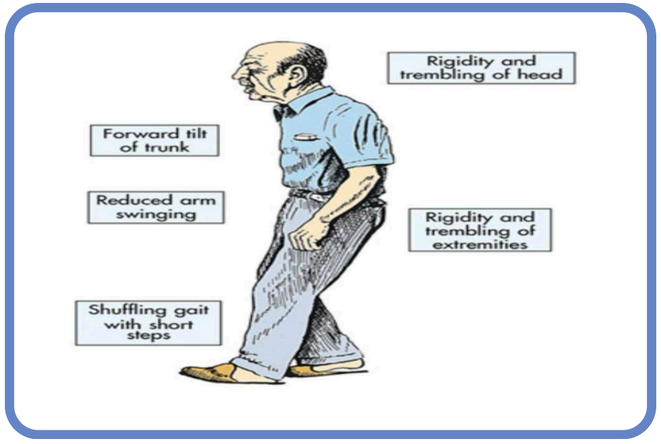
Management:

- Initially respond to L-dihydroxyphenylalanine (L-DOPA), but this treatment does not slow disease progression or reverse morphologic findings.
- Over time, becomes less effective
- Another Tx: deep brain stimulation

Symptoms:

1. Tremor: involuntary shaking, at rest, disappears with movement, begins in a limb, often in the hands or fingers. Patients might rub their thumb and forefinger back-and-forth (pill-rolling tremor.)
2. Slowed movement (bradykinesia): steps may become shorter, difficult to get out of a chair. Patients drag their feet as they try to walk (Shuffling gate)
3. Rigid muscles (rigidity): The stiff muscles can be painful and limit the range of motion.
4. Impaired posture and balance. stooped posture (leaning forward), and balance problems.
5. Loss of automatic movements.: decreased ability to perform unconscious movements, including blinking, smiling or swinging arms during walking
6. Speech changes. Patients might speak softly, quickly, slur or hesitate before talking.
7. Writing changes. It may become hard to write.
8. Diminished facial expressions (Masked facies).
9. Slow voluntary movement.

Pill rolling tremor



Huntington Disease (Chorea)

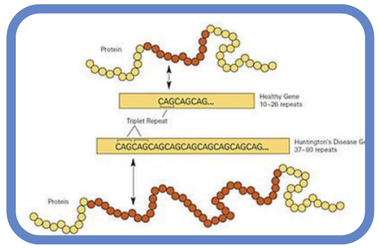
اللَّهُمَّ إِنَّكَ عَفُوٌّ تُحِبُّ الْعَفْوَ فَاعْفُ عَنَّا

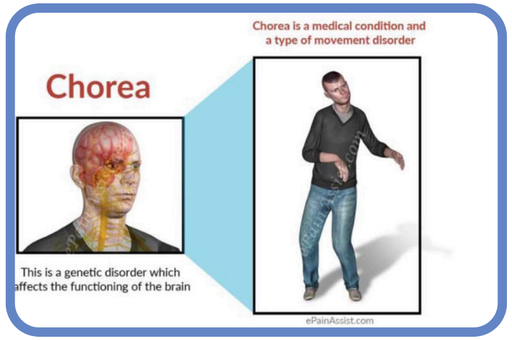
Definition:

- Autosomal dominant movement disorder associated with degeneration of the striatum (caudate and putamen).
- **Involuntary jerky movements of all parts of the body; writhing movements of the extremities.**
- Progressive, death after an average 15 years.
- Early cognitive symptoms (forgetfulness, thought and affective disorders, severe dementia).

Pathogenesis:

- **CAG trinucleotide repeat expansions in huntingtin protein gene located on 4p16.3 (Polyglutamine).**
- Normal alleles contain 11 to 34 copies of the repeat.
- **Disease-causing alleles: number of repeats is increased (may be hundreds)!**
- Larger numbers of repeats results in earlier-onset disease.
- Mutant protein is subject to proteolysis → fragments can form large intranuclear aggregates → toxic
- Age of onset: 40-50 years; related to the length of CAG repeats (more repeats; earlier age of onset).
- Anticipation: Further expansions of the CAG (glutamine-encoding) repeats during spermatogenesis → (paternal transmission) → earlier onset in the next generation.





اللهم بلغنا ليلة القدر، واجعلنا فيها من عتقائك من النار

لا تنسوني من صالح دعائكم

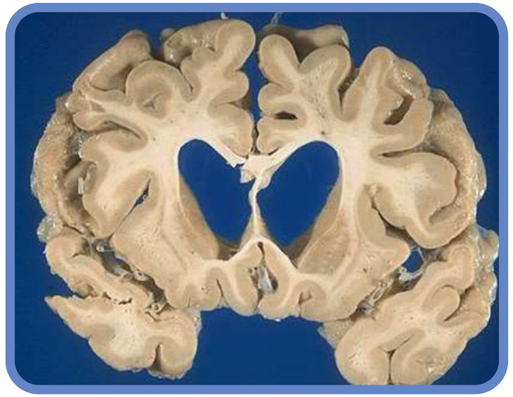
Morphology:

Macroscopic:

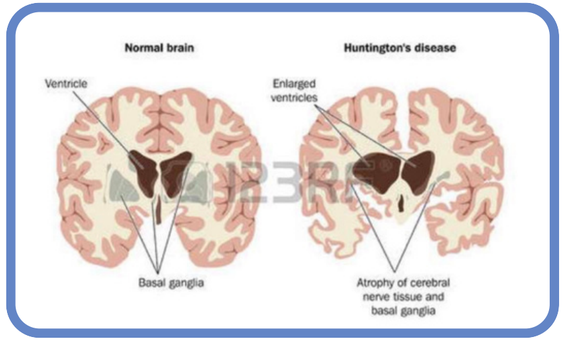
- Brain is small
- Striking atrophy of the **caudate nucleus and the putamen**
- Secondary atrophy of globus pallidus
- Atrophy frequently also is seen in the **frontal lobe.**
- **Dilated lateral and third ventricles**

Microscopic:

- Severe loss of neurons from affected regions of the striatum + gliosis Spiny neurons that release γ-aminobutyric acid (GABA), enkephalin, dynorphin, and substance P are especially sensitive, disappearing early.
- Intranuclear inclusions (aggregates of ubiquitinated huntingtin protein)
- **Strong correlation between degree of degeneration in the striatum and severity of motor symptoms; and between cortical neuronal loss and dementia.**



Enlargement of the ventricles seen here is due to atrophy of the head of the caudate.



Several members of a large family are affected by the onset of decreasing mental function and motor coordination when they reach middle age. Their extremity movements are marked by choreoathetosis. Genetic testing reveals increased trinucleotide CAG repeats. Which of the following intracranial structures is most likely to appear grossly abnormal with radiologic imaging of these affected persons?

A. Caudate nucleus
B. Midbrain
C. Temporal lobe
D. Locus ceruleus
E. Spinal cord

A

A 66-year-old man is finding that he has more difficulty getting up and moving about for the past year. He is annoyed by a tremor in his hands, but the tremor goes away when he performs routine tasks using his hands. His friends remark that he seems more sullen and doesn't smile at them, but only stares with a fixed expression on his face. He has not suffered any loss of mental ability.
Which of the following conditions is he most likely to have?

A. Amyotrophic lateral sclerosis (ALS)
B. Huntington disease
C. Parkinson disease
D. Niemann-Pick disease
E. Tuberous sclerosis

اللهم لک الحمد حتی ترضی، ولک الحمد إذا رضیت، ولک الحمد بعد الرضا

C

اللهم اجعل أجر هذا العمل صدقة جارية عن روح **عمر عطيه عوده المرابي**

- اللَّهُمَّ اغْفِرْ له وَارْحَمْهُ، وَاعْفُ عنْه وَعَافِهِ، وَأَكْرِمْ نُزُلَهُ، وَوَسِّعْ مُدْخَلَهُ، وَ اغْسِلْهُ بمَاءٍ وَثَلْجٍ وَبَرَدٍ، وَنَقِهِ مِنَ الخَطَايَا كما يُنَقّى الثَّوْبُ الأبْيَضُ مِنَ الدَّنَسِ.
- اللَّهُمَّ أبدله داراً خيراً من داره، وأهلاً خيراً من أهله، وأدخله الجنّة، وأعذه من عذاب القبر ومن عذاب النّار.
- اللهمّ يمّن كتابه، ويسّر حسابه، وثقل بالحسنات ميزانه، وثبّت على الصراط أقدامه، وأسكنه في أعلى الجنات، بجوار حبيبك محمد صلّى الله عليه وسلم.
- اللهم اغفر لحينا وميتنا وشاهدنا وغائبنا وصغيرنا وكبيرنا وذكرِنا وأنثانا اللهم من أحييته منا فأحيِه على الإسلام ومن توفيته منا فتوفه على الإيمان اللهم لا تحرمنا أجره ولا تضلنا بعده.
- اللهم اغفر له وارفع درجته في المهديين، واخلفه في عقبه في الغابرين، واغفر لنا وله يا رب العالمين، وافسح له في قبره، ونوّر له فيه.
- اللَّهُمَّ أنزل على أهله الصّبر والسلوان وارضهم بقضائك.

اللهم لا تفجعنا بأنفسنا ولا أهلنا ولا أحبتنا، اللهم أعوذ بك من فواجع الأقدار ومن مصائب الدنيا وتقلب حوادثها، اللهم إنا نخاف الفقد فلا تحملنا ما لا طاقة لنا به.