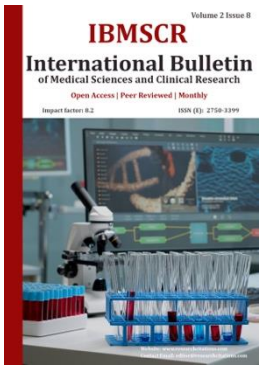

PARKINSON'S DISEASE CLINIC, DIAGNOSIS AND PRINCIPLES OF ITS DEVELOPMENT

Abdurasulov Sardor Sultanmurodovich
assistant.
Akhrorova Shakhlo Botirovna
associate professor, DSc,.
Department of Neurology, Bukhara State Medical Institute named after Abu Ali ibn Sina
axrorova.shahlo@bsmi.uz
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Abstract. Parkinson's disease (PD) is caused by a chronic neuroprogressive disease of the CNS with degeneration of nigrostriar neurons and disturbance of basal ganglia function. V 1817 g. the pain was described first D. Parkinsonom pod nazvaniem "trembling paralysis". The prevalence of BP with regard to age is 1%, the average age of onset is 60–65 years, and 5–10% of cases of pain begin at the age of 40 years; mujchiny boleut v 1.5 cups, chem ginseng. Etiology BP neizvestna. Predpolagaetsya, chto v razvitii zabolevaniya lejat age, geneticheskie i sredovye faktori.

Keywords: Parkinson's disease, Clinic, diagnosis of Parkinson's disease

Main part. PD is predominantly sporadic, but if close relatives have PD, the risk of developing it doubles. Only a small number of PD cases (10%) are associated with hereditary factors. Perhaps, genetic predisposition increases the sensitivity of the nigrostriatal system to the influence of damaging factors and aging processes. The role of environmental influences in the genesis of PD is studied: infections, intoxications, exposure to metals, pesticides, consumption of well water in rural areas, etc. According to the modern concept of PD pathogenesis, degeneration of nigrostriatal neurons is caused by intracellular metabolism disorders: oxidative stress, glutamate excitotoxicity, excessive calcium ion intake into cells, increased activity of intracellular proteases, impaired mitochondrial respiration with neuron energy deficiency, impaired iron metabolism. These factors lead to activation of apoptosis; However, the trigger mechanism, interaction, and sequence of pathogenetic factors of neurodegeneration remain unclear. Pathomorphological studies in PD reveal degeneration of nigrostriatal neurons, neurons of the locus coeruleus, and intracellular inclusions that are products of protein degeneration — Lewy bodies. The main neurotransmitter disorders in PD are deficiency of dopamine synthesis, excess of the excitatory amino acid glutamate and the neurotransmitter acetylcholine, and insufficient synthesis of norepinephrine and serotonin. Clinical manifestations of PD occur with a decrease in the amount of dopamine in the caudate nucleus and putamen by at least 70%. Symptoms of PD develop gradually, gradually, involving the limbs on one side. The core of the clinical picture of PD is hypokinesia, resting tremor, rigidity, and postural instability. Hypokinesia is manifested by decreased motor activity, which is expressed by a violation of the initiative to perform movements, slowness, and a decrease in the amplitude (amplitude decrement) of all actions. With severe hypokinesia, the patient has difficulty getting up from a chair, turning in bed with difficulty; when walking, he slouches, with his arms bent at the elbows and pressed to the body (the "supplicant" pose), walking slows down, the step is shortened; a shuffling or mincing gait, stamping and freezing in place occur. Speech disorders are characteristic: dysphonia, bradylalia, monotony, dysarthria. Resting tremor usually begins with the distal parts of the upper limbs and

resembles hand movements "when counting coins or rolling pills." Subsequently, the tremor involves the legs and lower jaw. Rigidity in PD is manifested by a plastic increase in muscle tone, increasing during the examination. Postural instability, which occurs at advanced stages of PD, manifests itself as unsteadiness when walking, frequent falls, propulsions. Patients need to use support devices (cane, tripod). In addition to movement disorders, PD is accompanied by depression (70% of cases), cognitive (45%) and psychotic disorders (20–40%). Autonomic disorders are also characteristic of the disease: orthostatic hypotension, constipation, urination disorders, seborrhea, salivation and pain syndromes. Depending on the predominance of a particular symptom in the clinical picture of PD, the following clinical forms are usually distinguished: akinetic-rigid, tremor-rigid and mixed forms.

It is customary to distinguish 5 degrees of PD severity (disease stages according to Hoehn-Yahr):

- Stage 1 — unilateral symptoms of Parkinsonism (hemiparkinsonism);
- Stage 2 — bilateral symptoms of Parkinsonism without postural disorders;
- Stage 3 — moderate postural instability joins in;
- Stage 4 — significant limitation of motor activity, but independent movement is still possible;
- Stage 5 — the patient is bedridden or wheelchair-bound. In the late stages of PD, certain features (clinical pathomorphosis) appear, which include motor (motor fluctuations, drug-induced dyskinesias, gait disturbances, falls, freezing, and akinetic crises); and non-motor (autonomic, cognitive, neuropsychiatric) disorders.

The factors in the pathogenesis of motor fluctuations and drug-induced dyskinesias in the late stages of PD are the loss of the buffering function of nigrostriatal neurons and non-physiological pulsatile stimulation of dopamine receptors, reflecting fluctuations in the concentration of levodopa in the plasma; changes in the function of postsynaptic DA receptors; increased glutamatergic transmission; impaired dopamine storage, its release into the synaptic cleft, as well as changes in the pharmacokinetics and pharmacodynamics of levodopa as the disease progresses. Motor fluctuations are manifested by the phenomenon of "wearing off the effect of a single and daily dose" of levodopa, the phenomenon of "on-off", and freezing.

The phenomenon of wear off of the effect of the dose is manifested by a shortening of the duration (less than three hours) of the action of a single dose of levodopa. The phenomenon of "on-off" is manifested by a rapid onset and rapid cessation of the effect of a single dose of levodopa. Freezing is characterized by a sudden loss of motor activity for several seconds or minutes. Drug-induced dyskinesias occur in 50% of PD patients 5 years after the start of taking levodopa drugs. Clinically, they are manifested by choreoathetosis and dystonia of the limbs, oromandibular dyskinesia, spasmodic torticollis, torsion dystonia, and postural disturbances. In the late stages of the disease, patients may experience long periods of decompensation lasting from several days to several weeks, as well as akinetic crises - severe episodes of akinesia accompanied by dysphagia, autonomic disorders, hyperthermia, oliguria, confusion. The causes of decompensation and akinetic crises in the late stages of PD may be a violation of the regimen for taking antiparkinsonian drugs, their complete cancellation ("drug holidays"); taking drugs that block dopamine receptors (neuroleptics, cinnarizine); exacerbation of concomitant somatic diseases, stress; operations, injuries, dehydration. PD can only be diagnosed with certainty by autopsy.

Clinical diagnosis of PD requires the presence of hypokinesia and at least one of the two main symptoms of parkinsonism - resting tremor and rigidity. In 2015, members of the International Movement Disorders Society developed fundamentally new clinical criteria for Parkinson's disease.

Clinically, "certain" PD is diagnosed if the clinical picture:

1) lacks absolute exclusion criteria;

2) contains two or more confirmatory criteria;

3) lacks "red flags".

Clinically "probable" PD is diagnosed if the clinical picture:

1) lacks absolute exclusion criteria;

2) contains "red flags" (no more than two), compensated by confirmatory criteria.

Confirmatory criteria for PD:

1) obvious and dramatic response to dopaminergic therapy;

2) presence of levodopa-induced dyskinesias;

3) resting tremor in the limbs;

4) hyposmia or cardiac sympathetic denervation based on cardiac scintigraphy.

Absolute exclusion criteria:

1) severe cerebellar symptoms;

2) vertical gaze palsy or slow vertical saccades;

3) signs of frontotemporal dementia or primary progressive aphasia in the first 5 years of disease;

4) parkinsonism limited to the lower limbs for more than 3 years;

5) therapy with dopamine receptor blockers or dopamine-depleting drugs;

6) lack of response to high doses of levodopa;

7) impairment of higher cortical forms of sensory disturbances (graphesthesia, stereognosis), limb apraxia, primary progressive aphasia.

"Red flags":

1) rapid progression of gait impairment requiring use of a wheelchair within 5 years from disease onset;

2) no progression of motor symptoms for 5 or more years;

3) early, marked bulbar disturbances in the first 5 years of disease;

4) respiratory disturbances (daytime or nighttime inspiratory stridor or frequent sighs on inhalation);

5) severe autonomic failure in the first 5 years of disease: a) orthostatic hypotension; b) urinary incontinence or retention in the first 5 years of disease;

6) recurrent falls (more than one per year) associated with impaired balance in the first 3 years of disease;

7) dystonic antecollis or contractures in the arms or legs in the first 10 years of disease;

8) absence of any of the characteristic non-motor manifestations, despite the duration of the disease: sleep disorders, autonomic disorders, hyposmia, psychiatric disorders;

9) presence of pyramidal signs;

10) bilateral symmetrical parkinsonism. PD should be differentiated from secondary parkinsonism (vascular, toxic, drug-induced, post-traumatic, tumor, occurring with normotensive hydrocephalus); as well as "parkinsonism plus" in multisystem degenerations of the central nervous system (multisystem atrophy, progressive supranuclear palsy,

dementia with Lewy bodies, Fahr disease, Alzheimer's disease, hepatocerebral degeneration, etc.).

Conclusion. The main treatment options for PD are pharmacotherapy, medical and social rehabilitation, exercise therapy, and neurosurgical treatment. PHARMACOTHERAPY Drug therapy for PD should be aimed at stopping and reducing the neurodegenerative process in nigrostriatal neurons (neuroprotective therapy) and normalizing the biochemical imbalance (symptomatic therapy). Neuroprotective therapy is promising for possibly reducing the rate of PD progression. Drugs with a putative neuroprotective effect in PD include drugs with an antioxidant effect (MAO B inhibitors); dopamine receptor agonists; dopamine transport inhibitors

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