

Modern Diagnostic Methods for Alzheimer's Disease

Yusupov Shokhzod Saydali ogli

Clinical Resident, Department of Neurology
Samarkand State Medical University

Jabborova Zamira Bakhridin qizi

Clinical Resident, Department of Neurology
Samarkand State Medical University

Yuldoshev Jaloliddin Bakhodir ogli

Clinical Resident, Department of Neurology
Samarkand State Medical University

Abdiqodirov Botir Anvar ogli

Clinical Resident, Department of Neurology
Samarkand State Medical University

Kasimov Arslanbek Atabaevich

PhD, Associate Professor, Department of Neurology
Samarkand State Medical University

Abstract: The article provides a literature review on the problem of diagnosing dementia in Alzheimer's disease - a neurodegenerative brain disease with progressive deterioration of cognitive functions and emotional disorders, in which patients die 5-10 years after diagnosis. There are many methods for diagnosing Alzheimer's disease, however, accurate diagnosis is only possible through postmortem brain examination - autopsy. Therefore, issues of antemortem diagnosis of this disease remain relevant.

Key words: dementia, Alzheimer's disease, diagnosis, neuroimaging methods, cognitive impairment.

Introduction.

The relevance of the problem of early diagnosis of late-onset dementias, especially Alzheimer-type dementias, is due to the high frequency of Alzheimer's disease (AD), the prolonged disabling course of the disease, high economic costs for treatment and patient care, which often require lifelong placement in specialized institutions. Thus, in 2000, about 20 million patients with dementia were identified worldwide, in 2020 their number may increase to 41 million, and in 2040 - to 81 million [9].

According to data from S.I. Gavrilova et al. (1995), the prevalence of Alzheimer's disease for the Moscow population aged 60 years and older is 4.4%. Among all patients, 2.1% suffer from moderate and severe dementia. It has been established that the frequency of dementia increases with aging from 2% at age 60 to 20% at age 80. Among people over 65 years old, approximately 9% have mild or moderate dementia, 5% have severe dementia [2].

The total cost of caring for AD patients, considering the severity of dementia (MMSE scale), increases depending on the stage of dementia. The highest direct costs for caring for patients with late-stage AD are due to placing patients in specialized institutions. In patients with initially mild AD, the main cost savings depend on the time of transition of the disease to moderate and severe forms.

Total costs depending on AD stage and MMSE scale scores were: for mild dementia from 836(30MMSEpoints)to836(30MMSEpoints)to4861 (21 MMSE points); for moderate dementia - from 5929(20MMSEpoints)to5929(20MMSEpoints)to26129 (11 MMSE points); for severe dementia – from

26496(10MMSEpoints)to26496(10MMSEpoints)to33177 (1 MMSE point) [25]. The greatest increase in costs (7.6 times) occurs when transitioning from mild stage (mild dementia) to moderate stage; transition to severe stage is accompanied by a 2.2-fold increase in costs.

In the Russian Federation, medical costs for maintaining dementia patients (excluding medication therapy costs) amount to 74.8 billion rubles per year (according to modeling data), with most of these expenses falling on the shoulders of patients' relatives [9].

Early diagnosis of Alzheimer's disease is the subject of scientific research worldwide, which is due not only to the importance of timely initiation of symptomatic treatment, but also to the need to provide social and psychological support to patients' relatives as the disease progresses.

The following approaches have been proposed to solve the problem of earlier Alzheimer's disease diagnosis: application of neuroimaging methods (CT, MRI, etc. [7]); genetic studies (apolipoprotein e-allele on chromosome 19, etc.); development and implementation of new psychodiagnostic methods, widespread use of neuropsychological scales [2, 4].

According to ICD-10, the antemortem diagnosis of Alzheimer's disease is based on the presence of the following obligatory signs:

- presence of dementia syndrome; development of multiple cognitive function deficits;
- gradual, barely noticeable onset and steady progression of cognitive function disorders;
- absence of clinical or special paraclinical study data that could indicate that cognitive function disorders are caused by any other disease or damage to the central nervous system;
- signs of cognitive impairment should be detected outside states of consciousness clouding.

Reliable confirmation of diagnosis is only possible with autopsy data, postmortem brain examination [1].

According to ICD-10, the following types of AD are distinguished:

1. Dementia in Alzheimer's disease with early onset (or Alzheimer's disease, type 2; presenile dementia of Alzheimer type).
2. Dementia in Alzheimer's disease with late onset (or Alzheimer's disease, type 1; senile dementia of Alzheimer type), where there is clinically established disease onset time after 65 years or usually after 75, or later.
3. Dementia in Alzheimer's disease, atypical or mixed type. This should include dementias that do not fit the description and diagnostic guidelines for presenile and senile AD, as well as mixed forms of AD and vascular dementia.

Stages of mild, moderate, and severe dementia are determined based on Clinical Dementia Rating (CDR) scale criteria [2, 4], as well as according to criteria for initial and moderate dementia stages according to ICD-10.

Currently, increasing attention is being paid to vascular changes in Alzheimer's disease. One-third of patients with Alzheimer's disease have significant cerebrovascular pathology due to small vessel damage; cerebral amyloid angiopathy, microvascular degeneration, hyaline fibrosis of arterioles and small vessels are common [8].

Differential diagnosis of dementia in Alzheimer's disease is conducted with the following diseases: depressive disorders, delirium, organic amnesic syndrome, other primary dementias (Pick's disease, Creutzfeldt-Jakob, Huntington's), secondary dementias in somatic diseases, intoxication, forms of mental retardation, but most often AD must be differentiated from vascular dementia.

Neuropsychological methods are used to assess cognitive functions. They represent various tests and trials for memorizing and reproducing words and drawings, recognizing images, solving intellectual tasks, studying movements, etc.

Psychometric scales are used in AD diagnosis [2]:

- Mini-Mental State Examination (MMSE), Folstein M.F. et al., 1975;
- Hachinski Ischemic Scale, Hachinski V.C., 1978;
- Frontal Assessment Battery (FAB), Dubois B., 1999;
- Clock Drawing Test (CDT), Brodaty H., 1997, Shulman K., 1986, Sunderland T., 1989;
- A.R. Luria neuropsychological examination methodology (1965) adapted for this patient population, etc.

Complete neuropsychological examination allows identifying clinical features of cognitive impairments and making a topical diagnosis. However, the use of complex tests, while increasing method sensitivity, leads to decreased specificity of obtained results, as their performance largely depends on patient age and education level.

Therefore, so-called screening neuropsychological scales are widely used in outpatient practice worldwide, allowing confirmation of cognitive disorder presence in general and their quantitative assessment. An example of such a

screening scale is the "Mini-Mental State Examination" (MMSE).

The Hachinski Ischemic Scale is used for diagnosing vascular dementia and distinguishing it from Alzheimer-type dementias. Despite obvious shortcomings (non-stroke forms of dementia are not detected, which primarily relates to Binswanger encephalopathy, as well as mixed vascular atrophic dementias), it allows rapid diagnosis of main forms of late-onset dementias.

Neuropsychological methods are used in diagnosing, primarily, mnemonic disorders in AD. Thus, increased forgetfulness of current events is usually the earliest sign, appearing as a monosymptom. Subsequently, other cognitive impairments join memory disorders - apraxic syndrome, speech disorders of amnesic or sensory aphasia type.

In AD, all types of long-term memory are impaired: episodic, semantic, procedural, and involuntary. The volume and retention time of traces in working memory also decrease. Retrograde amnesia in AD is often accompanied by pronounced confabulations.

Unlike AD, memory disorders in benign senile forgetfulness are a monosymptom, do not progress, and do not lead to gross social interaction disorders. Providing semantic cues during reproduction significantly improves information acquisition and reproduction. This sign is often used as a differential diagnostic criterion for normal age-related memory changes and pathological memory decline in early AD stages.

Auditory-verbal memory in normal aging suffers more than visual or motor memory. A very common cause of cognitive impairment in old age is depression, which can be both situationally conditioned and related to organic brain damage. Depression is also common in AD.

Emotional disorders in Alzheimer's disease are determined using methods:

- BDI - Beck Depression Inventory;
- HADS - Hospital Anxiety and Depression Scale (A.Zigmond, R.Snaith, 1983) - adapted Russian version (A.V.Andryushenko, M.Yu.Drobizhev, A.V.Dobrovolsky, 2003);
- HDRS - Hamilton Depression Rating Scale;
- GDS - Geriatric Depression Scale (GDeprS), Yesavage J.A. et al., 1983

Paraclinical studies are an important part of the diagnostic process. Laboratory examination of biological material in demented patients is indicated for differential diagnosis with toxic lesions or metabolic disorders. It is necessary to conduct laboratory tests such as complete blood count, blood electrolyte levels, blood sugar, blood creatinine, liver enzymes, thyroid function assessment, levels of vitamins B1, B12, folates in blood serum, serological tests for syphilis, HIV tests, urine examination.

Lumbar puncture is desirable when metastatic or infectious CNS involvement is suspected, in clinical picture of normal pressure hydrocephalus, when cerebral vasculitis is suspected [4].

Genetic testing is performed using numerous markers that help establish early-onset Alzheimer's disease. Mutations in the presenilin 1 gene (PS1, chromosome 14) cause the most common early familial forms of AD and are apparently the most "aggressive" genetic factors. Their pathological manifestation is characterized by high penetrance and does not depend on other environmental factors or genotype.

To date, more than 45 different missense mutations scattered throughout the coding part of the gene and one "splicing" mutation associated with familial Alzheimer's disease have been discovered. The only marker for the more common senile form of the disease (sporadic form) is apolipoprotein ε-allele on chromosome 19 [1].

Among neurophysiological research methods, **electroencephalography (EEG)** is most accessible [14, 21]. Pathological EEG changes in Alzheimer's disease: increase in slow-wave activity (predominantly its theta range, more often low or medium amplitude) and delta activity, alpha rhythm reduction in the form of decreased amplitude and smoothed regional differences compared to age norm. One-third of patients show generalized bilaterally synchronous theta and delta waves exceeding the main activity in amplitude [8].

Currently, the most commonly used **neuroimaging methods** that allow antemortem study of brain structure are magnetic resonance imaging (MRI) and computed tomography (CT) [3, 5]. Diagnostic CT signs confirming AD diagnosis are signs of total and regional brain matter atrophy, determined by the degree of subarachnoid space and ventricular expansion [7].

According to G.Roman et al. (1993), the presence of CT and MRI signs characteristic of vascular pathology does not exclude the diagnosis of Alzheimer-type dementia, and H.Chui et al. (1992) recommend considering such cases as combined vascular-Alzheimer dementia [6].

The nuclear magnetic resonance phenomenon underlies functional MRI, perfusion MRI, diffusion-weighted MRI, MR spectroscopy. V.C. Hachinski (1987) proposed the term leukoariosis (from Greek - leuko - white and ariosis -

rarefaction) to describe periventricular and subcortical hypodense areas on CT and hyperintense on MRI [16, 17, 18, 19]. The term leukoaraiosis applies to both CT and MRI [10].

In patients with Alzheimer's disease, white matter lesions are detected more often than in healthy elderly people [8]. However, despite years of research, the clinical significance of white matter changes is not definitively clear.

Functional methods are important in differential diagnosis of dementias, especially for distinguishing AD from vascular dementia, frontotemporal dementia, dementia with Lewy bodies, or depression.

Functional radioisotope methods include single-photon emission computed tomography (SPECT) and positron emission tomography (PET). SPECT in brain examination is used to assess regional cerebral blood flow. In Alzheimer's disease, decreased hemoperfusion in the parietal-temporal region is detected [23, 24].

PET is a method assessing glucose metabolism level in the brain after intravenous administration of radiopharmaceutical - fluoro-2-deoxyglucose (FDG). PET is performed both at rest and during patient performance of cognitive tests. Alzheimer's disease is characterized by decreased metabolism level in the parietal-temporal region. The magnitude of this decrease correlates with the degree of cognitive decline [2].

In 10-20% of cases, clinical and radiological signs of Alzheimer's disease and vascular dementia are detected in the same patient. This condition is defined in ICD-10 as mixed dementia.

Conclusions: Thus, considering the prevalence of Alzheimer's disease, the increase in the number of elderly people, economic costs and their dynamics with disease progression, it is necessary to improve the organization of gerontopsychiatric care and search for simple, accessible, modern methods of early Alzheimer's disease diagnosis.

Neuroimaging methods (MRI, CT) occupy an important place in primary and differential diagnosis of Alzheimer's disease. The role of psychodiagnostic methods in assessing mental status is increasing, especially cognitive functions and affective spectrum disorders - for diagnosis verification according to clearly established ICD-10 clinical signs of dementia in Alzheimer's disease.

References:

1. Winblad B. Alzheimer's disease: epidemiology, economic costs and therapeutic strategies // Alzheimer's disease and aging: from neurobiology to therapy: materials of the second Russian conference October 18-20, 1999. - M.: Pulse, 1999. - P. 24.
2. Gavrilova S.I. Mental disorders in primary degenerative (atrophic) processes of the brain // Guide to psychiatry: in 2 volumes. Vol.2 / A.S. Tiganov, A.V. Snezhnevsky, D.D. Orlovskaya et al. / ed. A.S. Tiganov. - M.: Medicine, 1999. - P. 57-117.
3. Damulin I.V., Levin O.S., Yakhno N.N. Alzheimer's disease: clinical-MRI study // Neurological Journal. - 1999. - No. 2. - P. 34-38.
4. Zharikov G.A., Roshchina I.F. Diagnosis of Alzheimer-type dementia in early stages of its development // Psychiatry and psychopharmacotherapy, supplement No. 2. - 2001. - P.23-27.
5. Zharikov G.A., Savvateeva N.Yu., Gavrilova S.I. Computer and magnetic resonance tomography in diagnosis of "mild" dementia (clinical-catamnestic study) // Journal of Social and Clinical Psychiatry - 1997 - Vol.7, issue 3 - P. 5-14.
6. Iznak A.F., Gavrilova S.I., Chayanov N.V. et al. EEG mapping in patients with Alzheimer-type dementias // Issues of gerontopsychiatry. - M.: USSR Ministry of Health, 1991. - P. 51-58.
7. Kolykhalov I.V. Clinical and computed tomographic comparisons in Alzheimer-type dementias: abstract of dissertation ... candidate of medical sciences. - M., 1993. - 25 p.
8. Ponomareva N.V., Selezneva N.D., Kolykhalov I.V. Neurophysiological mechanisms of brain activity in Alzheimer's disease // Issues of gerontopsychiatry. - M., 1991. - P. 58-66.
9. Sluchevskaya S.F., Shigashov D.Yu. Economic costs for treating Alzheimer-type dementias (DAT) in patients over 60 years old with calculation of predicted value for 2015 in St. Petersburg // Social and Clinical Psychiatry. - M., 2007. - P 47
10. Almkvist O., Wahlund L.O., Andersson-Lundman G. et al. White matter hyperintensity and neuropsychological functions in dementia and healthy aging. // Arch. Neurol. - 1992. - No. 6 (49). - P. 626-632.