Alzheimer dementia – a problem of individuals, families, medicine and society

Alchajmerova demencija – problem pojedinca, porodice, medicine i društva

Smiljana Kostić

Neurology Clinic, Military Medical Academy, Belgrade, Serbia

Since ancient times the term dementia, derived from the Latin word demeans (“no mind”), has marked a specific, acquired state of impaired intellectual and mental abilities of an adult which interfere with his her social and working abilities, making him her dependent on others.

At the beginning of the 2nd century Roman poet Junius Juvenal described how the weakness of the mind is worse than any physical illness, "Sed omni membrorum damno maior dementia, quae nec nomina servorum nec vultum agnoscit amici cum quo praeerit cenavit nocte, nec illos quos genuit, quos eduxit". ("But worse than any loss in body is the failing mind which forgets the names of slaves, and cannot recognize the face of the old friend who dined with him last night, nor those of the children whom he has begotten and brought up").

According to the assessment of the group of experts commissioned by the Alzheimer Disease International in 2005 about 24 million people suffered from dementia at that time, with 4.6 million new cases arising every year. The lifespan of the world's population has extended and there is a trend of increase of the elderly population. It is predicted that in 20 years the number of people affected by dementia will be nearly doubled. A frightening prediction says that by the year 2050 115 million people will be suffering from this disease and that 1 out of 85 persons will be demented.

Alzheimer dementia (AD) is the most common and accounts for about 70% of all dementias. The prevalence rates increase with age and double every 5 years after age 65.

Based on its age of onset, AD is classified into early onset AD, before the age of 65, accounting for 1–5% of all cases, and late-onset AD, after the age of 65, which occurs in 95% of patients.

Although there are no significant differences in the clinical symptoms of the two types of the disease, it is considered that the early onset AD is connected with faster progression and a different inheritance patterns. Mutations in three genes (APP, PSEN1, PSEN2) that participate in the encoding of proteins involved in the pathophysiological processes of the synthesis of the amyloid precursor protein and amyloid-beta (A\(\beta\)) are inherited autosomal dominant with high penetrance. In late-onset sporadic form there is an increased tendency towards manifestations of the disease in relatives of the patients, and the risk is doubled if the disease exists in the first instance relatives.

AD is result of a progressive neurodegenerative process whose pathological characteristics represent diffuse extracellular senile plaques made up of A\(\beta\) and intracellular neurofibrillary tangles consisting of tau protein aggregates, associated with reactive microgliosis, dystrophic neurites and neuronal and synaptic loss. In its clinical course this multifactorial neurodegenerative disease progresses from the prodromal phase to the late stages and histopathological substrate often cannot fully explain the clinical features of the disease.

Today we know that the pathological process begins decades before the first manifestation of the clinical symptoms and it is still assumed that the disorder of A\(\beta\) protein metabolism, the amyloid cascade, in the central nervous system is the initial and significant factor causing the disease. Hence, the main therapeutic strategies aim at modifying the abnormal production, accumulation and depositing of A\(\beta\).

Application of drugs that could potentially change the course of the disease would find its place in the earliest stages, asymptomatic- molecular, prodromal and early onset AD.

Until recently, the diagnosis of the disease, according to the valid criteria of Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association (NINCDSADRDA) from 1984, relied mainly on clinical characteristics of the disease reaching the reliability level of probable, but definite diagnosis requested an autopsy, histopathologic confirmation.

In the light of new knowledge, with a reliable and early recognition of the disease being the aim, diagnostic criteria...
for AD have been revised with a more precise definition of the clinical phenotype, including neuroimaging biomarkers: structural (MRI), metabolic (FDG PET), molecular (Aβ ligand PET), as well as biomarkers of cerebrospinal fluid (Aβ 1-42, total tau and p-tau).

Since AD is a disease of a still unknown etiology with a modest impact of so far available therapies, knowledge of risk factors is significant. An increased risk of illness showed a correlation with age, the presence of mild cognitive impairment, family manifestation of the disease, the presence of the APOE ε4 allele, vascular risk factor and traumatic brain injury. Identification of populations at risk leaves space for the preventive measures and neuroprotective strategies.

Among protective factors the concept of "cognitive reserve" is emphasized. Individuals with intellectually enriched life-styles, such as those with high educational and occupational attainment, have a reduced risk of expressing AD pathology clinically. Mediterranean diet, as well as regular physical activity also have a protective effect and are associated with a reduced risk of a progression from mild cognitive impairment to AD.

In terms of treatment of AD in the past decades a large number of drugs with potential disease modifying effect were examined but they have not given significant results. The encouraging results of experimental therapies with anti-amyloid beta monoclonal antibodies in the early stages of AD have been published recently, and we are expecting the results of other clinical studies in search for a cure that would stop or slow down the pathological processes.

The current treatment of AD is still based on the use of symptomatic drugs from the group of acetylcholinesterase enzyme inhibitors and NMDA receptor antagonists that have a modulating effect on the neurotransmitter activity and lead to a certain improvement in cognitive status, functionality, and behavioral symptoms.

Dementia is a growing issue throughout the world and is getting the status of the priority problem in the health care system worldwide. This disease leads to significant physical, psychological and social disability of patients and represents an enormous worry and burden for the family that takes care of the patient, as well as a great burden for the society. Financial expenses of the treatment of dementia in the United States range from 159 to 215 billion $ per year, which exceeds the cost of treating cardiovascular and malignant diseases. The largest economic cost of the treatment is set aside for the provision of institutional and long-term home care, followed by medical services.

According to the last official census in 2011 Serbia has a population of 7.2 million people, of which 17.4% are over 65 years old. Epidemiological studies have not been conducted yet, but it is estimated that approximately 80,000 people live with dementia. In 2004 the first pilot population survey was conducted in Belgrade and the estimated prevalence of unspecified dementia F03 was 6.7% which indicated the need for more reliable diagnosis by conducting broader population studies, as well as the education of professionals and the public. In Serbia there is only one specialized clinic for patients with dementia, a few centres and outpatient clinics, mainly in larger cities. There is the lack of specialized institutions for long-term care and the majority of patients are placed in residential care institutions of the elderly. There is also the lack of daily care centers for dementia patients and the support services for patients and their families, which would contribute to the prolongation of stay of those patients in local communities. Most of the costs and almost the entire burden of care for the patients are born by the families of patients themselves. In the past decade a lot of efforts were made to raise awareness about the disease in the general population, to train health professionals and improve communication between general practitioners, families and institutions of the tertiary level. There remains the problem of delayed and misdiagnosis, as well as failure to recognize the seriousness and severity of the problems that these patients and their caregivers face every day. That leaves us to think, as individuals and as a society, about the future that could become our cruel present.

REFERENCES