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Editorial

Depression and Cognitive Impairment

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Review by Sukiasyan and Tadevosyan published in this issue describes risk factor for development of depression. They provide a comprehensive list of these factors except that they are glossing over the issue of cognitive impairment. They are wrong when they call attention and short-term memory deficit in elderly patient "dementia" and state that these symptoms can be completely reversible with appropriate treatment. Unfortunately, there is currently no effective treatment for cognitive impairment and dementia occurring in many elderly patients. Cognitive impairment (CI) has very complex relationship with depression which may include difficulty diagnosing depression in a person with dementia, dementia being a risk factor for development of CI, depression being one of the first symptoms of developing CI, depression and dementia having some common pathogenetic processes, and depression having some specific consequences if it occurs in a person with dementia.

Diagnosing depression in a person with CI: Most of the scales for detecting depression and measuring its severity depends on patient's description of symptoms. This method may not be applicable in persons with CI because one of the impairments by be language ability. Therefore, using patient's response may not be possible or reliable, in this case, observational scales have to be used [1,2]. In addition, some symptoms of depression may be different in people with CI. For instance, irritability is considered a specific symptom of depression in Alzheimer's disease [3]. It was proposed that different criteria should be used for diagnosis of depression in people with Alzheimer's disease [4]. However, it is important to realize that even if symptoms of depression do not fulfill the diagnostic criteria, the subthreshold depression is also deleterious for the patient and should be treated [5].

Is depression a risk factor for developing CI.? Several studies found that many persons who had depression in early life were at higher risk for developing dementia when they were aging [6]. However, more recent studies with longer follow-up found that depressive symptoms in the early phase of the study, corresponding to midlife, do not increase the risk of dementia [7]. In addition, treatment of depression with antidepressants did not change the incidence of dementia in later life [8]. Results of these studies indicate that symptoms of depression before development of CI are markers of incipient dementia, which is already developing, instead of being a risk factor. Therefore, occurrence of depressive symptoms in older person who has no depression history should always be a warning about possible development of CI.

Common pathogenetic processes: Cooccurrence of depression and CI may indicate that both conditions. may share some pathogenetic factors. These factors may include neurotransmitter involvement, vascular changes and beta amyloid deposits. Some neurological degenerative diseases, and especially Alzheimer's disease, cause serotoninergic and noradrenergic denervation [9,10] and loss of serotonin receptors [11]. High occurrence of depression in individuals developing Alzheimer's disease can be expected because of these monoaminergic deficits. The importance of serotonin for depression development is supported by the most effective medications which are selective serotonin reuptake inhibitors (SSRIs). Treatment with antidepressants that potentiate the effect of serotonin may be similar to treatment of CI with cholinesterase inhibitors potentiating the effect of acetylcholine which is depleted in Alzheimer's disease.

Vascular etiology of depression was proposed already 20 years ago [12]. Recent studies found that white matter hyperintensities increase the risk of depression development 8.1 times [13] and it is proposed that reduced white matter microstructural integrity, is a pathophysiological mechanism of late-life major depressive disorder [14]. Presence of white matter hyperintensities predicted development of functional disability in depressed individuals [15] and these changes are also hallmarks of one type of vascular dementia - Binswanger disease [16,17]. Accumulation of beta amyloid in the brain is one of the main pathological markers in Alzheimer's disease. A longitudinal study found that elevated beta amyloid levels are associated with a 4.5-fold increase likelihood of developing significant depressive symptoms during the 54-months follow-up [18]. Therefore, it was proposed that late-life depression could be considered a predementia state and the persons with this condition could be candidates for participation in anti-amyloid drug trials [19]. However, beta amyloid may not be always involved because one study found that people with subjective and mild cognitive impairments and depressive symptoms did not have pathological and biochemical markers of Alzheimer's disease [20].

Consequences of depression in persons with CI: Depression by itself has serious consequences for affected person's quality of life. In cognitively intact persons, that includes reduced well being, reduced quality of life, worsening health status, greater disability, increased morbidity and mortality [21]. In persons with CI and dementia, depression has also other consequences. The most important is an increased risk of development of reactive aggression [22] which happens when persons with depression reject care provided by their care providers [23,24]. Depression is also increasing the risk of development of agitation [25]. It important to realize that these behavioral symptoms of dementia could be improved by treatment with antidepressants if the treatment is effective [26,27].

Unfortunately, the depression in people with CI is often unrecognized and untreated or undertreated [28]. It is important for both primary physicians and physicians treating institutionalized persons with CI to keep in mind that depression should be always considered when persons with CI exhibit behavioral symptoms of dementia, such as abusive behavior or agitation.

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