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Editorial

Cognitive Function in Autoimmune Disease

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In carrying out its functions in everyday life, humans need cognitive functions that work optimally. By definition, cognitive function is a broad term that refers to the mental processes involved in acquiring knowledge, manipulating information, and thinking. Cognitive functions include perception, memory, learning, attention, decision making, and language skills. Therefore, this decline in cognitive function will cause problems related to daily routine activities. For example, cognitive dysfunction will cause attention deficits, impaired verbal and nonverbal learning, impaired short-term memory and visual and auditory work, problem-solving, speed, and motor function.

The spectrum of cognitive dysfunction varies from mild cognitive impairment to severe dementia involving memory, language, thinking and judgment problems that interferes with daily functioning. Several causes cause a decline in cognitive function. Most of the main risk factors are age and several other risk factors such as family history, education level, history of head trauma, exposure to pesticides or other toxins, physical inactivity, chronic diseases such as Parkinson's, heart problems, stroke, and diabetes. Other causes can also come from the presence of an inflammatory process in brain tissue due to an abnormality of blood flow. It can be in blockage of blood flow, an infection process, inflammation, or an autoimmune disease characterized by abnormal regulation and activation of the immune system. This process will result in the infiltration of mononuclear and polymorphonuclear cells, which will release cytokines and chemokines. Increased levels of peripheral inflammatory cytokines, oxidative stress, and decreased brain-derived neurotrophic factors are associated with decreased cognitive function and impaired cognitive tasks. The study conducted by Maeda et al. showed that rheumatoid arthritis patients had a cognitive decline in verbal function, memory, and attention.(1) Furthermore, a study

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conducted by Vitturi et al. showed that more than two-thirds of patients with rheumatoid arthritis had impaired cognition.[2]

Pathomechanism

Several pathomechanisms play roles in cognitive dysfunction in autoimmune diseases.

- *Involvement of arterioles and venules*. Studies show the presence of vasculopathy in the small blood vessels in the brain of patients with systemic lupus erythematosus (SLE). Destructive and proliferative changes involving the vessel wall were found, with extravasation of fibrin and red blood cells. Greater vascular involvement is seen in Kawasaki disease, although studies suggest the vasculitis in Kawasaki disease is temporary.[3] In systemic vasculitis, one study demonstrated a mild impairment of abstract reasoning, nonverbal memory, and mental speed in positive antineutrophil cytoplasmic antibody (ANCA) patients.[4]
- *Autoantibody-mediated damage.* This mechanism could explain what happens in SLE. Autoantibodies play a significant role in the pathomechanism of SLE. Studies have shown the deposition of an antigen-antibody complex with secondary inflammation of the choroidal vessels leading to the neuropsychiatric symptoms of SLE. For SLE, several factors in cognitive dysfunction are immunological factors, inflammation, microglial activation, leakage from the blood-brain barrier, excitotoxic mediators, and aging markers.[5] In Behcet's disease, the study of Cavaco et al. demonstrated the possibility of impaired cognition in the absence of significant neurologic symptoms.[6]
- *Blood brain barrier (BBB) impairement*. Increased permeability of the BBB can be caused by the deposition of immune complexes, activation of complement and cytokines. This makes it easier for neurotoxic autoantibodies to enter the brain causing cognitive dysfunction.[7]
- *Role of Pro-inflammatory cytokines*. Pro-inflammatory cytokines are produced by immunocompetent neuronal, glial, BBB endothelial cells and systemic infiltration. At low levels, cytokines can be neurotrophic, but if excessive they can activate microglia, which causes neuronal death and increased BBB permeability
- *Vitamin D deficiency* is an independent predictor of poorer cognitive performance in SLE patients. In addition, vitamin D has a role in neuronal survivability by preventing oxidative stress and inhibiting the formation of free radicals
- *Treatment Effect*. The use of corticosteroids can impact memory impairment, especially in the older age group. This is associated with increased expression of glucocorticoid receptors on CA1 hippocampal neurons. As a result, chronic steroid exposure impairs synaptic plasticity and cognition, decreases neurogenesis, and causes dendritic atrophy

Diagnosis

Establishing a diagnosis is a challenge in itself. Decreased memory, frequent repetition of questions, changes in mood and habits, visual disturbances, difficulty recognizing faces from family, or disorientation of place and time are symptoms of cognitive impairment. Any change from the patient's previous habits is a marker that needs further investigation. Mild cognitive disturbances may characterize by general confusion or concussion-like symptoms or mood disturbance and forgetfulness. The gold standard for the identification of cognitive impairment, in particular, mild cognitive impairment, is MoCA (Montreal Cognitive Assessment). In addition, other modalities such as

the MMSE (Mini-Mental State Examination) can also be used, which is also intended to assess cognitive impairment empirically. These instruments use a simple cognitive task (e.g., match) to determine the level of cognitive impairment present in the patient. Both instruments are easy to use in daily clinical practice as part of the routine daily process. For SLE, other Instrument can use such as ACR Neuropsychological Test Battery (ACR - SLE Battery), The Hopkins Verbal Learning Test-Revised (HVLT-R), Controlled Oral Word Association Test (*COWAT*) and Automated Neuropsychological Assessment Metrics (*ANAM).*[5] Tracking cognitive performance over time can provide an early picture for diagnosis and management

Treatment

The main focus is the treatment of the underlying autoimmune disease and the predominant symptom. Several case reports show that improving the autoimmune disease underlying disease will improve cognitive symptoms. Not all cognitive dysfunctions require specific pharmacological therapy. Non-pharmacological approaches are also thought to improve cognitive function. A regular, supervised exercise program may be a practical approach to improving cognitive function in addition to cognitive behavioral therapy and cognitive rehabilitation.

Until now, there is still no specific pharmacotherapy aimed at managing cognitive disorders in patients with autoimmune diseases. Some agent use to treat cognitive dysfunction with limited evidence and study. Aspirin, anti malaria, ACE inhibitor are some of studied agent but no recent RCT.[5]

References

1. Meade T, Manolios N, Cumming SR, et al. Cognitive Impairment in Rheumatoid Arthritis: A Systematic Review. Arthritis care & research. 2018;70(1):39-52. Epub 2017/04/04. doi: 10.1002/acr.23243. PubMed PMID: 28371512.
2. Vitturi BK, Nascimento BAC, Alves BR, et al. Cognitive impairment in patients with rheumatoid arthritis. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2019;69:81-7. Epub 2019/08/27. doi: 10.1016/j.jocn.2019.08.027. PubMed PMID: 31447371.
3. Lim L, Lippe S, Silverman E. Effect of autoimmune diseases on cognitive function. In: Dulac O, Lassonde M, Sarnat HB, editors. Handbook of clinical Neurology 112: Elsevier 2013.
4. Mattioli F, Capra R, Rovaris M, et al. Frequency and patterns of subclinical cognitive impairment in patients with ANCA-associated small vessel vasculitides. Journal of the neurological sciences. 2002;195(2):161-6. Epub 2002/03/19. doi: 10.1016/s0022-510x(02)00015-1. PubMed PMID: 11897248.
5. Ernes M, Rahman PA. Diagnose and Management of Cognitive Disorders Systemic Lupus Erythematosus (SLE). Clinical and Research Journal in Internal Medicine. 2022; 3(1);250-263. DOI: https://doi.org/10.21776/ub.crjim.2022.003.01.6
6. Cavaco S, da Silva AM, Pinto P, et al. Cognitive functioning in Behçet's disease. Annals of the New York Academy of Sciences. 2009;1173:217-26. Epub 2009/09/18. doi: 10.1111/j.1749-6632.2009.04670.x. PubMed PMID: 19758154.
7. Seet D, Allameen NA, Tay SH, et al. Cognitive Dysfunction in Systemic Lupus Erythematosus: Immunopathology, Clinical Manifestations, Neuroimaging and Management. Rheumatology and therapy. 2021;8(2):651-79. Epub 2021/05/17. doi: 10.1007/s40744-021-00312-0. PubMed PMID: 33993432; PubMed Central PMCID: PMCPMC8217391.