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MANAGEMENT OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS: CURRENT APPROACHES AND FUTURE PERSPECTIVES

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Abstract:
The neuropsychiatric systemic lupus erythematosus (NPSLE) is a multifactorial disorder with worse outcomes on a patient's life. Disease have heterogeneous and uncommon neuropsychiatric (NP) manifestations including the central and peripheral nervous system. Clinical presentation is challenging due to deficits of standard for proper management. The clinical manifestation of non-SLE does not differ with NP symptoms. Subsequently, individualized therapeutic strategies based on the severity of symptoms were applied. Symptomatic therapy is an adequate method to treat mild NP patients while the same method is ineffective to treat the patient with severe signs of NPSEL. MRI with other different techniques can be used to identify the NP and SEL. Further, the article is a review of the diagnosis, current and future management of NPSEL.

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INTRODUCTION:

The chronic multisystem inflammatory auto-immune disorder, systemic lupus erythematosus (SLE) can be described with the involvement of neuropsychiatric, which is an emerging clinical challenge for the protection of viscera, having a huge contribution to increasing the economic burden and responsible for high mortality and morbidity. [1] Disease has a broad spectrum of clinical presentation with the non-specific and heterogeneous class of neuropsychiatric (NP) manifestations. Its clinical assessment is difficult because of similarities in the attribute of NP symptoms to SLE. [2] The lack of existence of laboratory, radiological biomarker and deprivation in the establishment of a diagnosis and guiding therapy decisions in neuropsychiatric SLE (NPSLE). The recommendation of clinical diagnostic approach through multidiscipline and therapeutic approach for an individual based on the severity of diseases' symptoms. The prevalence of NPSLE is different for the different population as it based on the type of syndrome present. [3] in this article we will discuss the epidemiology, diagnosis, treatment along with the potential future therapies to treat the individuals with NPSLE.

Epidemiology:

Epidemiological history of SLE and NPSLE alludes to the difference of prevalence of both disorders depend on age, sex, and ethnicity. It is confirmed by evidence that SLE is significantly greater in women of childbearing and its female to male ratio is 15:1. However, females are at greater risk to develop the NP, and escalated risk of seizers in males was reported. [4] The embodiment of NP are more observed time after time in Africans, Hispanics, and Asians than in white individuals. In a cohort study of Maryland LUMINA demonstrated that a more deleterious effect of NP was found in white patients. The controversy was found between the prospective and retrospective studies regarding the prevalence of NPSLE which varied from 17.6% to 44.5%. [5]

A large number of studies entailed minor, non-specific symptoms included mild depression and anxiety to some extend are specified by investigator-dependent. After neglecting these minor issues the reported prevalence 4.4% and the incidence rate 7.8/100 person/year for the peripheral nervous system PNS. [6] Afterword, the comparison of previous data (myelopathy shows prevalence 22% rather than 1-1.5) demonstrated that the proportion of the major central nervous system substantially enhanced. [8] NPSLE more worsen the SLE which impair the quality of life, contribute to morbidity and mortality. A recent study reported NPSLE increases the 10% mortality rate in the general population. [7]

Diagnostic Approach in NPSLE:

Diagnose patients with NPSLE should be carried out by considering all the investigations performed for non-SLE patients. Diagnosis at a clinical level can be performed by using the laboratory, electrophysiological, neuroimaging data, based on clinical performance. [9] the autoantibodies (aPL, b2-glycoprotein antibodies) offer the instructive knowledge for diagnosis of NPSLE specifically for patients with cerebrovascular disease. An intimation about the serum anti-ribosomal P antibodies has an association with lupus psychosis. [10] In a study it is suggested that there is a connection between the NPSLE and N-methyl-D- aspartate antibodies but another study found contrary to this evidence. The measurement of autoantibodies would be a better option for the diagnosis in patent with optic neuritis and myelopathy but avoid to recommend for clinical practice because of the shortfall of specificity. [11] In clinical practice of NPSLE magnetic resonance imaging (MRI) can be used which is a neuroimaging technique, able to highlight the brain and spine abnormalities, identify the lesion due to NPSLE and diagnose the tumor or infection. [12] In a study of MRI majority of patients with no abnormalities and merely white matter hyperintensities are measured, have no association with NPSLE. New emerging MRI techniques have been proposed to identify the patients of NP and SEL such as diffusion-weighted imaging, proton magnetic resonance spectroscopy method, and nuclear imaging techniques' includes emission tomography and single-photon emission computed tomography. Although, to use these techniques in clinical practices more evidence is needed. The multimodal imaging test can be used as a single imaging test alone is not enough to detect the brain injury in these patients. [13]

General Treatment:

i. Symptomatic Therapy

To treat the patients with NPSEL multimodal management is needed. Symptomatic therapy is required for various patients with NPSLE. The first step treatment (drugs) given to a patient with SLE having signs of a seizure, psychosis disease, movement disorders, and headache instead of considering them underlying symptoms of NPSLE. Symptomatic therapy is an adequate method to treat mild NP patients while the same method is ineffective to treat the patient with severe signs of NPSEL. Immunosuppressive and anti-thrombotic medicines are recommended in these cases. In the case of

psychiatric disease anti-depressive, anti-psychiatric agents are advice in accordance with disease indication. Another therapy, anti-epileptic therapy has given according to risk assessment likely, severe brain injury, brain abnormality, focal neurological sign, and partial seizures. Phenytoin or barbiturate mostly used to treat generalized seizures and carbamazepine, valproic acid can be used to handle partial seizures. To manage the symptomatic pain nonsteroidal anti-inflammatory can be used and migraine for localized headaches. [1]

ii. Nonpharmacological Intervention

Particularly inquest reported the patients in case of SLE are normally encounter cognitive issues while their incidence is between 17-66 percent. Although patients ordinary show mild abnormality in cognitive functions, immunosuppressant therapies are given to them. Some psychologic factors are basically the cause of cognitive dysfunctioning like lack of sleep, the sensation of pain, frustration, and depression. The SLE is not more associated with cognitive dysfunctioning based upon the unavailable symptomatic therapies. Furthermore, those who have been reporting for the dysfunction of cognitive abilities are mostly treated with antidepressive drugs. [17]

Potential Future Therapies:

The mechanism of pathogenesis behind the NPSLE is known improperly. But the drug development has been advanced in the order to learn the SLE immunopathogenesis which cytokines and other costimulatory modulation. However, experimental evidence on these advanced therapies is not sufficient. But the known pathogenesis of NPSLE enables us to discuss the treatment and effects of these drugs from this perspective. so, to go with ease effect of rituximab suggests the B cell's helping contribution in the pathogenesis of NPSLE. A United State and European licensed drug belimumab have a stimulating effect of antibodies against the BLyS are now using for the SLE treatment. Even though, the explanation of organ system-oriented efficacy has not been empowered by BLISS designs or trials. [18]

On the other hand, therapies trials are preceding focused on phase II and III (tabalumab and blisibimod respectively). SLE patients have been checked for Atacicept, which has receptors on APRIL and BLyS. The preceding results indicated the increased levels of APRIL and BLyS together in the CSF of the patient. With exception of NPSLE patients found with elevated APRIL in CSF comparative to the asymptomatic patients of SLE and of neurologic issues. In the etiological prospect of NPSLE patients, the local production of APRIL and BLyS has been revealed in the brain with a significant role in the cause. Consequently, the antagonist action of cytokines shown an advantageous effect in NPSLE patients. However further research in concerned therapies is on the way to come up but the patients who kept the severity of CNS exhibition were not part of any trial, which impose a limited conclusion in this regard. [19]

DISCUSSION:

A study attempted on neuropsychiatric systemic lupus erythematosus (NPSLE) which heavily impacts the quality of life with worse disease outcomes. The pathogenesis of NPSEL is multifactorial and its management is multimodal. The finding shows that 32 patients (19%) out of 169 died within 6 years after the diagnosis. Its mortality rate has been enhanced up to 9.5% with severe symptoms. [15]

The finding of one more research for diagnosis of neuropsychiatric systemic lupus erythematosus shows that 15 patients diagnosed with NPSEL and 16 without the NPSEL, the age of patients varies from 18 to 58 years (females), correlation of white matter dysfunction has existed for patients with NPSEL while smaller degree was correlated in patients with non-NPSEL. [16]

CONCLUSIONS:

The treatment of NP patients is challenging for the physician because of the rare appearance and understanding of symptoms even in patients with SLE. Notably, the lack of evidence for better characterization of NPSEL and deficit of proper management seem a hinder for timely treatment. Therefore, more evidence, findings, and understanding are required to target the exact barriers to approach a better management system.

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