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Review Article

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Review on Diagnosis and Management Approach of Multiple Sclerosis

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ABSTRACT

The most prevalent non-traumatic debilitating illness affecting young individuals is multiple sclerosis (MS) (2). Both industrialized and emerging nations are seeing an increase in the incidence and prevalence of MS, whose underlying etiology is still unknown. In addition to some well-known environmental variables, such as vitamin D or ultraviolet B light (UVB) exposure, Epstein-Barr virus (EBV) infection, obesity, and smoking, MS is a complicated illness with several genes that can influence disease vulnerability (3). The Medline, Pubmed, Embase, NCBI, and Cochrane databases were searched for studies of patients with non-alcoholic fatty liver disease. Incidence, etiology, and management options were analyzed. The etiopathogenesis of MS is convoluted. The processes through which genetic and environmental risk factors for the illness alter risk are still largely unclear, despite significant improvements in their detection. Discovering these processes might result in the identification of novel and more focused therapy targets as well as disease pathways.

Key words: *Multiple sclerosis, Diagnosis, Disease course, Epidemiology, Phenotypes, Prognosis*

INTRODUCTION

The most prevalent non-traumatic debilitating condition that affects young individuals is multiple sclerosis (MS) [1]. Both industrialized and emerging nations are seeing an increase in the incidence and prevalence of MS [2], whose underlying etiology is still unknown. In addition to some well-known environmental variables, such as vitamin D or ultraviolet B light (UVB) exposure, Epstein-Barr virus (EBV) infection, obesity, and smoking, MS is a complicated illness with several genes that can influence disease vulnerability [3].

The classification of multiple sclerosis as an organ-specific T-cell-mediated autoimmune disease has existed for some time. However, the conventional T-cell autoimmune dogma is called into question by the efficacy of B-cell targeted treatments [4-6]. Relapsing-remitting illness is thought to be caused by early inflammation, whereas

secondary and main progressive MS is thought to be caused by delayed neurodegeneration [7]. The long-term prognosis for MS patients is improving due to the development of increasingly potent biological treatments and an active strategy for treating MS, particularly the treatment of a target of no apparent disease activity (NEDA) (pwMS). A limited percentage of MS patients may be cured with more intensive immune reconstitution therapy which causes a portion of MS patients to go into long-term remission [8].

Those with more advanced MS have optimism that recent successful studies of disease-modifying treatments would halt the disease's progression while preserving its remaining function [9]. The conventional two-stage concept of the natural history of MS is strongly challenged by the observation that therapies appear to be effective at various phases of the disease cycle [10].

Epidemiology

Multiple sclerosis often develops between the ages of 20 and 40 in young adulthood. Females are two to three times more likely to be impacted than males, and in some parts of the world, this disparity appears to be growing [11]. The prevalence of multiple sclerosis is 33 per 100 000 individuals worldwide, with substantial regional variation. Asia and countries in sub-Saharan Africa have the lowest prevalence (2.2 and 2.1 per 100 000 people, respectively), while North America and Europe have the highest prevalence (140 and 108 per 100 000 people, respectively) [12]. However, there is significant regional variation within Asia (0.77 per 100 000 in Hong Kong; 85.80 per 100 000 in Iran) [13]. According to recent studies, the frequency is rising in several areas, including northern Japan (18.6 per 100 000) [14]. Regardless of frequency, multiple sclerosis incidence appears to be rising internationally [15].

The exact causation of multiple sclerosis is unclear, although it is generally recognized to have a multifactorial origin where genetic and environmental variables interact in a complicated way to influence a person's risk for developing the illness. Therefore, it is believed that a variety of changeable environmental variables, which are mostly governed by the major histocompatibility complex, have a role in deciding whether a person will develop multiple sclerosis in genetically vulnerable people. Strong evidence supports the link between Epstein-Barr virus infection, smoking, poor vitamin D levels, and an elevated BMI during adolescence, all contributing to a greater chance of developing multiple sclerosis among environmental variables that have been evaluated. Some of these elements, like vitamin D levels and smoking, may also affect how the multiple sclerosis condition develops in the future [11].

Particularly among those with comorbidities such as mental illnesses, cerebrovascular and cardiovascular disease, diabetes, or cancer, multiple sclerosis patients have a higher death rate and a lifespan expectancy of only around ten years compared to the general population [16]. However, during the past 60 years, people with multiple sclerosis have experienced an increase in survival rate, according to two recent studies utilizing national samples from Denmark and Norway [17].

Signs and symptoms

Multiple sclerosis (MS) and the field of primary demyelinating diseases of the central nervous system (CNS) as a whole produce a staggering number of publications every day, each one focusing on a different aspect of the disease, making it impossible to keep up with the vast amount of new information. As might be expected, the majority of studies focus on topics like the etiology and pathophysiology of MS, which are currently poorly understood or require further research. Over the last two decades, claims of novel therapeutics that purportedly alter the course of MS have proliferated in the literature; these treatments are known as "disease-modifying medications" (DMD). Unquestionably, the identification of DMD has advanced our understanding of the illness, opened up new avenues for study, and raised hopes for a potential solution. Even so, second-line DMD drugs must be weighed against their superior efficacy, which must be weighed against their inferior safety profile [18], as the first-line drugs act on the inflammatory, but not the neurodegenerative, mechanisms of the disease. As a result, the impact on long-term disability is minimal.

A thorough and customized treatment intervention is required for MS patients to manage the disease's symptoms and physical manifestations and improve their quality of life. It is important to keep in mind that MS is a neurological condition with unexpected clinical symptoms, a protracted duration, and a high risk of impairment.

Among the various therapeutic modalities used across the world to treat the condition, symptomatic therapy and rehabilitation techniques are of utmost significance. To better appreciate the role of symptomatic therapy, both pharmaceutical and non-pharmacological, it is necessary to identify the physiopathological changes occurring in the demyelinating lesions that impair the function of the nerve fibers during the disease. Because of its intricacy

and the presumption that such mechanisms are the domain of biophysical and biochemical sciences, this issue is not usually covered in the literature aimed at neurological doctors.

Patients with MS have a partial or complete loss of physiological functioning during relapses, which is accompanied by several unpleasant symptoms such as paresis, hypoesthesia, visual impairment, diplopia, or ataxia. Every day at MS Clinics, patients' clinical symptoms and disease stages vary greatly from one another, as is attested to by the high degree of patient variability. The range of conduction qualities presented by the damaged axons affects the clinical manifestation in addition to the location of MS lesions.

Diagnosis

Only clinical and/or radiological evidence of lesions in the CNS that are dispersed in space (DIS) and time (DIT) can establish the diagnosis of multiple sclerosis. The existence of DIS and DIT was solely determined by clinical evidence before the MRI was accessible. However, the most recent criteria now make use of MRI results to confirm the existence of DIS and DIT. This frequently enables an earlier diagnosis, which, when necessary, can lead to earlier treatment. Using the 2010 McDonald criteria, the diagnosis of multiple sclerosis can be made after the emergence of a clinically isolated condition (CIS) if it meets the DIS and DIT criteria [19].

The McDonald's criteria can substantially aid in the diagnosis of multiple sclerosis, but it is important to remember that they are only helpful when used in the right clinical setting. Furthermore, the diagnosis of multiple sclerosis is still regarded as a diagnosis of exclusion, and all other diseases should be taken into consideration and ruled out, and the diagnostic criteria should only be used for individuals presenting with characteristic CIS symptoms. The existence of brain and spinal cord lesions in multiple sclerosis may be found by MRI, which is also useful for ruling out other disorders [20]. Recent publications provide specific recommendations for using brain and spinal cord MRI in the clinical diagnosis of multiple sclerosis [21]. One of the most crucial paraclinical instruments for making the diagnosis of multiple sclerosis is the MRI. The 2001 McDonald criteria [22], which initially considered the MRI, have since been refined and adjusted to simplify them without sacrificing sensitivity and specificity [23].

Multiple sclerosis frequently includes intracortical lesions. Three studies have examined the value of adding intracortical lesions as a new location to satisfy DIS criteria since the 2010 criteria were published. Collectively, these investigations discovered that adding intracortical lesions to the criterion improved specificity without reducing sensitivity, increasing the criteria's accuracy [24]. However, because intracortical lesions are difficult to image and identify in most centers, it was suggested that these lesions be combined with the juxtacortical topography [25].

As part of the standard diagnostic process for multiple sclerosis, blood tests are frequently required. Routine auto-antibody testing, however, is not always helpful for individuals who have a typical CIS [26]. As a result, it would be sensible to test for autoantibodies only in the presence of other symptoms that are indicative of other autoimmune illnesses.

Risk factors

Decades ago, it was established that there were genetic components to the risk of MS. Strong evidence for a genetic foundation for the illness comes from familial clustering of the condition, which increases risk based on how genetically close a person is to the proband and higher prevalence of MS in specific racial groups. Multiple DNA mutations that are quite common in the community, according to family and population statistics, may be the cause of MS heritability [27].

Environmental risk factors

Numerous environmental elements and exposures have been linked to an increased risk of developing MS. However, few have been investigated in sufficient numbers and with reduced bias, and even fewer of those results have been repeatedly duplicated. With an emphasis on those that have been linked more recently, this article analyzes the factors with the greatest damning evidence for an involvement in MS, such as limited sunlight exposure, vitamin D insufficiency, obesity, and smoking [28].

Human herpesvirus Epstein-Barr Virus (EBV) is quite common. People of many races and ethnicities have repeatedly demonstrated an association between adult- and pediatric-onset MS and EBV seropositivity, or the presence of antibodies suggesting past exposure to EBV [29]. In fact, serologic evidence of past EBV infection is present in virtually all adult MS patients. Epstein-Barr nuclear antigen 1 antibody titers are greater in MS patients.

Ultraviolet radiation exposure and vitamin D

At higher latitudes, MS incidence and prevalence are higher. Numerous research investigating how sun exposure and vitamin D affect the risk of MS was inspired by this discovery. Studying the separate impact of these factors on the likelihood of having MS is challenging since ultraviolet exposure causes the skin to manufacture vitamin [30, 31] D. However, it appears that both UV radiation and vitamin D are linked to a decreased risk of developing MS, and not all of the UV radiation's effects may be fully explained by its role in vitamin D production [32].

Obesity

Obesity and the risk of MS have been linked in several cohort and case-control studies. Obesity throughout youth and early adulthood, but not later in life, appears to be linked to a future risk of MS, much like many other environmental risk factors. Overtly obese people are in the greatest danger, while others who are only slightly overweight may also be at higher risk [33].

Smoking

A large case-control study and pooled analysis of several smaller studies have shown that smoking is a risk factor for MS [34].

Lifestyle risk factors

The investigation of the relationship between different nutrients or dietary components and the risk of a disease can be impacted by a variety of biases, including recollection bias, measurement bias, and confounding, in particular. It is extremely challenging to demonstrate the relationships between the observed connections and their causes.

Treatment

The cornerstone of relapsing-remitting MS therapy is disease-modifying medications. Some of the most common disease-modifying treatments are glatiramer acetate, dimethyl fumarate, fingolimod, interferon-beta preparations, natalizumab, and mitoxantrone. Once MS has been identified, therapy should start right away. A decrease in the activity of MRI lesions is a short-term objective. Preventing secondary progressive MS is one of the long-term objectives. Following the start of therapy, the main concerns are patient compliance and medication toxicity monitoring [30].

- Glatiramer acetate is a combination of artificial polypeptides that may act as a ligand for major histocompatibility complex (MHC) molecules. Binding restricts activation and promotes the growth of regulatory cells. Additional potential methods for neuroprotection and repair [30]. Subcutaneous administration is used. Although glatiramer acetate is well tolerated, it is ineffective for the treatment of MS progression.
- There are several potential modes of action for interferon-beta preparations. Interferon-beta affects T and B-cell activity, which may change cytokine expression, contribute to the restoration of the blood-brain barrier, and may lessen matrix metalloproteinase production. Depending on the formulation, administration can either be subcutaneous or intramuscular. Flu-like symptoms and a temporary exacerbation of the patient's current neurologic problems are examples of side effects.
- An injectable humanized monoclonal antibody called natalizumab prevents leukocyte adherence to vascular endothelial cells. Leukocyte migration into the central nervous system is prevented by this medication. Usually, natalizumab is well tolerated. During intravenous administration, light headaches and flushing are frequent side effects [30].
- Mitoxantrone is a chemotherapy drug that is injected intravenously that inhibits both RNA production and DNA repair. A potential impact on cellular and humoral immunity may serve as the MS treatment's mechanism of action [31]. Numerous negative consequences, such as baldness and amenorrhea, have been seen.
- An oral medication called fingolimod has immunomodulatory effects that may be related to the suppression of T-cell migration. Hepatotoxicity, lymphopenia, and bradycardia are examples of potential adverse effects.

Patients with primary progressive MS, secondary progressive MS, and progressive-relapsing MS appear to largely represent neurodegenerative processes. Since disease-modifying medicines are less successful, their effects on disease progression have ranged from potential benefit to negligible. Young individuals with rapid disease progression appear to benefit the most [31].

The following guidelines illustrate how to manage sudden relapses:

1. Treatment of a potential underlying issue that may have led to a recurrence (such as an infection or metabolic derangement)
2. Treatment of symptoms depending on particular neurologic symptoms
3. A brief corticosteroid course to aid in recovery
4. Rehabilitation with physical and occupational therapy participation

CONCLUSION

A chronic CNS condition with a strong immunological component, multiple sclerosis primarily affects younger persons worldwide. Lesions that are dispersed in both time and space are the clinical, radiological, and pathological hallmarks of multiple sclerosis. Early diagnosis and treatment have been made possible by improvements in imaging technology and continuous diagnostic criteria refinement, and efforts are being undertaken to further improve the definitions of disease phenotypes. The outlook for people with multiple sclerosis varies greatly from patient to patient. Clinical, imaging and laboratory indicators might help predict clinical course and optimize treatment in specific patients when combined with clinical judgment. A significant unmet need in the clinical practice of multiple sclerosis will be filled by future research that will enable the creation of more precise biomarkers for disease classification and prognosis, enabling prompt customized therapy.

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