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Chapter

Introductory Chapter: Multiple Sclerosis

Stavros J. Baloyannis

1. In the labyrinth of multiple sclerosis

Multiple sclerosis (MS) remains a crucial unsolved problem in the field of neurosciences, being also a serious cause of suffering for millions of patients worldwide affecting the quality of life, the personal and social economy, and the psychosomatic homeostasis substantially in the majority of the patients.

The etiopathological background of the disease, which is a progressive inflammation of the CNS [1, 2], inducing demyelination in the white matter and degenerative alterations in the gray matter in various areas of the brain hemispheres, the cerebellum, the brain stem, and the spinal cord, may provoke a multitude of polymorphic clinical phenomena inducing a variable type of physical, mental, and social disability in the suffering people [3, 4].

The incidence of MS varies considerably across geographic regions, with high rates in high latitude and low in the tropical zone, affecting three times more women than men at any age, though the climax is between 20 and 40 years. Approximately 2.5 million people in the world suffer from multiple sclerosis nowadays, and 700,000 among them are registered in Europe [5–7].

Many genetic factors, MHC and non-MHC, may play an important role in the innate immune mechanisms and in the modulation of the immune system under the influence of the many exterior environmental risk factors and viral infections [8, 9]. Among the viruses, the infection with Epstein–Barr virus (EBV), which is a common human herpes virus, seems to have a considerable association with the incidence of MS, particularly among pediatric patients [10–12].

A large number of patients have from onset the experience of relapses and remissions of the various neurological phenomena, lasting for many years, whereas a substantial number of untreated patients face the tragedy of the continuous deterioration of their physical and mental condition, resulting in a serious irreversible disability eventually, though primary progressive forms starting from the onset of the disease may also occur in approximately 10–15% of patients [13, 14].

Energy failure is obviously the substantial cause of the functional impairment in the majority of patients who suffer from multiple sclerosis. That cause is reasonably associated with demyelination, neuronal degeneration, and axonal loss, based on a wide spectrum of innate autoimmune mechanisms, inflammatory reactions, mitochondrial dysfunction, cytokine interactions, intracellular and interstitial edema, and perivascular cell reactions [15, 16].

2. The multiform suffering

The multiform clinical manifestations of the disease vary from person to person, from time to time, from age to age, and most of them are unstable and

changeable in the majority of the cases even from the initial stages of the disease. Vertigo, nausea, vomiting, hiccups, motor deficits, tremors, dysarthria, cutaneous sensory deficits, sensory phenomena from mucosae, cerebellar dysfunction, gait instability, diplopia, vision impairment, visual field defects, dyschromatopsia, phosphenes, hearing impairment, painful conditions, neuralgia of the trigeminal nerve, autonomic dysfunction, sphincter insufficiency, fatigue, and cognitive decline, such as episodic memory deficits and impaired visuospacial estimation, emerging early in the disease compose a part of the frequently resizing pattern of the disease [17].

Particularly, cognitive decline, which would be attributed to the association of gray and white matter lesions [18], in addition to disconnection and dissociation syndrome, is frequently underestimated in the initial stages of the disease, necessitating neuropsychological evaluation by properly designed tools for MS patients [19]. In fact, cognitive phenomena are evident in the same degree of severity during all the stages of the disease, concerning all clinical subtypes [20, 21]. Cognitive rehabilitation, which is essential for the improvement of the quality of life of the patients, may include various methods and technics enabling the patients to overcome common problems of everyday life and to cope harmoniously with the disease burden, improving skills and capacities on the basis of the neuronal plasticity and the principle of functional reorganization of the brain [22, 23].

Language disorders are not rare phenomena in patients who suffer from MS [24]. The naming deficit, semantic paraphasia, impaired verbal fluency, grammar and syntax deficits, and the loss of high-level language skills necessitate the appropriate speech therapy [25].

3. Searching for the truth

Diagnostic criteria for multiple sclerosis have been proposed and introduced for many years and have been revised over times [26]. Most of them may simply facilitate the approach of the diagnosis of the disease. In general, the clinical estimation of the patients and the incorporation of data from the paraclinical investigation, especially from MRI [27], diffusion imaging, resting state functional MRI, magnetic resonance spectroscopy, evoked potentials, optical coherence tomography (OCT) [28], OCT angiography, and immunological analysis of the CSF, may lead to a prompt diagnosis of the disease even in patients with atypical clinical manifestations and marked course heterogeneity [29, 30].

In the cases that clinical and neuroimaging data are atypical or inadequate for posing the diagnosis of MS, the findings of oligoclonal band and immunoglobulin G (IgG) level in the cerebrospinal fluid analysis, in correlation with the serum data, would be a strong argument of intrathecal inflammation, advocating in favor of the diagnosis of MS [31].

However, in the differential diagnosis of multiple sclerosis, a substantial number of other conditions mimicking the clinical manifestations of the disease should be under consideration [32]. Among them, the neuromyelitis optica spectrum disorder (Devic's disease) would be differentially diagnosed on the basis of anti-aquaporin 4 antibody (AQP4-IgG) [33], the acute disseminated encephalomyelitis (ADEM) on the basis of the clinical profile and the neuroimaging data [34], the MOG antibody disease on the basis of the level of MOG antibodies [35], and the antiphospholipid syndrome by the detection of lupus anticoagulant and anticardiolipin antibodies [36]. In addition systemic lupus erythematosus, small vessel disease, and Susac's syndrome have a substantial place in the expanded spectrum of the differential diagnosis of MS [37].

Disease activity is usually estimated by the clinical relapses and the MRI findings of contrast-enhanced lesions, enabling the detection of new lesions on T2-weighted images. However, a reasonable criticism and a periodic reevaluation of the adopted diagnostic criteria would be of substantial importance for the accuracy of the prompt diagnosis of MS [38, 39].

4. Perspectives on resolution

There is no definite targeted therapeutic approach for MS [40–42]. The application of many current treatments aims at ameliorating the quality of life of the patients by reducing the disability progression and stabilizing the clinical condition of the patients [43].

The introduction of interferon in 1993 opened the horizons of many potential therapeutic options of various efficacy and side effects, which turned to raise many reasonable controversies from the viewpoint of the heterogeneity of the disease, the obscure etiopathological background, and the complexity of the pathophysiological mechanisms [44].

An efficient therapeutic strategy should be based on a clear knowledge of the pathogenetic mechanisms of the disease. The investigation of the role of the myeloid cells and the infiltration of the CNS by peripheral lymphoid and myeloid cells may be crucial for a deeper understanding of the progression of the disease and the chronicity of the clinical phenomena [45, 46].

Novel therapeutical attempts aiming at modulating the activities and reactions of myeloid cells might be hopeful in treating MS patients at the initial stages of the disease. In addition the application of autologous EBV-specific T cell therapy may improve the clinical condition of the patients, ameliorating consequently the quality of life in a substantial number of them [47–49].

Non-pharmacological therapies [50], such as appropriate diet [51], proper environment, physical exercise [52], psychological relaxation [53] and progressive muscle relaxation therapy (PMRT), psychotherapy [54], cognitive behavioral therapy [55], music therapy [56], and emotional, social, and spiritual support [57] may also play a considerable beneficial role in the amelioration of the quality of life in the large majority of the patients.

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