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Review

Multiple sclerosis: Therapeutic applications of advancing drug delivery systems

Sanam Dolati[a,b,c], Zohreh Babaloo[b,c], Farhad Jadidi-Niaragh[b,c,d], Hormoz Ayromlou[e], Sanam Sadreddini[a,b,c], Mehdi Yousefi[b,c,*]

[a] Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[b] Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[c] Department of Immunology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[d] Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[e] Department of Neurology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

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ABSTRACT

Multiple sclerosis (MS) is an inflammatory autoimmune disease of the central nervous system, which is accompanying with demyelination, neurodegeneration and sensibility to oxidative stress. In MS, autoreactive lymphocytes cross the blood–brain barrier (BBB) and reside in the perivenous demyelinating lesions which create various distinct inflammatory demyelinated plaques situated predominantly in the white matter. The current MS-related therapeutic approaches can be classified into disease-modifying therapies (DMTs) and symptomatic therapy. DMTs suppress circulating immune cells, inhibit passing the BBB and decrease the inflammatory responses. Recent advances have remarkably delayed disease development and improved the quality of life for numerous patients. In spite of major improvements in therapeutic options, there are some limitations regarding the routes of administration and the necessity for repeated and long-term dosing in which cause to systemic disadvantageous consequences and patient non-compliance. Nanotechnology presents promising approaches to improve autoimmune disease treatment with the capability to overcome many of the limitations common to the current immunosuppressive and biological therapies. Here we emphasis on nanomedicine-based drug delivery approaches of biological immunomodulatory mediators for the treatment of multiple sclerosis. This comprehensive review details the most successful drugs in MS therapy and also focuses on conceptions and clinical potential of novel nanomedicine attitudes for inducing immunosuppression and immunological tolerance in MS to modulate abnormal and pathologic immune responses.

Contents

* Corresponding author at: Immunology Department of Immunology Faculty of Medicine Tabriz University of Medical Sciences Tabriz, Iran.
E-mail address: Yousefime@tbzmed.ac.ir (M. Yousefi).

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1. Introduction

Charcot, Carswell, Cruveilhier and others were identified the clinical and pathological characteristics of multiple sclerosis (MS), more than 100 years ago [1]. MS is a chronic immune-mediated demyelinating disease of the central nervous system (CNS) accompanying with a relapsing-remitting (RR) or a progressive course that followed by axon damage and paralysis. MS usually appears in people with 20–50 years old and women are usually more predisposed to evolving MS [2,3]. MS has been affected about 500,000 people in the US and 2.5 million individuals worldwide and approximately 20000 MS patients died all over the world in 2012 comparing to 12000 in 1990 [4,5]. MS exhibit a diversity of chronic physical, neurological and psychological symptoms containing muscle weakness, weak reflexes, muscle spasm, difficulty in move, miss coordination and unbalance [6,7]. While the etiology of MS remains elusive, it seems that disease beginning and progression is affected by the genetic, infectious, immunological or environmental factors [8]. Remarkable advancements are recently achieved regarding the novel treatment options for RRMS [9]. At this time, there are numerous disease-modifying therapies (DMTs) approved or under clinical development for the treatment of relapsing forms of MS [10]. Nanotechnology is a novel promising approach which exerted an enormous contribution in diagnosis and treatment of CNS-related disorders [11]. Nanomaterials exhibit a widespread field of actions in MS therapy; they help to attain efficient systems for CNS drug/gene delivery, tolerance inducing vaccine, tolerance-inducing nanocarriers and platforms for screening restarting therapeutics [12]. The present review is focused on available treatments and nanomaterials at the neuro-immune interface and provides an outlook into the near future to improve treatment of MS.

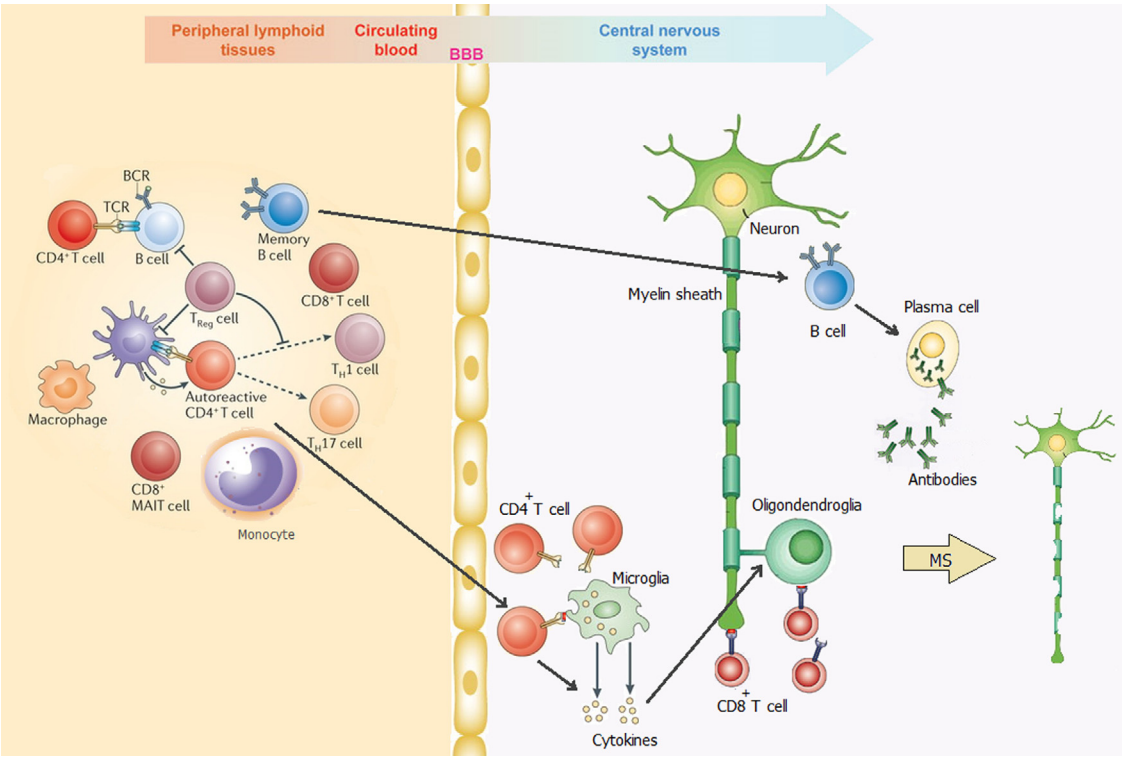

Fig. 1. MS Immunopathogenesis: In MS, two steps are essential to induce an immune response in central nervous system (CNS): myelin sheath damage and inflammation. Demyelinating white matter lesions accompanied by infiltrates of mononuclear phagocytes, B lymphocytes, plasma cells, and dendritic cells and CD8+ T cells, differentiated CD4+ T helper 1 (TH1) and TH17 cells into the CNS. After clonal expansion, B cells mature to plasma and release large amounts of antibodies. Reactivation of immune cells leads to heightened production of inflammatory cytokines. These cytokines attract other immune cells, such as macrophages, which release injurious immune mediators and direct phagocytic attack on the myelin sheath.