Benign Multiple Sclerosis: A Distinct Clinical Entity with Therapeutic Implications

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Abstract This chapter describes the natural history of multiple sclerosis and, in particular, reviews the controversy regarding the entity of benign multiple sclerosis. Based on the Olmsted County population prevalence cohort study performed at the Mayo Clinic, MS patients with EDSS scores of 2 or lower followed for a period of 5–10 years have a very small risk of developing disability over the next 10–20 years. Based on these findings, this chapter reviews the indications, efficacy, mode of action, and side effect profiles of the currently approved and available disease-modifying agents for the treatment of multiple sclerosis. The efficacy of these agents is discussed based on the concepts of evidence-based medicine and the natural history of the disease. We review the arguments for and against treating all patients with MS. The authors propose an individualized approach to the use of these agents in the MS population.
1 Introduction

The past decade has witnessed significant advances in the understanding of the pathophysiology of MS and in the development of novel disease-modifying agents (DMA). The use of DMA in the treatment of patients with MS has drastically increased not only in the United States but throughout the rest of the world. Currently, in the United States, most patients given a diagnosis of relapsing-remitting MS are commenced on a DMA. Controversy still exists regarding how early DMA should be commenced and whether all patients with relapsing-remitting MS should in fact be treated [21, 54]. To answer these questions, it is important to know the natural history of the disease.

The public associates a diagnosis of MS with the need for a wheelchair and certain disability. This misinformation may motivate many patients with a recent diagnosis of MS or a clinically isolated syndrome to initiate long-term DMA. In order for the patient and physician to make the best therapeutic decision for the patient, both parties must study DMA efficacy, the side effects, mode of administration, and costs, and review the natural history of the disease.

In this chapter, we will describe the natural history of MS and review the controversies regarding the entity of benign MS. We will review the indications, efficacy, mode of action and side effect profiles of the currently available FDA approved DMA. We will discuss the importance of evidence-based medicine and natural history studies in treatment decision making. We will review the arguments for and against treating all patients. We will discuss a possible change from the blockbuster to a more individualized patient care approach.

2 Natural History of Multiple Sclerosis: Disability Progression

Upon receiving a diagnosis of MS, patients are generally most concerned with their long-term prognosis. Long-term follow-up studies of MS natural history cohorts from many different regions including Lyon, France [10, 11], Gothenburg Sweden [14, 58], Olmsted County, Minnesota, USA [50, 51, 57], London, Ontario, [67, 69] and British Columbia [65] Canada provide useful information on the accumulation of disability in MS. Most of these natural history studies define the course of the disease over a long period of time in an untreated population.

These studies have relied heavily on the use of the expanded disability status scale score (EDSS) as an outcome measure [35]. The EDSS, a measure of impairment, ranges from a level of zero (no disability) to ten (death). Three cutoff scores used consistently throughout natural history studies include EDSS 3 (or 4 in some), moderate dysfunction including monoparesis or mild hemiparesis; EDSS 6, which indicates a need for unilateral assistance (need for a care); and EDSS 8 (or 7 in some), in which the patient is restricted to a wheelchair but retains effective use of arms. Time from onset (or diagnosis) of MS to the assignment of one of these disability scores has been estimated in many studies and provides information regarding the rate of accumulation of physical disability.