CHAPTER I

INTRODUCTION

Multiple slcerosis (MS) is not uncommon in Thailand. It is an inflammatory disease of the central central nervous system, characterzed by primary destruction of myelin. The most widely considered hypothesis is that MS is an autoimmune disease (1,2) and either autoreactive T-lymphocytes, autoantibodies or both are involved in the pathogenesis. Myelin basic protein (MBP) is thought to be the most important autoantigen in MS (3). However with regards to antibodies against MBP, its occurence in patients with MS is controversial. Some suthors have reported high percentage of anti-MBP antibodies is serum and CSF(4,5) but others have not(6-12). In this study, we used enzyme-linked immunosorbent assay(ELISA) to detect anti-MBP antibodies in serum and/or CSF of patients with MS and other neurological diseases, and to determine whether anti-MBP antibodies will be present exclusively in subjects with MS and other immune mediated neurological diseases.

Background

Immunopathogenic process has been well demonstrated in many diseases of the central nervous system such as multiple sclerosis, allergic encephalomyelitis (post-infectious and post-vaccinal encephalomyelitis) (13), as well as neuropsychiatric SLE (13).

Multiple sclerosis is not uncommon in Thailand, and is one of the major causes of neurological disability among young and middle-aged adults. The most currently and widely accepted concept is that MS is the result of an immune reaction directed against self myelin antigens.(1,3,14) Myelin basic protein has long been considered as " MS antigen " or autoantigen becauses of its encephalitogenic role in experimental allergic encephalomyelitis.(14) Some evidences suggest that genetic susceptibility is an important factor but just alone is not sufficient for the development of MS.(1) Exogenous agents such as viruses may be important in triggering demyelination.(1,15) Several immunopathogenic hypotheses have been proposed but the widely considered and supported ones are either autoimmunity or immune destruction of persistently infected oligodendrocytes or both.(15) Cytotoxic T cells, antibodies-directed killing (injury by complement, ADCC, opsonization), lymphokines and activited macrophages could be effectors in demyelination.(15)

The diagnosis of MS is based primarily on clinical criteria.(16) However, advances in laboratory, neurophysiologic and neuroimaging techniques have aided in the diagnosis of this disease, and led to the formulation a of new diagnostic criteria by Poser et al(17). The jphysician must realise that accurate diagnosis is extremely important for all concerned. Nevertheless, it is extremely defficult to differentiate between initial attack of MS

from other central nervous system diseases, and the diagnosis of MS is almost impossible without exclusion of viral infection and other disorders as well as long term follow up.

No CSF abnormalities are specific for MS. Aproximately 90% of patients with clinically definite MS and 30-40% of those with possible MS have oligoclonal banding in ltheir CSF.(18) CSF IgG index:

$$\text{CSF IgG index} = \frac{(\text{CSF IgG}/\text{CSF albumin})}{(\text{serum IgG}/\text{serum albumin})}$$

is reported to be abnormal in 80-90% of clinically definite MS patients.(18) Some investigators have suggested that daily IgG synthesis rate is more sensitive.(19) The rate is greater than 3 mg/day in mor than 90% of established MS.

Antibodies to MBP as well as evidences of intrathecal synthesis of the antibodies could be found in MS by different assays such as radioimmunoassay (5), enzyme immunoassay (20,21) and immunoblot.(21) The occurence of antibodies against MBP in patients with MS is controversial.(4-12,20,22-32) Recently, Warren and Catz(5) demonstrated that by using radioimmunoassay, free form anti-MBP antibodies could be detected exclusively in CSF of MS patients with clinical exacerbations, and bound form antibodies to MBP were found

in all MS patients with stable or progressive disease but not in clinical remission cases. If these findings are confirmed, anti-MBP antibodies could be a diagnostic and/or prognostic marker for MS. However, while some investigators reported high percentage of this antibodies in MS patients,(4,5) others reported negative results.(6-12) The main reasons for these discrepancies include differences in methodology and patient selection, or myelin basic protein may not be the only encephalitogen.(21)

In this study, we used enzyme-linked immunosorbent assay (ELISA) to detect anti-MBP antibodies in serum and/or CSF of patients with MS and other neurological diseases, and to determine whether antibodies to MBP will be present exclusively in MS patients with exacerbations. We also analyed CSF samples of patients with clinally definite MS dring exacerbation to evaluate the sensitivity of the IgG index and the IgG synthetic rate.