THE TREATMENT OF MS WITH IMMUNOSUPPRESSANTS

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Multiple sclerosis (MS) is a progressive and disabling neurological disease the precise cause and disease pathogenesis of which remain unknown. There is no specific disease marker in MS and the diagnosis is based on clinical and MRI-evidence of temporal and spatial dissemination of demyelinating lesions in the central nervous system. Pathologically, MS is considered to be heterogeneous and there are at least four different patterns of demyelination. Of these, two patterns (Types I-II) appear to have T-cell, or T-cell plus antibody mediated inflammatory changes; two other patterns (Types III-IV) are non-inflammatory, and are considered to be caused by a non-immune process of primary oligodendrocyte dystrophy. Despite the knowledge of pathogenic heterogeneity, it has not been possible to reliably categorise MS patients into inflammatory and degenerative subpopulations based on their clinical, radiological and laboratory features. Consequently, current diagnosis of MS selects a patient population with a specific clinical syndrome rather than a specific disease.

Immunosuppressive therapy, as a whole, is not an effective treatment option for wider population of MS patients. It is not difficult to appreciate that immunosuppressants would not be effective or even desirable as a choice if the disease pathogenesis is purely degenerative, i.e., primary oligodendrocyte dystrophy. However, there may be sub groups of clinically diagnosed MS patients who would respond to specific immunosuppressive therapy because of an inflammatory pathogenic process (Types I and II). Examples of such cases would be acute MS, often presenting with MRI or histological changes of concentric sclerosis of Balo, and patients with the clinical phenotype of optico-spinal MS associated with anti-aquaporin 4 antibody in the spectrum of Devic's disease (neuromyelitis optica). In addition, there are a small number of patients with multiphasic and recurrent acute disseminated encephalomyelitis (ADEM) who are currently classified as MS and are likely to respond favourably to immunotherapy. Plasma exchange and monoclonal antibodies are probably the most effective treatment for acute MS, Devic's disease and recurrent ADEM. Currently, natalizumab appears to be the most effective therapy for actively relapsing and potentially disabling MS and rituximab is the treatment of choice for Devic's disease.

The uncertainty of immunosuppressive therapy in MS is essentially the product of non-targeted treatment aimed at an unselected and heterogeneous patient population with a clinical phenotype of MS. With better knowledge and increasing experience, select immunotherapy can be used successfully to treat much smaller but well defined patient subgroups in order to prevent rapid progression of disability from highly active demyelinating disorders of central nervous system.

References

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