MULTIPLE SCLEROSIS
Multiple Sclerosis
Jun Yan
July 2012

Multiple sclerosis (MS) means multiple scars or lesions. It is a chronic inflammatory demyelinating disease of the central nervous system (CNS). CNS consists of the brain and the spinal cord. In MS, the myelin sheath of the neuron of CNS is damaged, scientifically it is called demyelination. This disease affects about 2 million people worldwide. In Australia there are over 20,000 people living with MS. Based on the study of experimental autoimmune encephalomyelitits (EAE), an animal model used to study MS in the laboratory, MS is considered to be an autoimmune disease mediated primarily by some special peripheral T cells, which is a type of peripheral leukocyte or white blood cell.

The pathological hallmark of MS is demyelination and axonal damage of the CNS. Axons in CNS are wrapped up by many layers of myelin sheaths, this is myelination. Myelinatation can increase the speed of electrical impulse conducted by axons. In the CNS myelin sheath is an outgrowth of a type of glial cell, called oligodendrocytes. When the myelin sheath is damaged, the transmitting of electrical impulse between nerves will be decreased or blocked. Demyelination can lead to axonal damage. Demyelinated lesions can occur anywhere within the brain and spinal cord, leading to disease complexity and heterogeneity of clinical signs and symptoms. For example, people can have problems with vision when demyelination occurs in the Parietal lobe of the brain. Common symptoms of MS include fatigue, weakness, spasticity, balance problems, bladder and bowel problems, numbness, vision loss, and tremors. Importantly patients with MS easily get depression.

Clinically MS can be divided into three major groups: relapsing remitting MS (RR-MS), secondary progressive MS (SP-MS) and primary progressive MS (PP-MS). There is a high degree of clinical diversity within these groups. In addition, there is a small proportion of people with MS who are relapsing progressive or benign MS.

RR-MS:

There are about 80-85% of people with MS are diagnosed with RR-MS. The mean age of RR-MS onset is about 30 and the female and male ration is 3:1. This is where the patient has progressively worse episodic period of neurological impairment (it can also called inflammatory attacks), followed by a period of improvement, complete or incomplete recovery before the onset of another attack. People with RR-MS can lead a moderately normal life in the early periods of the improvement phase, however, the worry and threat of another attack always weighs heavily on their mind and their quality of life declines as the cycle of relapse and remission progresses over time. The treatment for RR-MS involves management of symptom or to modifying the number and severity of relapses. Unfortunately these treatments are not cure of the disease.

SP-MS

About half of the patients with RR-MS then enter the next phase of progressive clinical deterioration, called SP-MS. SP-MS is characterized by a steady deterioration without relapses. By this stage, people may be wheelchair bound and require assistance for the most basic needs. Clinically, spinal cord atrophy can be found in SP-MS as compared with RR-MS; Cortical demyelination from mild to prominent. The average age for SP-MS is about 40. The ratio of female to male is 3:1.

PP-MS

Similar to SP-MS, patients with PP-MS don't have relapsing course and remission period. The disease starts with a steady decline in function from onset. There are about 10 to 15% of people with MS who have PP-MS, which is defined as a disease course without any clinical attacks or remission from onset. The incidence of PP-MS is similar in females and males and PP-MS tends to appear at a later age (about 40) than does RR-MS. PP-MS differs from RR-MS and SP-MS in the clinical course; that is differential diagnosis and treatment response.

Pathogenesis of MS:

The question that puzzles people deeply is what initiates the neuroinflammatory reaction in MS lesion. Unfortunately we still don't know the answer.

Medical research from the 19th century and early 20th century has shown that MS development is related to three factors: geography distribution, genetic effects and the body's own immune system. It is considered that people from low latitude, eg. Northern and southern equator have increased prevalence of MS than from high latitude. Genetic predisposition to MS has been seen through the study of twins. The susceptibility to MS in twins isvery high when one of them is diagnosed with MS. Further genetic related evidence is the genotype study of human leukocyte antigen A (HLA). HLA is the general name of a group of genes which allow the immune system to distinguish between foreign invaders and the body's won tissue. HLA is located in human chromosome 6. It has many different types of this gene. Among these gene types, HLA DRB1*1501 has been found in majority of people with MS. It is often considered that the pathogenesis of MS is a complex interaction between genetic and environmental factors. MS is generally considered to be an autoimmune disease although the exact cause is still unknown. The studies in the later 20th and 21st century have paved the road to investigate pathogenesis of the disease in the molecular level with depth. One of the cutting-edge genetic techniques called Genomic Wide Association study (GWAS) has allowed scientists to examine all the genetic differences in thewhole chromosome between people with and without MS. Although GWAS study requires high-resolution analysis and is time consuming, it has pushed MS research to another new level.

Treatment of MS

There is no cure for MS at the moment. Because we don't know what causes MS. Existing therapies are mainly for RR-MS. There are a wide range of treatments to be chosen to help patients to modify the immune system, suppress the disease and improve the symptoms. Many drugs are designed to target on T cells which has been considered to be involved in MS pathogenesis.

The treatment for progressive MS still remains elusive. There are only a few treatments available for secondary progressive MS. These medications are mainly used to reduce the disease progression. Treatment for PP-MS is not available.

Many studies have shown the differences at some molecules in the cells between RR-MS and progressive MS. These may contribute to the design of new therapeutic approaches to the treatment of progressive MS.