Innovation immunomodulatory treatment – case study of men diagnosed with relapsing-remitting multiple sclerosis (MS)

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ABSTRACT

Multiple Sclerosis (MS) is a complex disease that interferes with environmental factors and genetically predisposed conditions. This is a chronic, inflammatory disease of the central nervous system in which demyelination of neural tissue occurs. It is most often the case for young people with a slightly higher prevalence among women than men. Occurrence is rising in countries far from the equator, and the highest incidence is observed in temperate white people. This disease is characterized by so-called "rolls" that can last from 24 hours to several weeks. At this time there is a sudden increase in the existing symptoms or the appearance of a new one. The first signs of the disease are often mild and tend to cease quickly. The name reflects the spread of the pathological process in various places in the nervous system as well as the spread of changes over time. Regardless of the recognized form, the effect of MS is disability and reduced quality of life, which hinders self-reliance, self-care and freedom of movement. This paper is a case study of 49-year-old patient diagnosed with relapsing-remitting MS included in the experimental program of immunomodulatory treatment.

Keywords: sclerosis multiplex, SM, immunomodulatory, treatment, disability, experimental
1. INTRODUCTION

Multiple sclerosis (MS) is a chronic, inflammatory disease of the central nervous system that results in demyelination of the nervous tissue. [1]. Described in 1868 by Jean-Martin Charcot. Mostly young people are sick - the peak occurs on the 20th - 40th year of life. Statistically 6 out of 10 cases are diagnosed among women [2]. In general, SM is a disease that damages the myelin sheath around nerve cells, which impairs the proper transmission of impulses along the nerve pathways in the brain and spinal cord. The name reflects the distribution of the pathological process at various points in the nervous system and the spread of time changes [3].

The occurrence of MS increases in countries far from the equator. The highest incidence was observed in white people living in temperate climates [4]. The disease is not considered to be hereditary, but there is evidence of genetic factors in the predisposition to disease [5].

Many researchers believe that the main role in the pathogenesis of MS play autoreactive T lymphocytes. In patients with acute attacks, autoreactive T lymphocytes were isolated that produced proinflammatory cytokines, while cell clones isolated during remission demonstrated increased production of anti-inflammatory cells. In patients with MS, cerebrovascular microcirculation was characterized by high expression of MHC II cells, which may lead to activation of autoreactive T lymphocytes [6].

1.1. Symptoms

SM is characterized by a series of intermediate symptoms. They are related to the disorder of the body function, which was responsible for the part of the brain that was damaged. This disease is characterized by so-called "rolls" that can last from 24 hours to several weeks. At this time there is a rapid increase in the existing symptoms or appearance of a new one. The first signs of the disease are often mild and tend to cease quickly. At first the disorder is poor and the patient rarely goes to the doctor [7]. In the further development of the disease the change arrives and more and more tissues are affected by dysfunction.

Table 1. Symptoms due to occurrence [8].

<table>
<thead>
<tr>
<th>Place of occurrence</th>
<th>Symptoms</th>
</tr>
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<tbody>
<tr>
<td>Nervous and sensory system</td>
<td>Lhermitte’s symptom (&quot;current propagates&quot; along the spine); Imbalance, motor coordination disorder, loss of control of the limbs, paresis; dizziness, impaired concentration and logical thinking, short-term memory loss; changes in stimulus reception - decreased sensitivity to touch or hypersensitivity to heat, tingling sensation, numbness, hot flushes; slurred speech (dysarthria) - change of rhythm, speech slowed, slurred; blurred vision - strabismus, double or blurred vision, nystagmus, optic neuritis, pain on movement eyeball, blurred vision, difficulty in recognizing the color vision loss in one or both eyes</td>
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### Muscular system

- Feeling of muscle weakness and real muscle weakness; paresis, spasticity with increased muscle tone, stiffness and muscle spasms; gait ataxia, difficulty in movement; muscle tension disorder; tremors and lack of body coordination.

### Digestive system

- Difficulty swallowing; dysfunction of intestinal function at the level of digestion and drainage.

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1. 2. Diagnosis

SM may not present any symptoms for many years, so it is very difficult to recognize it at an early stage. In more than 25% of patients, the first symptom is deterioration or visual disturbance and a change in limb sensation. The first trigger of the disease, the most common is viral infection. The final diagnosis is made on the basis of visible changes in brain [9]. This involves, however, the advanced form of the disease. In order to differentiate a disease for multiple sclerosis, a person must have two cases of dementia associated with severe nerve conduction deterioration of at least 24 hours and the interval between them should not be less than 30 days. Clinical trials are then performed, the results of which are evaluated by McDonald's criteria. They analyze multiprocessing and time variations [10]. However, if the patient has gone through only one view of the disease, additional tests are needed. MS may present similar symptoms as other neurological or autoimmune diseases [11].

1. 3. Types

MS may have different paths. Its definition is important, it differentiates treatment and also requires different diagnostics. In the United States in 1996, the National Multiple Sclerosis Society awarded four forms of MS:

1) Relapsing-remitting - most common (80%); the earliest symptom is demyelination of cells within the brain; there are distinguishable periods of illness and remission;

2) Secondary progressive - permanent deterioration of health over the next 6 months; quickly leads to disability; occurs after 10-15 years in more than half of patients with relapsing-remitting;

3) Primary progressive - one of the rare (about 10%); usually recognized around the age of 40 or later; demyelinating changes mainly in the spinal cord; symptoms gradually worsen without violent exacerbations;

4) Progressive-relapsing - the rarest and the heaviest; symptoms worsen gradually; often sudden deterioration occurs; no remission; symptoms persist and quality of life is not improved [3].

2. EDSS SCALE

The main tool for assessing the severity of symptoms and disability, also widely used in scientific research, is the Expanded Disability Status Scale (Figure 1). It is based on finding...
the presence of neurological symptoms on a scale of 1 to 9. The higher the scale, the higher the degree of disability of the patient [12].

![Expanded Disability Status Scale (EDSS)](image)

**Figure 1.** Expanded Disability Status Scale (EDSS) [13].

3. TREATMENT

MS can be supported by therapies that allow to slow down the disease or recover lost nerve functions. Modifying therapies are used for this purpose, usually with the help of interferon derivatives, the human protein involved in the response of the immune system [14].

3.1. EAE

So far, no effective and no side effects of MS treatment have been lacking. A commonly used experimental model imitating SM is Experimental Autoimmune Encephalomyelitis (EAE), which can be caused by genetically predisposed mice, rats or rhesus monkeys [15].

Disease-specific Th1 CD4+ lymphocytes, that produce IFN-γ, IL-2, TNF-b are responsible for the development of the disease. Th2 lymphocytes, CD8+ T lymphocytes, macrophages, B lymphocytes and possibly NK cells are also involved. EAE became possible to explore the complex interactions between cells of the immune system and the nervous system that underlie multiple sclerosis [16].

4. CASE STUDY

The patient, now a 49-year-old male, was diagnosed at age 35. The first symptoms occurred at the age of 20 and included optic neuritis. Probable cause of the first “rolls” of the disease was very strong stress and viral infection. On the day of diagnosis, EDSS disability was rated at 3, now it is 6 - the patient requires walking support.
Relapses since 2004 occurred every two years, then every year. It is treated with Solu-Medrol. Doctors diagnosed relapsing-remitting form. The patient is receiving immunomodulatory treatment from January 2013. Every six months, in the form of infusion Ocrelizumab he takes.

4.1. Ocrelizumab – mechanism of action

It is a humanized CD20 protein-bound monoclonal antibody that is located on the surface of B lymphocytes at various stages of development leading to selective B cell death that expresses CD20. Its effects depend on the form of MS. It is believed that, in relapsing-remitting about half the “rolls” becomes weaker or disappear. Patients with primary-progressive - one third had a worsening condition, but after ocrelizumab, the patients were better at performing fitness tests and brain imaging studies.

Like every medicine, ocrelizumab has side effects. Because it modifies the immune response, patients are more at risk for infectious diseases and some cancers. This is a breakthrough study showing a drug that slows the progression of primary-progressive type of MS. Although, the results are not fulfilling the dreams of patients and doctors, but it is still the first effective treatment [17].

5. PROGNOSIS

Prognosis in MS is various. It depends on the triggering factor, age, gender, race and timing of the diagnosis. The average life expectancy of people with MS is comparable to healthy, while dramatically change the quality of life [18].

Indicators of good prognosis are visual and sensory disturbances, while walking difficulties can herald a faster developing disease. Surprisingly, the hope is that the first symptoms are quickly resolved because they are characterized by rapid regression. If the patient complains only one symptom, it can also indicate a milder disease development. One third of the patients are able to work after 15-20 years of illness and 15% will not experience the second “rolls”. Health deteriorates more rapidly in men, but they suffer less frequently.

It is not possible to predict the exact course of MS, but the first five years of disease may suggest how it will behave in the individual case [19].

References


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