MULTIPLE SCLEROSIS RELAPSING REMITTING PROGRESSIVE TYPE

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ABSTRACT

Multiple sclerosis (MS) is the most common neurologic demyelinating disease in high-income countries. The causes of MS are multifactorial involve genetics and the environment in which immune cell infiltration occurs across the blood-brain barrier, causing inflammation, demyelination, gliosis, and neuroaxonal degeneration substantia grisea in the central nervous system. A 23-year-old female patient was treated with four limbs weakened since two weeks ago accompanied by blurred vision, pain, cramps, and stiffness in the back muscles and legs. The patient has experienced the same complaint before. Clinical findings reveal lhermitte signs, atrophy papillae, and tetraparesis. On thoracic vertebral MRI examination without contrast and brain MRI with contrast obtained multiple sclerosis lesions. Patients receive steroid and antidepressant therapy. MS needs to be studied further because this number of cases began to emerge.

Keywords: Autoimmune; Demyelination; Lhermitte Sign; Multiple Sclerosis

INTRODUCTION

Multiple sclerosis (MS) is the most common neurological demyelinating disease in high-income countries. The median global prevalence of MS increased from 30 per 100,000 in 2008 to 33 per 100,000 in 2013.\textsuperscript{1} Multiple sclerosis is caused by infiltration of immune cells across the blood-brain barrier, causing inflammation, demyelination, gliosis, and neuroaxonal degeneration of the grisea substantial of the central nervous system (CNS).\textsuperscript{2} Causes of MS are multifactorial, involving both genetics and the environment. The gene most strongly associated with MS is the HLA-DRB1 * 1501 MHC class II haplotype linked to immune function.\textsuperscript{3,4,5} Additionally, MS has been linked to vitamin D deficiency, connected to several other autoimmune diseases.\textsuperscript{3,6}

CASE PRESENTATION

A twenty-three-year-old woman was treated at the neurology department of RSUD M. Djamil with weak four limbs since two weeks ago. These conditions had occurred gradually since one year ago, where conditions began with weakness in both legs. These conditions were followed by weakness in both arms, which was felt two weeks later. The weakness started in the left arm, followed by the right arm. Since two weeks ago, she only could move his toes and often let go of holding objects. These conditions accompanied by blurred vision since one week ago. Pain, cramps, stiffness in the back and legs muscles, and irritability and anger have often occurred for one year. For two months, the patient has also had a catheter attached.

She had experienced the same complaint in 2016, 2017, and January 2018. A history of blurred vision also occurred 2x in June 2017 and September 2017. In December 2017, an MRI of thoracic vertebra without contrast was performed where multiple tubular-shaped lesions were seen in the spinal cord as high as Th3- Th6 with transverse myelitis impression (Figure 1).
In January 2018, lumbar puncture was performed with macroscopic smooth flow, clear color, none +1, pandy +1, and microscopic cell count of 1 / mm3, CSF glucose 91 mgs / dl, blood glucose 195 mgs / dl, and protein 800 mgs / l. Contrast brain MRI was performed with results within normal limits. In February 2018, an MRI of the thoracic vertebrae without contrast was performed, showing a small size cystic spinal cord dilatation with hydrosyringomyelia as high as C1-Th12 and susp. Multiple sclerosis at the level of Th1-2 and Th4-5 (Figure 2). The neurosurgeon performed a drain with an indication of hydrosyringomyelia. After the operation, the patient can stand by holding the wall. Physical examination showed a moderate general condition, cooperative composition with blood pressure (BP) 110/70 mmHg, pulse 108 x/minute. Lhermitte's sign was found, and on funduscopy, the impression of papillae atrophy of the right and left ocular. Visus OD 1/300 and OS 1 / ∞. Superior motor strength 344/443 and inferior 111/111. Sensory hyperesthesia is found at the level of the C5 dermatome and below.

Urinary retention and sweat secretion are impaired at the level of C5-6 dermatome and below. Physiological and pathological reflexes are increased. Laboratory test when she was admitted showed anemia (Hb = 9.8 g / dl (normal level = 12-14 g / dl)) and mild hypokalemia (K = 3.3 mmol / L (normal level = 3.5-5.1 Mmol / L)).

Based on clinical findings, physical examination, and investigations, the patient was diagnosed with relapsing-remitting multiple sclerosis (RRMS). During hospitalization, patients received methylprednisolone 4 x 250 mgs (iv), ranitidine 2x 50 mgs (iv), ibuprofen 2 x 400 mgs (oral) and fluoxetine 1 x 10 mgs (oral). She showed clinical improvement in the form of improvement in limb weakness and improvement in vision. During treatment, the patient also received gabapentin 2 x 300 mgs (oral) to reduce pain, cramps, and stiffness in the back muscles.

At the time of treatment, a brain MRI was performed in contrast to the results showing multiple hyperdense lesions in the left lateral paraventricule and left parietal lobe (on T2, Flair, and DWI), the lesion did not enhance post contrast administration with multiple sclerosis impressions.
The patient went home with motor strength 344/222 and vision 1/60 ODS and was given 2x300 mgs gabapentin, 2x400 mgs ibuprofen, 2x150 mgs ranitidine, and 3 x 8 mgs methylprednisolone.

DISCUSSION

Multiple sclerosis (MS) is an autoimmune disease, which rarely occurs. Because of this rarity, MS is a diagnostic challenge in itself. MS is usually diagnosed between the ages of 20 and 40 and twice as many women as men. Cause of MS is multifactorial, combining genetic and environmental factors. However, MS's cause remains largely unknown. Pathological feature of MS is that it is characterized by involving the brain, spinal cord, and optic nerve. Focal lesions are thought to be caused by immune cells' infiltration, including T cells, B cells, and myeloid cells, into the parenchymal of CNS where the injury is located.

This patient's clinical features are visual disturbances (optical neuritis), weakness of all four limbs (myelitis), pain, cramps, stiffness in muscles and joints, and phases of relapse and remission. The MS course can be relapse-resolution or progressive but usually involves multi-phases and multi-focal (disseminated in time and location). Where reversible episodes of neurologic deficit last for several days to weeks characterize the early stages of the disease. Over time, clinical and cognitive deficits develop become irreversible. A minority of patients have a progressive course of the disease from baseline.

The clinical features of myelitis in MS are usually asymmetrical, progressive over hours to days, and usually, there is spinter involvement. Optic neuritis may be acute or subacute with bilateral or unilateral visual impairment, sometimes accompanied by retroorbital or ocular pain that worsens with eye movement. There is usually a complete or partial improvement in the patient.

Apart from physical complaints, these patients also tend to be more sensitive and easily irritated and tired. Mood changes that occur in MS, including depression (50%), euphoria, and psychosis. Fatigue is common in MS patients, where it reaches 84%. Various forms of fatigue can occur due to MS disease or caused by related factors such as depression, lack of sleep due to nocturia or seizures, poor appetite. Depression in MS may involve cytokines that are essential components of immune activation during inflammation and are involved in an oligodendrocyte injury, axonal degeneration, and neuronal dysfunction, significant MS pathology features. Cytokines are molecules produced by immunocompetent cells that mediate and coordinate communication between cells of the immune system.

Pain, cramps, and stiffness in joints and muscles also occur in these patients. Impaired muscle function in MS patients can manifest in involuntary muscle stiffness or movement and limited muscle function capacity, which focuses on spasticity, spasms, and weakness. The primary mechanism of spasticity is the hyperexcitability of α motor neurons caused by decreased secondary descending inhibitory signals that damage of CNS.

Lack of inhibition of the oligointramedular pathway in the brain or polysynaptic in the spinal cord,
physiologically mediated by the neurotransmitter γ-aminobutyric acid (GABA), results in reflex hyperactivity. Symptoms include muscle stiffness and/or spasms, pain or discomfort, loss of function in the upper / lower extremities, and difficulty maintaining a standing or sitting posture with excessive reflexes, clonus, seizures. Spasticity increases with stress and harmful stimuli (e.g., pain, pressure, urinary tract infections, and usually shows spontaneous fluctuations (usually increases at night).11

Imaging examination that must be done to establish MS is MRI. Besides, evoked potential (EP) can also be performed, especially visual evoked potential (VEP) and CSF examination. On MRI examination, you will see a Disseminated Lesion in Space (DIS) image on the T2 section at least 2 out of 4 areas, including periventricular, juxtacortical, infratentorial, and spinal cord.12

EP examination aims to measure the electrical activity of the brain against stimuli in specific sensory nerve pathways. EP can detect a decrease in electrical conduction caused by damage due to demyelination along a pathway. However, the degree of damage is so small that it is not visible on clinical examination.12

CSF examination is performed to help determine MS's diagnosis and rule out other possible diagnoses, especially intracranial infections. In CSF, an increase in the immunoglobulin G (IgG) index will be obtained, or the discovery of ≥ 2 oligoclonal bands (OCB), indicating a demyelination process due to inflammation. IgG and OCB tests have high sensitivity but are not specific for MS. OCB can also be found in other diseases such as SLE, paraneoplastic syndrome, neurosarcoidosis, meningitis, neurosyphilis, intracranial masses, vascular lesions, and hereditary neurological diseases.12 The more important CSF message is to rule out other possible diagnoses. The high incidence of infection in Indonesia requires considering the possibility of infection before establishing a diagnosis of MS.

The MS diagnosis was confirmed by the revised McDonald Criteria of the International Panel on the Diagnosis of MS (Table 1). She had ≥ two attacks; there is clinical evidence, so it does not require additional data to make a diagnosis. MS is divided into several types based on the course of the disease in the form of relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS), progressive relapsing MS (PRMS), and benign MS (Table 2).12 She was admitted to the RRMS type.

MRI examination of the spinal cord in MS very rarely extends beyond two vertebral segments. Generally, the lesions are short, asymmetrical, and located in the spinal cord section's posterior segment.12

At the time of complaint of relapse, the patient received high intravenous doses of methylprednisolone therapy. Treatment in MS is divided into therapy at relapse and long-term therapy. They are using corticosteroids, intravenous immunoglobulin (IVIG), or plasma exchange at the time of relapse. Glucocorticoids in the form of IV or oral methylprednisolone at a dose of 0.5-1 g per day for 3-5 days. Long-term therapy in the first line uses interferon-β, glatiramer acetate, and fingolimod, while in the second line using mitoxantrone, natalizumab,13,14,12

In addition, we can also use immunosuppressants mycophenolate mofetil (MMF), azathioprine, methotrexate, and cyclophosphamide. But its effectiveness still needs further study. Studies show that 55% of patients do not experience any worsening of the condition with cyclophosphamide therapy. Other studies have shown the same effect of both azathioprine and MMF. Further research is needed about the effectiveness of immunosuppressants in MS.2,14

Apart from immunomodulation and immunosuppressive therapy, symptom-specific therapy is an important component of MS patients' comprehensive management. This therapy aims to reduce complaints that can lead to impaired functional ability and quality of life. She received phenytoin, gabapentin, and pregabalin therapy to reduce
spasticity and pain. To reduce spasticity can use diazepam 5-30 mgs/day, gabapentin 300-3600 mgs/day, tizanidine 2-4 mgs/day or baclofen 10-120 mgs/day.\textsuperscript{2,11,14} To reduce pain in joints and muscles then can use amitriptyline 25-150 mgs/day, gabapentin 200-1600 mgs/day, 200-400 mgs/day lamotrigine or 150-600 mgs/day pregabalin.\textsuperscript{2,14,15} To overcome fatigue in these patients, can use amantadine, modafinil, pamoline.\textsuperscript{16}

Depression can be viewed as a clinical symptom and a complication of MS, so the management of depression is an integral part of general MS management. To treat depression in these patients, fluoxetine 1x10 mgs was used. The approach to treating depression in MS patients can be carried out in three approaches, namely (1) by trying and minimizing side effects and potential drug interactions such as escitalopram and sertraline, which are serotonin selective reuptake inhibitors (SSRIs) that have a relatively low side effect load and little or no significant risk for drug interactions. SSRIs do not have significant anticholinergic effects (sedation, dry mouth, constipation, indecisive urination), antihistaminergics (sedation, weight gain), or antiadrenergic (orthostatic hypotension). (2) antidepressants whose side effects reduce MS symptoms other than depressive symptoms such as bupropion, fluoxetine, and venlafaxine, which actively improve fatigue symptoms in MS or desipramine, mirtazapine, and paroxetine are sedation and stimulate the patient's appetite, which is useful for people with insomnia and loss. appetite. (3) antidepressants that are useful in simultaneously treating MS depression and also help treat comorbid conditions apart from depression in the form of tricyclic antidepressants (such as nortriptyline and desipramine) can help incontinence (because they are anticholinergic) as well as treat neuropathic pain or duloxetine, which are also effective in treating pain. Neuropathy or bupropion is indicated for the treatment of smoking and depression.\textsuperscript{16}

Multiple sclerosis (MS) is an inflammatory disease of the CNS that results in progressive neurological regeneration and neurological disability. MS most commonly affects young adults, especially women. Many cases of MS are starting to emerge along with the improvement of supporting tools such as imaging that complement the clinical findings of MS patients so that the diagnosis can be made early, sensitive, and precise.

REFERENCE

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