MULTIPLE SCLEROSIS (MS)

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The information below has been instigated by the fact that we get a lot of calls and are asked about how to treat Multiple Sclerosis (MS). This information is to facilitate communication and to save time.

INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune disease due to a combination of stressful factors such as early infancy or childhood viral infections stimulating the immune system, later in life complicated by recurrent stress leading to recurrent attacks of rogue and dysfunctional immune system coding. It is more likely to develop in patients of northern European lineage. It is more prevalent in colder climate countries. Females are almost twice as likely to suffer from MS. It has four main forms: relapsing-remitting, seen in 4/5 of patients, primary progressive which starts at somewhat older age and is seen almost equally in both sexes, secondary progressive which may follow the relapsing-remitting form, and relatively benign form with a few attacks (relapses) followed by years or decades of no new attacks unless the patient is exposed to a major stress - more common in females. According to a European data base center (NEMJ, 11/16/2000), the primary progressive form takes a median time of around one year to start showing disability. This is in contrast to a median time of 11 years in relapsing-remitting course.

MS is not diagnosed by the process of exclusion. It is diagnosed by careful history taking, thorough neurological examination, and tests such as MRI (not CAT Scan), physiological tests such as evoked potentials (BAER, SER, VER) and laboratory tests, such as serum and CSF immunological changes. Monitoring the T-cell lymphocyte function test may help in prognostication and treatment of MS.

DIAGNOSIS

The diagnostic tools in order of importance are:

1. A careful history taking which if taken in detail will provide vital information in regard to how the very first attack in childhood or early teenage years started as a viral infection (measles, infectious mononucleosis, whooping cough, etc). The same history gives a detail of the nature of the disease and helps with prognostication in regard to the fact that the patient may have had multiple attacks which may have been mistaken for the patient being hysterical or malingerer or Munchausen's Syndrome (blaming the patient for being a liar), etc.

2. A careful neurologic examination which specifically, quite frequently reveals evidence of thoracic spinal cord and/or brain stem involvement with sensory loss over the face, chest, trunk, or abdominal regions.

3. MRI. Unfortunately, there are a lot of false positive and false negative MRI's. The MRI shows typical changes in MS, but the damages to the white matter of the brain and spinal cord can be quite variable. Other diseases may mimic MRI changes seen in MS. For example, patients who have had early childhood viral infections may show multiple areas of abnormal density which may be the result of nothing but the original viral infection. Other patients may have had a head injury which may show abnormalities similar to MS. MRI should be taken for its value in regard to its limitations, but it is a useful test in research studies to find out if more plagues are evolving. In this regard, it also helps with the study of medications trials for MS.

4. The next series of informative tests are evoked potential tests. These are totally harmless and are done in the form of visual, auditory, or somatosensory evoked potentials. The test simply gently stimulates the nerves to the eye, inner ear, or to the spinal cord, and record the delay of conduction of the impulse from periphery to the brain. In at least 1 out of 5 patients with MS, evoked potentials may be quite abnormal in face of no abnormality on MRI.

5. Another test that seems to be out of vogue now-a-days is the spinal fluid evaluation. The lumbar puncture and the spinal fluid can be quite important in diagnosis and in prognostication of the disease, and more importantly in differential diagnosis. It can reveal other diseases that mimic MS. It can reveal the severity or lack of severity of the MS reflecting itself in the tests on the spinal fluid such as infections. Obviously, in this day and time, only less than 10% of such patients require spinal tap, but if there is doubt about diagnosis and there is need for more definitive diagnosis, this test should not be ignored.

TREATMENT

The disease should be treated as aggressively as is safe. The common practice of "wait and see" is asking for more permanent damages due to MS. At the present time, there are plenty of medications that can be used in a rational fashion, suppressing the disease and proportionately reducing the damages caused in the central nervous system by MS. The treatment should be tailored to the type and severity of the MS individually. Four-fifths of the patients suffer from the intermittent (relapsing-remitting) type of MS. The prognostic factors are influential to the outcome of the treatment. Early treatment is imperative in all forms of MS. The response to treatment is individualized. However, the relapsing-remitting type of MS which shows a tendency for few and far in between attacks of flare-up of the disease, especially in a young female, and in a patient who has not been exposed to multiple stressors (such as husband with poor understanding of the disease, or intake of alcohol, or frequent viral infections), is more likely to respond positively to the treatment and to have less residuals from it.

On the other hand, male patients in the late youth or middle ages, with frequent attacks of illness, and with a tendency to be exposed to stress either due to the work environment or due to financial reasons will have a worse prognosis.

In the relapsing-remitting MS patients, there has been a tendency for starting the treatment with IV corticosteroid (Prednisolone) followed by oral corticosteroid by mouth. The usual schedule is 4-5 days of IV Prednisolone followed by a few weeks of corticosteroid by mouth. First of all, there is no proof that this form of treatment will do better than the newer forms of treatments.

Secondly, repetitive treatment with corticosteroids has a tendency to cause suppression of the function of the adrenal glands and secondarily, make the patient more susceptible to suffer from frequent infections, and severe chronic fatigue syndrome (CFS). So, in these patients it may make sense to start IV Prednisolone for 4 days, then to follow with newer medications listed below.

There is a tendency to limit the treatment to corticosteroid therapy for a few weeks with no subsequent treatment until the next attack. This may leave the patient unprotected. As soon as possible, the patient should be treated with one of the Interferon or copolymer type of medications.

Early treatment with Interferon and or Glatiramer acetate (GA, a.k.a. Copolymer-1 or Cop-1) is far more effective than corticosteroid treatment. Immune therapy plays a major role in the treatment of MS. Beta Interferon is an effective form of treatment, but causes too many side effects. In our experience, only less than 25% of the patients could successfully continue the treatment with Beta Interferon. It has a harsh effect on the immune system, resulting in practically intolerable inflammation, fever and other immune system dysfunctions in the majority of patients. Among the patients who can tolerate Beta Interferon, the relapse rate is

decreased by up to 30%, which is a major improvement for prevention of reoccurrences in MS.

Glatiramer acetate (GA / Copaxone) inhibits the myelin - reactive T-cells by blocking human leukocyte antigen (HLA), as well as antagonizing the T-cell receptor. GA (Cop-1) exerts a strong inhibitory role in the proliferation of myelin basic protein (MBP).

Interferon Beta 1a (Avonex) is well tolerated, and is quite effective in improving the MS pathology, reducing the progression of neurological impairment and reducing the relapse rate. It is better tolerated than Beta Interferon. Copolymer- 1 is also effective in the treatment of remitting relapsing attacks of MS. The combination of Cop-1 and Avonex is even more effective in the treatment of more progressive and destructive MS patients. The combination works better due to the fact that Cop-1 acts as a complimentary agent; whereas Avonex interferes with antibody formation, the Copolymer-1 (Cop-1) as drone or a decoy to protect the brain from the destructive effect antibody against brain tissue.

IV immunoglobulin treatment is quite effective in the management of MS. The published articles in MED-LINE from January 1981 through January 1995 reported the effect of IVIG in 189 patients, only ninety-eight (52%) of the patients responded with improvement with the help of IVIG. Since January 1995, there have been other large studies. Five hundred fifty MS patients were treated with IVIG, showing reduction and prevention of recurrence of the disease. Achiron, in multiple trials of IVIG treatment, found this form of treatment very effective in reducing the relapses (exacerbations) of MS.

Hyperbaric oxygen has not proven to be effective in treatment of MS. Total lymphoid radiation is too harsh and harmful, and should not be considered for treatment of MS. TNF (tumor necrosis factor) and anti-CD4 antibodies are being studied by Compston in Cambridge, England. Results are not finalized.

Certain forms of chemotherapy such as 4-aminopyridine (4AP) treatment are helpful in more severe MS patients. The chemotherapy with 4AP is not similar to chemotherapy for cancer. In MS, chemotherapy should be applied in conservative doses, avoiding hair loss and bone marrow suppression.

Weiner and colleagues have been reporting their experience with oral vaccination (ingestion of myelin antigens) and have noted some promising results in their preliminary study. This form of treatment is assumed to selectively stimulate T-cells secreting anti-inflammatory Cytokines.

MS usually causes severe pain in over 60% of patients. The pain itself is a strong stressor instigating flare-up (relapse) of MS. Treatment with anticonvulsants such as Tegretol (non-generic), Klonopin® (non-generic), and Depakote help in the management of severe pain. Analgesic antidepressant treatment with

Trazodone or Desipramine (not Amitriptyline), opioid antagonists, Tramadol (Ultram) are the minimum requirements.

MS can lead to sensitization of spinal cord, causing myoclonic seizures. Treatment of choice is Klonopin (non-generic). Spasticity should be managed by Zanaflex, Baclofen (oral or pump).

The stress of bed rest and inactivity on one hand, and the stress of too much work and isometric exercise are very harmful to any immune system disease (e.g., Lupus, MS, Arthritis, CRPS, etc).

The stress of tremors, spasticity, and chronic fatigue syndrome (CFS), should be aggressively counteracted: for CFS, treatment with proper analgesic antidepressants at night time to prevent insomnia is essential: Trazodone 50-250 mg at bed time, or Desipramine or Doxepin (at 25 to 200 mg doses) is usually well tolerated. If the CFS is quite disabling in spite of the above-mentioned treatments, supplemental doses of Effexor 37.5 to 75 mg in the morning are helpful.

In more advanced stages the immune system modulated by the sympathetic system becomes exhausted, and leads to hypertension. After several months the hypertension changes to hypotension (especially orthostatic hypotension) causing dizziness, CFS, and unsteadiness. The hypertension responds best to alpha blockers such as Hytrin. The hypotension responds best to treatment with Promantine (Midodrin). The hypotension responds best to treatment with Promantine (Midodrin).

Treatment with Amitriptyline (Elavil) should be avoided: it may aggravate hypotension, CFS, as well as causing weight gain (an average of 6-7 Kg in the first year).

SSRI antidepressants may partially and temporarily help CFS, but in the long run suppress any sexual desire in over ½ - ¼ of patients causing stress, marital problems, and agitation. SSRI should not be treatment of choice for MS. Treatment with Effexor is helpful to relieve CFS.

OTHER COMPLICATIONS

1. MANAGEMENT OF MS SIDE EFFECTS

The treatments should not be just limited to counteracting the plague formation of multiple sclerosis, but it should also address the disabling complications of MS. Here are some of the disabling complications.

Pain. Over 60% of MS patients suffer from pain. This has been one of the most disabling and most ignored complications. Treatment with Carbamazepine (Tegretol brand-name) is quite effective for sharp or stabbing or electric shock

type of pain. If the patient has a burning type of pain, then the treatment of choice would be Gabapentin (Neurontin). Valproate (Depakote) is also helpful for treatment of pain or severe headache. If the patient has deep pain in the bones and muscles, then the treatment of choice would be increasing activity, mobilizing the patient, and in addition, treating the patient with analgesic, such as Tramadol (Ultram).

Analgesic antidepressants are treatment of choice in practically every MS patient with pain. The antidepressants are not given because the patient is depressed, or has any kind of psychiatric disease. It is given because it prevents the pain. It also usually provides good sleep. Some antidepressants such as Zoloft, Paxil, and Prozac don't have any significant analgesic value. In addition, they can aggravate the chronic fatigue syndrome and in 1 out of 5 patients they can suppress sex desire which would complicate the marital relationship. The treatment of choice is with antidepressants such as Trazodone, Desipramine, or Doxepin. These three antidepressants are quite effective without serious side effects. The use of Amitriptyline (Elavil) should be avoided because it has a tendency to cause obesity (up to 8kg in the first year, and then up to 6kg the years after). Also, it aggravates the CFS, and can cause low blood pressure.

2. NEUROPATHIC PAIN AND

COMPLEX REGIONAL PAIN SYNDROME (CRPS/RSD) IN MS

In approximately one fifth of MS patients, neuropathic pain (pain accompanied by inflammation, hypersensitive skin, and temperature and circulatory changes) is seen as a complication of MS leading to sympathetic nerve dysfunction. The treatment of choice is a combination of antidepressants (such as Trazodone or Doxepin) and anticonvulsants (Depakote, Trileptal, and Klonopin®) as well as nerve blocks and epsom salt bath are quite effective.

3. CHRONIC FATIGUE SYNDROME

For the treatment of CFS (which the Social Security Courts accepted as the most disabling type of chronic disease, treatment of choice is Effexor. In MS patients who have problems with fatigue plus anxiety, which is totally expected, plus a tendency for depression, Buspirone (Buspar) at the dosage of 5-15mg 3 times a day is very effective and has the least side effects. The MS patients should stay away from benzodiazepine (BZ) type of tranquilizers and sleeping pills such as Xanax, Ativan, Librium, Valium, etc. These medications suppress the formation of endo-BZ in the brain, resulting in severe chronic fatigue, withdrawal anxiety and depression, and inactivity. They should be replaced with Buspar. The two exceptions are Klonopin® and Serax which do not suppress the formation of endo-BZ's.

4. MUSCLE SPASMS

For muscle spasms, spasticity, flexor spasms, and poor mobilization, the treatment of choice is Zanaflex, and if the patient can not tolerate Zanaflex, then Baclofen. If the spasticity progressively deteriorates, then Baclofen infusion pump through the spinal fluid can provide excellent relief, and can help mobilize the patient. For spinal cord sensitization (myoclonic jerks, or falling attacks) Klonopin® (non-generic) is helpful.

The above medications have the potential of having serious side effects, especially if given in large doses and in combination with a lot of other medications. The patient has to consult with his/her doctor, and also has to read about the side effects and educate herself/himself. The above information is nothing but to help educate the people about the subject of MS, and it does not at all imply that someone can just read about it and practice on herself.

Physical therapy is essential to prevent the patient ending up in a wheelchair or a nursing home.

5. URINARY TRACT COMPLICATIONS

Bladder complications are quite serious. In mild cases, the treatment with Detrol or Elmiron can be helpful, but urologist consult is a must, and the urinary complications should be treated as aggressively as possible. One of the common causes of death (which happens infrequently in MS) is kidney infection secondary to MS.

6. FOOD

Correction of diet is imperative. MS is a disease of stress. Certain foods aggravate stress such as chocolate, hot dog, cold cuts, alcohol, 5'C (candy, chocolate cookie, cake, and cocktail), and any guts meat i.e., liver, kidney, etc. The patient should never skip a meal because fasting or skipping meal causes fluctuation of blood sugar and secretion of adrenaline which contributes to more stress and more weight gain. Also, inactivity is a major stressor and aggravator in this regard.

Finally, the worst of all treatments and alternatives is to tell the patient that there is no cure for MS and to do nothing for the patient. Interestingly, this is a common practice among the clinicians and should be strongly discouraged.

Avoidance of stress (e.g., marital problems), proper diet (please refer to the 4F diet) and exercise are essential.

Acknowledgment: I am most grateful to Mr. Eric Phillips for his indispensable, and extensive research and preparation of this report.