NEURO-OPHTHALMOLOGIC MANIFESTATIONS OF DEMYELINATING DISEASES

CRISTINA PLEŞA[1], ADINA GRIGORESCU[2], MONICA TANTU[3], MAGDA DIACONU[4], PAUN CAZIA[5]

[1] Emergency Clinical Hospital "Prof.Dr. D. Gerota" Bucureşti, [2] Endocenter Clinic Bucharest, [3,5] Emergency Clinical Hospital Piteşti, [4] Emergency Clinical Hospital Craiova

Keywords: *demyelinization, autoimmune, optical neuritis*

Abstract: *Among all demyelinating diseases, the most frequent one in practice as well as in life is, beyond any doubt, multiple sclerosis (MS). Although the etiology of this condition is not known exactly (a lot of predisposing factors being involved), the disease has an obvious genetic predisposition and its pathogenetic mechanism is autoimmune. The clinical manifestations of MS are multiple and various, depending on the level the demyelinating injuries are produced at. The most frequent inception is through visual signs and symptoms, the neurological signs generally breaking out a bit later. The diagnostic of MS supposes firstly being familiar with the ways of manifestation of the disease, specific neurological and eye investigations and, of course, a closer cooperation between the neurologist and the ophthalmologist. It is equally important to establish the etiology of retro bulbar visual neuritis (a common manifestation of MS), through a strict history and specific paraclinical, biochemical and serological tests, so that the MS diagnostic should involve great responsibility on the part of the neurologist to inform the patient on the clinical manifestations and the progressive evolution of the disease. Since there still isn't any etiological treatment of MS, its treatment is immunomodulator / immunosuppressive, symptomatic and rehabilitating.*

Cuvinte cheie: *demielinizare, autoimun, nevrită optică*

Rezumat: *Dintre toate bolile demielinizante, cea mai frecvent întâlnită în practică şi în viaţă este fără îndoială scleroza multiplă (SM). Deşi etiologia afecţiunii nu se cunoaşte cu exactitate (fiind implicaţi mai mulţi factori predispozanţi), boala are totuşi o clară predispoziţie genetică, iar mecanismul patogenetic este unul autoimun. Manifestările clinice ale SM sunt multiple şi variate, în funcţie de nivelul la care apar leziunile demilienizante. Debutul cel mai des întâlnit este prin semne şi simptome vizuale, semnele neurologice apărând de regulă ceva mai târziu. Diagnosticarea SM presupune în primul rând cunoşterea formelor de manifestare ale bolii, investigaţii specifice neurologice şi oftalmologice şi bineînţeles o colaborare strânsă între neurolog şi oftalmolog. Este de asemenea important de stabilit etiologia nevritei optice retrobulbare (o manifestare comună a SM), printr-o anamneză riguroasă şi prin teste paraclinice, biochimice şi serologice specifice, întrucât diagnosticul de SM, implică o mare reponsabilitate a medicului neurolog de a informa pacientul cu privire la manifestările clinice şi la evoluţia progresivă a bolii. Întrucât nu există încă un tratament etiologic al SM, tratamentul este în principal imunomodulator/imunosupresor, simptomatic şi recuperator*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Demyelinating disease refers to any kind of affection that produces damage/destruction of the myelin sheath of the nerves in the Central Nervous System (CNS).

The most frequently met demyelinating disease is multiple sclerosis. (MS).

MS is a chronic disease which is characterized by axonal demyelination at the level of CNS, but through an inflammatory and degenerative device that are the base of neurological damage.

Described for the first time by Charcot in 1868, MS is an incompletely understood disease with unknown aspects regarding its etiology and pathogenesis. Conducting studies on monozygotic twins in comparison to bizygotic twins, it has been proved the certain existence of a genetic predisposition for MS. Apart from genetic factors, there are predisposing ones, such as environmental factors, infectious, smoking (although the device is still unknown).

No matter the etiology of the disorder, the pathogenetic device is considered of having autoimmune nature, a fact which has been scientifically proved through auto reactive HT1 lymphocytes. They activate themselves and migrate in the CNS where they are exposed to various auto antigens and, by reactivating themselves, they lead to inflammatory falls which has, as a final result, axonal demyelination as well as the loss of oligodendrocytes and axons. The necessary and compulsory condition for producing the inflammatory/immune assault upon the CNS structures is a complex, focal modification at the level of the blood-encephalic barrier which leads to modification of its permeability.

From the point of view of the correlation between these pathogenic and clinical processes, the inflammation or demyelination episodes manifest through clinical flares (falls followed by remissions), while the axonal degeneration is the major cause of the progressive and irreversible disability, which is more often met with progressive forms.

The damage may occur in every region on the CNS –

[1]Corresponding Author: Cristina Plesa, 39 Mircea Vodă street, M30 Flat,3rd Floor, Ap. 64, 3rd sector, Bucharest, Romania; e-mail: crisplesa@yahoo.com;
Article received on 07.04.2010 and accepted for publication on 28.04.2010
ACTA MEDICA TRANSILVANICA September2010; 2(3)197-199

visual nerve, spinal cord or in the cerebral parenchyma but most of the focuses are located in the white matter and specific-periventricular. Demyelination finds itself in different stages of evolution and may coexist with focuses of dysfunctional incomplete demyelination whose final stage is represented by the astroglial scar, from which the old name of *multiple sclerosis*.

The signs and neuro-ophthalmologic symptoms from MS are multiple and various, depending on the affected nerves. The disease may begin with motive symptoms (fatigue, ataxia, spasticity) or sensory (paraesthesia, feelings of burn or pain, Lhermitte sign etc.), but it most frequently starts with visual symptoms. On average, the period between the beginning of the visual symptoms and the neurological ones is 9 years.

Visual neuritis is the most often clinical symptom of presentation of Ms (25% of the cases), especially with young patients. It consists in the inflammation of the visual nerve with its demyelination, having as a result the reduction of visual ability of the respective eye (rarely bilateral). It is usually about a retro bulbar visual neuritis, only in third of the cases manifesting itself as papillitis.

It seems that about 78% of the visual neuritis cases are due to MS!

Visual neuritis manifests through different degrees of visual dysfunctions – from light to severe and even blindness. It is often accompanied by pain (or discomfort) at the movements of the affected eyeball – which precedes fogginess of the sight or occurs at the same time. The sight usually diminishes suddenly, stagnates for a few days and then it recovers spontaneously in a few weeks or months. The sight retrieves totally after the first attack, the visual prognosis diminishing with each subsequent attack. Even after the complete recovery of the visual acuteness, the examination of the fund eyes generally indicates a temporary visual atrophy (rarely generalized) – frequently met with optical neuritis in MS.

The most common brack of eyeshot which accompanies visual neuritis is the diffuse reduction of sensitiveness in central area (at 30 degrees), followed by arched scotoms, central or centrocecal scotom, bracks within the dial, etc.

Visual neuritis is also accompanied by discromatopsy, especially in red-green spindle and by an afferent pupillary brack.

Although the patient's sight is very weak or blurry, the fund eyes examination in the acute phase of retro bulbar neuritis (visual atrophy occurs later) – "the patient cannot see anything, the physician cannot see anything". Therefore, in this stage of the disease, the diagnosis is suggested by pupillary signals, by the bracks of the eyeshot, by the affectation of the chromatic sense and by the quick reduction of the sight. Visual evoked potentials (VEP) which reveal the delay of the conduct of the impulses through the visual nerve, represents an additional element for diagnosing, though it is nonspecific – alteration of VEP possibly reoccurring in the case of glaucoma or of ischemic visual neuropathy.

Very suggestive for MS is the fluctuation of the sight together with the growth of body temperature – either during a hot bath or after persistent physical activity (Uhthoff sign). The explanation consists in the alteration of neural conductivity through demyelinating nerves due to the high temperature.

In evaluating visual neuritis, for guiding the differential diagnosis, history is extremely important. The patient has to be asked whether he has been exposed to various toxins (mercury, lead, etc.), whether he is aware of certain diseases (sarcoidosis, lupus or other vasculitis, syphilis, etc.) or some viral or bacterial infection, whether he has taken medicines (etambutol, isoniazid, contraceptive, drugs) or whether he uses alcohol or tobacco excessively.

Another frequent visual signal which occurs in MS is *diplopia,* due to affecting the afferent visual system, with abnormalities of ocular movements. There are likely to occur *nystagmus* and *internuclear ophthalmoplegia*. Nystagmus in internuclear ophthalmoplegia is specific. Nystagmus occurs at the eye which is in abduction, at the horizontal look. When internuclear ophthalmoplegia is bilateral, nystagmus occurs at the eye in abduction in both directions, and the diagnosis of MS is almost certain. Less frequent visual signs in MS are paralyses of oculomotor muscles, hemianopsis intermediary uveitis (10% of the cases occur in the context of MS) and retinal periflebita.

Internuclear ophthalmoplegia, intentional tremors, cerebellar ataxia, motive and sensorial symptoms, emotional disturbances – all of these suggest MS.

Positive diagnosis of MS is set on the basis of the history, of the clinical signs and paraclinical investigations. Very useful and absolutely necessary for the diagnosis are complete ophthalmologic consultation, testing the eyeshot = VEP – which can trace alterations even in the absence of visual symptoms. Ophthalmologic examination should contain, beside fund eyes examination, testing the chromatic sense, the red glass exam (in the event of diplopia) and biomicroscopy and visual tonometer – for settling the differential diagnosis.

Blood tests and serological tests (for VIH, syphilis, Lyme disease) help establishing the etiology of visual neuritis.

The establishment of the diagnosis for sure of MS is done on the basis of cerebral NMR and cervical column (native and with contrast substance), possibly lumbar puncture with RCL examination and NMR spectroscopy.

Because of the fact that it is not known for sure the cause of the disease, despite the great number of researches for the past few years, there isn't an etiological treatment to lead to its cure. Numerous efforts for elucidation the pathogenic devices of the disease, are at the base of some therapeutical schemes that eventually lead to the alteration of the natural evolution of the disease.

The treatment of MS contains, beside the treatment which alters the natural evolution (immunomodulator, immunosuppressive), the treatment of the flare, the symptomatic and recovery ones.

In the case of acute flares of the disease, the treatment consists in administrating intravenous SoluMedrol, followed by Prednisolon orally. The scheme is established by the neurologist and it adapted to each case. It is not recommended the treatment only with corticosteroids orally administrated, as it doubles the rate of relapse of visual neuritis. After the acute phase treatment, immunomodulators are administrated (beta 1a/1b interferon, acetate glatiramer) or immunosuppressive (mitoxantrone, cyclophosphamide, methotrexate, etc.), depending on the form and progress of the disease.

Devie visual neuromyelitis is a pathological entity related to MS. It is a rare disease which can occur at all ages and which consists of bilateral visual neuritis quickly followed (within days or weeks) by transverse myelitis (demyelination of spinal cord) with paraplegia.

Schilder disease (diffuse mielinoclastic sclerosis) is also a very rare disease, progressive, generalized, which starts before the age of 10. It represents one of the causes of cortical blindness acquired by children of this age. It may cause bilateral retro bulbar visual neuritis or papillary edema (in 20% of the cases), because of the light growth of intracranial pressure. As the disease progresses, spastic paralysis occurs. The cause of this disease and its treatment are unknown, the decease intervening within 1-2 years form the inception of the disease.

BIBLIOGRAPHY

1. Coyle PK, Hammad MA – Atlas of multiple sclerosis. Science Press, London 2003. .
2. Freedman MS et al – International consensus statement on the use of disease - modifying agents in multiple sclerosis. Multiple Sclerosis, 2002; 8; 19-23.
3. Goodin DS et al – Disease modifying therapies in multiple sclerosis. Report of the Therapeutics and Technology Assessment Subcommitee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology, 2002; 58: 169-178.
4. McDonald WI et al – Recomended diagnostic criteria for multiple sclerosis: guidelines from the international panel on the diagnosis of multiple sclerosis. Ann Neurol, 2001; 50: 121-127.
5. National Multiple Sclerosis Society (NMSS) – Disease management consensus statement, Treatments > Medications Used in MS, site accesibil pe Internet la www.nmss.org
6. Panitch H et al – Randomized, comparative study of interferon â-1a treatment regimens in MS. The EVIDENCE Trial, Neurology, 2002; 59: 1496-15063
7. Samuels MA (edit.) – Manual of neurologic therapeutics, 7-th edition, Lippincott Williams & Wilkins, Philadelphia 2004.
8. Sharief MK – Dose and frequency of administration of interferon-b affect its efficacy in multiple sclerosis. Review article, Clin Drug Invest 2003; 23: 551-559.
9. Stamatoiu IC (sub red.) – Scleroză multiplă, Editura Medicală, Bucureşti, 1989.
10. Tuta S.-Multipla scleroza. Ghid therapeutic. 2002
11. Victor M, Ropper AH – Adams and Victor's Principles of Neurology, 7-th edition, McGraw-Hill, New York, 2001.
12. Thomas J. Walsh - Neuro-Ophthalmology: Clinical Signs and Symptoms, Fourth Edition
13. Myron Yanoff, Jay Duker – Ophthalmology, Second Edition, 2004
14. Jack Kanski – Clinical Ophthalmology, Fifth Edition, 2003