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NEURO-OPTHALMOLOGIC MANIFESTATIONS OF DEMYELINATING DISEASES

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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.

Rezumat: Dintre toate bolile demielinizante, cea mai frecvent întâlnită în practică și în viață este fără îndoială scleroza multiplă (SM). Deși etiologia afecțiunii nu se cunoaște cu exactitate (fiind implicați mai mulți factori predisponenți), boala are totuși o clară predispoziție genetică, iar mecanismul patogenetic este unul autoimun. Manifestările clinice ale SM sunt multiple și variate, în funcție de nivelul la care apar leziunile demielinizante. Debutul cel mai des întâlnit este prin semne și simptome vizuale, semnele neurologice aparând de regulă ceva mai târziu. Diagnosticarea SM presupune în primul rând cunoașterea formelor de manifestare ale bolii, investigații specifice neurologice și oftalmologice și bineînțeles o colaborare strânsă între neurolog și oftalmolog. Este de asemenea important de stabilit etiologia nevritei optice retrobulbare (o manifestare comună a SM), prin anamneză riguroasă și prin teste paraclinice, biochimice și serologice specifice, întrucât diagnosticul de SM implică o mare responsabilitate a medicului neurolog de a informa pacientul cu privire la manifestările clinică și la evoluția progresivă a bolii. Întrucât nu există încă un tratament etiologic al SM, tratamentul este în principal immunomodulator/ immunosupresor, simptomatic și recuperator.

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 –
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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 demyelinating, having as a result the reduction of visual ability of the respective eye (rarely bilateral). It is usually about a retrobulbar 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 retrieving 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 fundus generally indicates a temporary visual atrophy (rarely generalized) – frequently met with optical neuritis in MS.

The most common brack of eye-shoot 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 discromatopsia, 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 (Unthoff 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 abdution, 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, hemianopsia intermediary urvetis (10% of the cases occur in the context of MS) and retinal periflerteb.

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 fond 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 therapeutic 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 neurymelitis 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.
5. National Multiple Sclerosis Society (NMSS) – Disease management consensus statement, Treatments > Medications Used in MS, site accesibil pe Internet la www.nmss.org