CLINICAL ASPECTS IN MULTIPLE SCLEROSIS

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Abstract: *The first appearance of various combinations of motor, sensory, coordination, visual, and cognitive impairments, as well as symptoms of fatigue and urinary tract dysfunction compatible with central nervous system involvement in young patients, raises the possibility of multiple sclerosis. The gradual resolution of these symptoms during a period of days to weeks further supports this diagnostic entity. Clinically isolated syndrome is the first acute clinical demyelinating event with evidence of subclinical demyelination on the brain or spinal cord MRI. Pediatric multiple sclerosis represents a particular MS subgroup with provocative diagnostic. Problems of cognitive dysfunction and psychosocial adjustment have particularly serious implications in both children and teenagers with multiple sclerosis.*

Cuvinte cheie: *semne, simptome, scleroza multiplă, sindromul clinic izolat*

Rezumat: *Prima apariţie a diverselor combinaţii de tulburări motorii, senzitive, de coordonare, vizuale şi cognitive, precum şi simptome ca oboseala şi disfuncţia tractului urinar, compatibile cu implicarea sistemului nervos central la pacienţii tineri, ridică suspiciunea de scleroză multiplă. Atenuarea graduală a acestor simptome pe o perioadă de zile, săptămâni, susţine mai departe acest diagnostic. "Sindromul clinic izolat" este prima manifestare clinică acută de demielinizare cu dovada IRM a demielinizării subclinice la nivelul creierului şi măduvei spinării. Scleroza multiplă la copil reprezintă un subgrup particular cu diagnostic provocator. Problemele disfuncţiei cognitive şi a integrării psihosociale au implicaţii serioase particulare atât la copiii cât şi la tinerii cu scleroză multiplă.*

Multiple Sclerosis (MS) is an inflammatory, demyelinating, chronic disorder of the central nervous system (CNS) of unknown etiology, based on autoimmune mechanisms that attack myelin's proteins (mediated by T cells) and associating an axonal injury/damage process. It is characterized by the existence of demyelinative foci called plates. These vary in size from millimeters to centimeters, are multiple and they spread mostly in the white matter and the spinal cord.

MS represents the most frequent pathology in terms of young subject's handicap.

In Romania there are not recent statistics that show the exact number of Multiple Sclerosis patients. According to some epidemiologic studies made in the 80's, there are about 35-40 cases of MS in 100.000 people (1).

Although the disease usually has its onset at age 20-40, there are cases when it affects children or adults over the age of 50, women being affected twice as much as men (2).

Clinical manifestations are variable, depending on the way the plates are spread. The main myelinating paths of the CNS, motor, sensitive, cerebral and optical are involved.

There are several characteristics signs and symptoms that might suggest Multiple Sclerosis as a posible diagnosis, particularly in young subjects.

1. Motor disorders are due to corticospinal tract involvement. Patients may develop monoparesis, paraparesis, hemiparesis/ hemiplegia, quadriparesis/ quadriplegia. Lower extremities are usually more affected than the upper. Neurological examination shows weakness, spasticity, hyperactive reflexes, clonus, Babinski reflex, Hoffmann sign, the disappearance of abdominal skin reflexes.

2. Visual anomalies: optic neuritis is the frequent onset sign of MS (in about 25 % of the MS patients and mostly children), usually unilateral in adults and bilateral in children. It is characterized by partially or totally loss of vision, usually unilateral and sometimes bilateral (simultaneously or successively). Optic neuritis is preceded or accompanied by pain in the orbit accentuated at eye movement; it might recidivate on the same side or on the opposite one. Funduscopy results are normal in the beginning ("the patient sees nothing and the doctor sees nothing.") and later appears a pallor of the optic disc. The recovery of visual functions is complete in almost half of cases. After the recovery, a transitory decrease of visual acuity might appear again at effort or at an increase of the body's temperature (Uthoff phenomenon). The effect on the optic nerve is shown by the alteration of visual evoked potentials (the elongation of latency of the wave P100). More than half of the patients who present optic neuritis will develop other MS signs, the risk being lower if the MRI doesn't reveals demyelinating lesions (3-6).

3. Sensitive disorders: paresthesias under the form of tingling, constriction sensations; disesthesias (often described as a burning, itching, pins and needles); Lhermitte sign (an electrical sensation that runs down the back and into the limbs, and is produced by bending the neck). The objective disorders are mostly due to posterior columns involvement and affect the vibration sensation and the position of inferior limbs' fingers. Pain is a common symptom for MS patients (in almost 50% of the cases). There are different types of pain, such as: trigeminal neuralgia, joint pains, central pain (7,8).

4. Cerebellar events: gait and balance disorders, limbs

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or body ataxia, scanning speech and intention tremor, often invalidant. The combination of nystagmus, scanning speech and intention tremor is known as the Charcot's triad.

5. Brainstem impairment: diplopia is frequent, mostly connected with internuclear ophtalmoplegia (INO) by the impairment of the medial longitudinal fasciculi which is responsible for communication between the two eyes by connecting the abdcens nucleus of one side to the oculomotor nucleus of the opposite side. The presence of bilateral INO at a young adult is highly evocative of MS. The trigeminal neuralgia affects 1-2 % of the MS patients, manifests itself with intense pain episodes and hypesthesia in the trigeminal nerve, associated with the disappearance of the corneal reflex on the same side. We can also find a vestibular central syndrome with vertigo and nystgamus (deafness is rare, but the alteration of auditory evoked potentials is frequent), a pseudobulbar syndrome characterized by dysarthria and deglutition problems, and also a facial nerv paresis (3,9).

6. The bladder dysfunctions appear in at least 80% of MS patients, the most common problem is incontinence, but frequency, urgency, nicturia, sensation of incomplete urination also appear. These problems expose patients to repeated urinary infections (10,11).

7. The intestinal disorders are rare, patients complain of constipation, diarrhea and incontinence for feces.

8. Sexual dysfunction: in MS prevalence is 45-70% in women and 70% in men, the most commonly described symptoms in men are erectile and ejaculatory dysfunction and in women decreased libido, lack of orgasm, difficulty in vaginal lubrication (12).

9. Psychiatric disorders: depression is the most common disorder, characterized by irritability and anxiety associated with suicidal ideation, diurnal variation of mood, anger and euphoria (13.14).

10. The cognitive impairment occur in 40-60% of cases of MS regardless of clinical form. It may be the major source of social and occupational disability and the lower quality of life. The functions most affected are: memory, attention and processing speed information, rarely may occur a subcortical type dementia. Cognitive disorders associate with neocortical atrophy, third ventricular width, hippocampal atrophy, atrophy of corpus callosum (15-20).

More recent imaging and pathological studies have shown neocortical abnormalities in patients with MS, which can be detected in early stages of the disease and that, at least in part, do not correlate with the accumulation of lesions in the white matter. Third ventricular width may have a predictive value for cognitive dysfunction. Atrophy of corpus callosum is frequently observed in MS and the anterior body is especially interested (17,18,21,22).

11. Other symptoms:

a) Fatigue is common among patients with MS,

b) Paroxysmal symptoms are a group of symptoms that occur suddenly, are expanding in a few seconds, it takes seconds or minutes, occur several times during the day and leaves no residual deficits. Clinically, they can take very different aspects: pain, dysarthria, ataxia, paresthesias, tonic seizures (spasm in flexion of the hand and elbow with extension of the lower leg).

Depending on developments, The National Multiple Sclerosis Society classifies 4 types of disease:

- relapsing remitting (RRMS)
- secondary progressive (SPMS)
- primary progressive (PPMS)
- progressive relapsing (PRMS)

The most common is relapsing remitting form, affecting 80-85% of patients with MS. Usually this form begins with clinically isolated syndrome (CIS). CIS is the first neurological episode lasting at least 24 hours, caused by inflammation or demyelination of nervous tissue. This may be a monofocal episode represented by a single symptom (e.g. optic neuritis) or a multifocal represented by more symptoms (i.e. abnormal coordination, bladder dysfunction). Clinically is characterized by: optic neuritis, brainstem impairment (INO, nystagmus), myelitis, and other events such as facial paresis, vertigo, deafness, dysarthria, dysphagia, ataxia, spasticity. However, only 30 to 70% of patients with CIS developed MS later (18.24).

Brain damage (evidenced by MRI) associated with CIS are suggestive of MS. Thus, if initial MRI is abnormal (demyelination lesions), the possibility of developing MS is 60%. If initial MRI is normal (without injuries), the possibility of developing MS is 20% and then MRI should be repeated after 3-6 months. After this period, it is not recommended another MRI in the absence of symptoms. Early treatment of CIS with interferon ß late conversion to MS in high-risk patients (25,26).

When deficits always submit between relapses we are talking about a benign form of MS.

Secondary progressive form occurs in 65% of patients with RRMS beginning to decline gradually between neurological relapses without remission periods. The average time between onset of disease and the conversion from RRMS to the SPMS form is 19 years (27).

Primary progressive form is described in approximately 10-15% of those who have never had remission after the initial symptoms of MS. It is characterized by progression of disability from onset, without remission or improvement. Age of onset in the form of PPMS is higher than in the RRMS (around 40 years) (27).

Progressive relapsing form is described in individuals who have onset of neurological decline stable, over overlapping relapses. This is the least common of all forms of MS (27).

Pediatric MS represents approximately 3-4% of all cases of MS. Patients reported the occurrence of the first symptom before the age of 16 years. According to the International Pediatric MS Study Group, pediatric MS can be diagnosed by two clinical episodes of CNS demyelination that are separated by at least 30 days (28).

Children have a variety of symptoms including sensitive deficits, INO, abnormalities in the brainstem, motor deficits and gait disturbance. Some studies have shown that polysymptomatic manifestations are more common in children (50-70%) than in adults, although the monosymptomatic are not rare (30-50%). Among children with monosymptomatic symptoms, 30% will develop motor symptoms, 30% sensitive symptoms, 25% of brainstem, 10-22% have INO and 5-15% have ataxia. Acute disseminated encephalomyelitis as initial manifestation is encountered to 18-29% of patients (29-32).

Several clinical features are more common in young patients (under 11 years of age). These include frequent severe cognitive impairment, seizures, optic nerve dysfunction and brainstem and cerebellar involvment. A study shows that the number of relapses in children under 12 years is lower in the first 2 years of disease compared with those over 12 years. Cognitive impairment appear to be exceptional in children. However, preliminary data indicated that in 70% of them, cognition decline occurs after 2 years, compared with adults, in which cognitive impairment occurs gradually (33-35).

A proper management of Multiple Sclerosis may improve the social and professional activity and the quality of life in both young patients and children.

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