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HEADACHE AND MULTIPLE SCLEROSIS

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Abstract

Migraine is a disease not seen in the general population and in particular when the migraine is comorbid with other neurological diseases. This condition ensures that patients give little importance to this disease without acknowledging that this is likely to induce alterations in the quality of life often worse in the same multiple sclerosis (MS). The relationship between migraine and MS is still unclear. It is important that the physician has to consider a number of elements which differentiate the two clinical pictures in the context of a global vision that involves primarily the clinical evaluation and medical history, and subsequently the aid of instrumental and laboratory investigations. The recent development of new treatment options for MS requires professionals to be aware of the treatments for migraine and possible side effects that could limit or contraindicate the use of specific drugs. Patients with this comorbidity are "crushed" by the weight of two chronic diseases.

Key words: Migraine, Multiple Sclerosis, Neurological Diseases

Introduction

The prevalence of headache in patients with multiple sclerosis is relevant (1). The prevalence varies from 35.5 % to 70% and in particular criteria (ICHD -2) (2) shows that the most common form of headache in patients with multiple sclerosis is migraine in all its forms with a frequency of 2-3 times higher than the general population and in the proportion of 70% (the form with aura is present in 30% of cases), while tension-type headache is present in 30% of cases (2). Migraine with aura is prevalent visual symptoms (44 %) compared to the symptoms visual / sensory (38%) or only sensory (17%). These data show that the frequency of migraine with aura in patients with amyotrophic multiple substantially similar to patients without multiple sclerosis (1). From the literature it is clear that the frequency of chronic migraine , headaches caused by excessive use of drugs and the degree of disability caused by migraine crisis and rated according to the scale MIDAS , do not differ from the general population. Familiarity for multiple sclerosis is not different between patients with MS (MS or MS-migraineurs Mig) compared to MS patients but free from headache (headache - free MS or MS-NH) while the family history of migraine is 2, 5 times higher (49%) between the MS- Mig compared to MS- NH (19%). Migraine is more frequent in female patients Mig - MS compared with patients suffering from MS -NH in the ratio of 90 vs. 57%. In patients Mig - MS is more frequent presence of depressive disorder compared with patients in the MS -NH ratio of 36 vs. 21%. (see Table 1) .

The MS-Mig patients , particularly patients with migraine with aura , generally have relapses of demyelinating disease (three or more episodes / year) with a frequency greater than the MS- NH (25-30 % vs. 10 %) while the absence of relapse (often related to primary progressive MS) is higher in MS- NH compared to MS- Mig (9 vs 3 %) (1). The MS-Mig patients have higher incidence of cognitive disorders , mood swings, symptoms of brainstem dysfunction and visual compared to MS- NH. In particular, migraine is a significant predictor of anxiety and depression often associated with higher incidence of fatigue in chronic symptoms of MS (Table 2 and 3).

The scales of disability in MS is not generally differ between patients MS-Mig and MS- NH. Interestingly, the MS-Mig patients have an increased incidence of side effects compared with interferon beta in patients with MS- NH: 32% of MS patients had Mig - flu-like symptoms as well as migraine after all or nearly all injections compared to only 13% of patients MS- NH.

From the point of view of the neuroimaging (3) no particular differences between patients Mig - MS and MS- NH , in particular for the number or the distribution of T2-hyperintense lesions or gadolinium-enhancing

Physiopathogenetic Hypothesis

All this for some time already led to hypothesize an association between these morbid affections and several reports over the years have proved its existence. Clinical experience shows in fact a number of common features among these diseases: beginning at a young age , the prevalence in women, chronic evolution with exacerbations, frequent attenuation of symptoms with exacerbations during pregnancy or puerperium to stressful events both physical and mental (4). Migraine can be considered a symptom of MS, may be associated with a mood disorder or secondary to the use of specific drugs (eg interferon), can be considered a factor predisposing to multiple sclerosis or, according to more recent hypothesis, be a medical condition diagnosed when the MS is already present in subclinical phase as the initial symptoms is still scarce or absent.

An interesting fact is the increase in the frequency and duration of relapses of MS in MS-Mig compared to MS- NH patients (4). This fact can be interpreted in several ways:

-The migraine crisis may induce " inflammatory " alterations affecting the brain such as to predispose to an exacerbation of demyelinating disease. This assumption, however, is not endorsed by neuroimaging data do not show significant differences between MS-Mig ans MS-NH patients in particular in relation to T2 hyperintense lesions and gadolinium-enhancing

-A reduction of the pain threshold in patient perception of migraine aggravate the symptoms of MS.

- In migraine patients with aura the spreading depression can cause neurological deficits from which the unmasking of sub -clinical symptoms of multiple sclerosis. In this case the therapy for migraine should be implemented as early as possible in order not to induce worsening of neurological deficits of MS.
Currently, the pathophysiology of migraine recognizes a role in the periaqueductal gray (PAG), located in the midbrain and involved in pain modulation. Imaging studies during migraine attacks showed a continuous activation of the structures in particular within the PAG. A series of neuroradiological reports indicate that the presence of at least one plate to the midbrain in patients with MS is associated with an increased risk of headache with migraine features (IHS criteria -2). The data revealed a fourfold increase in the likelihood of developing a migraine-type headache and 2.5 times more likely to develop a tension headache compared to those patients who have lesions in this area . This evidence is not in relation to lesion load and the degree of illness. The PAG therefore seems to represent the collage between migraine and multiple sclerosis. Other physiopathogenetics theories indicate an alteration of the blood-brain barrier to a direct action of serotonin to cause an exposure of myelin T-cell.

The Relapse and the Aura

Relapse or relapse in multiple sclerosis is characterized by the appearance of new symptoms or worsening of existing symptoms, lasting at least 24 hours and is preceded by a period of neurological stability of at least one month (3). The clinical recovery after relapse is variable and often incomplete.
The migraine aura, based on the criteria ICHD - 2, is characterized by symptoms alone or in combination involving visual impairment in the majority of cases or sensory disturbances, motor, or language. These symptoms last for at least 5 minutes and no longer than 60 minutes. They do not involve neurological outcomes, have a clinical history usually stereotyped and may not be accompanied by headache (2). The differential diagnosis between relapse and aura is related to a careful history to be carried out before such a procession of symptoms.

Magnetic Resonance

Even the misinterpretation of MRI involves inaccurate diagnosis of multiple sclerosis. The differential diagnosis is more frequent neuroradiological with small vessel disease, encephalopathy characterized by a micro-angiopathy that can be damage ischemic cerebral vessels. The disease may be asymptomatic but typically involves isolated or associated with clinical symptoms such as headaches among them, cognitive decline, abnormal gait, stroke, mood disorders, urinary disturbances. This pathological condition, generally more frequent in the elderly population, and is associated with vasculitis, diabetes mellitus and hypertension.
MS is characterized by lesions on MRI generally oval in shape and mainly the periventricular regions, iuxtacortical and in the corpus callosum (3). The presence of "enhancement" after administration of Gadolinium is a crucial aspect. In particular, the injury to the surface of the bridge, to the base of the fourth ventricle and trigeminal tract are specific for the MS while the small vessel disease typically affects the central portion of the bridge.
Patients with migraine often have small hyperintense lesions , symmetrical , subcortical white matter regions typically periventricular, lobar, basal ganglia and thalamus (5). These injuries, no precise meaning and related factors such as smoking, hypertension, and use of oral contraceptives , are to be framed in the general clinical condition for a correct differential diagnosis (6).

Conclusions

Migraine is a disease not seen in the general population and in particular when the migraine is comorbid with other neurological diseases. This condition ensures that patients give little importance to this disease without acknowledging that this is likely to induce alterations in the quality of life often worse in the same MS. The relationship between migraine and multiple sclerosis is still unclear. It is important that the physician has to consider a number of elements which differentiate the two clinical pictures in the context of a global vision that involves primarily the clinical evaluation and medical history, and subsequently the aid of instrumental and laboratory investigations.

The recent development of new treatment options for MS requires professionals to be aware of the treatments for migraine and possible side effects that could limit or contraindicate the use of specific drugs. Patients with this comorbidity are "crushed" by the weight of two chronic diseases.

The study of this problem is of crucial importance not only for the diagnosis but also to avoid the negative synergism of disability caused by both diseases.

References

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Table 1 Demographic characteristics, co-existing medical conditions and family history in MS-Mig and MS-NH groups

	MS-NH	MS-Mig	*p*
N	73	94	–
Age in years (mean ± SD)	47 ± 13	43 ± 11	NS
% Female*	57%	90%	<0.001
Disease duration in years (mean ± SD)	13 ± 11	12 ± 11	NS
% Interferon beta-1 use	71%	64%	NS
Co-existing conditions			
Hypertension	12%	15%	NS
Diabetes	0%	4%	NS
Seizures	1%	4%	NS
Syncope	1%	7%	NS
Thyroid disease	8%	10%	NS
Fibromyalgia	0%	4%	NS
Mononucleosis*	5%	20%	0.006
Autoimmune disease	4%	12%	NS
Bipolar disorder	4%	3%	NS
Anxiety spectrum disorder	8%	16%	NS
Depression	21%	36%	0.028
Current smoker	18%	19%	NS
Family history			
Family history of MS	17%	10%	NS
Family history of migraine*	19%	49%	<0.001

MS-Mig MS and migraine group, *MS-NH* MS–no headache group, *NS* non-significant

* $p < 0.01$

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Table 2 Painful symptoms and analgesic use in MS-Mig and MS-NH groups

	MS-NH (%)	MS-Mig (%)	*p*	OR	CI
Brief, shooting pains into jaw*	5	27	<0.001	9.7	2.1–44
Shooting pains into back of head/neck*	11	45	<0.001	9.2	2.7–32
Facial pain*	10	32	0.001	6.6	1.6–27
Temporomandibular joint syndrome*	7	30	<0.001	4.8	1.4–16
Lhermitte's sign*	18	48	<0.001	5.2	1.9–14
Painful spasms*	29	48	0.012	3.7	1.4–9.6
Restless legs feeling, movement-relieved*	33	57	0.002	2.1	0.87–4.8
Frequent allodynia (not during headache)*	4	26	<0.001	5.3	1.2–23
Daily use of pain medication for non-headache*	6	21	0.006	7.3	1.2–46

* $p < 0.01$

Table 3 Non-pain symptoms in MS-Mig and MS-NH groups

	MS-NH	MS-Mig	*p*	OR	CI
Optic neuritis*	49%	77%	<0.001	2.8	1.2–6.4
Visual problems interfere with reading	22%	32%	NS	0.64	0.25–1.7
Brainstem symptoms*,[a]	27%	53%	0.001	2.4	1.0–5.7
Cognition "definitely affected"	24%	38%	0.039	1.8	0.67–4.9
Depression score (PHQ-9)	4.7	8.2	<0.001	NA	NA
Anxiety score (PHQ)	4.1	6.5	<0.001	NA	NA
Fatigue severity score	3.6	5.0	<0.001	NA	NA
Hours of sleep per night	6.7	6.8	NS	NA	NA
Epworth sleep scale score*	5.6	8.1	<0.001	NA	NA

* $p < 0.01$

[a] Double vision, facial weakness, deafness, abnormal taste, vertigo

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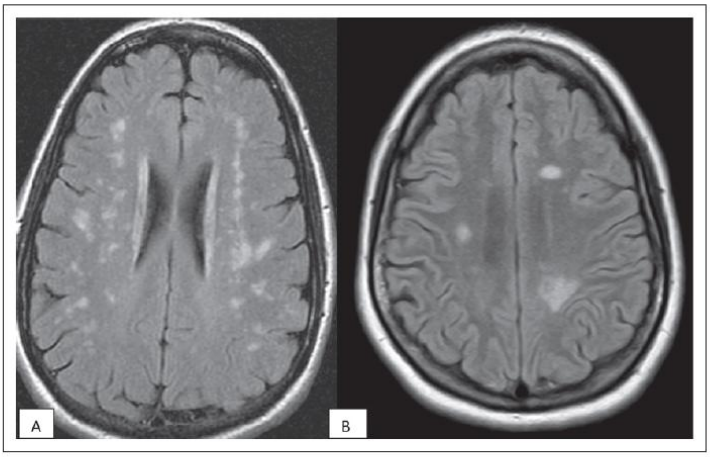

(A) Axial T2 FLAIR image of patient with small-vessel disease. (B) Axial T2 FLAIR image of patient with relapsing–remitting multiple sclerosis.

Angela Applebee, The Clinical Overlap of Multiple Sclerosis and Headache – Headache, 2012