Late onset multiple sclerosis

ANA CARVALHO[1,2], EVA BRANDÃO[1,3], JOANA GUIMARÃES[1,4], JORGE REIS[1], PEDRO ABREU[1,4], TERESA MENDONÇA[1], MARIA JOSÉ SÁ[1,5]
[1]*MS Clinic. Department of Neurology. Centro Hospitalar São João. Porto.*
[2]*Department of Neurology. Centro Hospitalar Vila Nova Gaia/Espinho.*
[3]*Department of Neurology. Centro Hospitalar Entre-Douro e Vouga.*
[4]*Faculty of Medicine. University of Porto.*
[5]*Health Sciences Faculty. University Fernando Pessoa. Porto.*
Portugal.

ABSTRACT. Late onset multiple sclerosis (LOMS) defined as the first presentation of multiple sclerosis (MS) over 50 years is unusual and frequently misdiagnosed. We analyzed whole MS population in our MS Clinic and we found a prevalence of 3.35%, a female/male ratio of 1.4:1, a high occurrence of motor function involvement at presentation (47%) and a severe evolution, similarly to those elsewhere described.
Key words: multiple sclerosis, late onset, differential diagnosis.

RESUMEN. La esclerosis múltiple de inicio tardío (EMIT), definida como la primera presentación de la esclerosis múltiple (EM) después de 50 años de edad, es rara y mal diagnosticada con frecuencia. Se analizó toda la población de la EM en nuestra Clínica de EM y se encontró una prevalencia de 3.35% de la EMIT, una relación hombre/mujer de 1.4:1, una alta incidencia de la disfunción motora en la presentación (47%) y una evolución grave, de una manera similar a los descritos en otras series.
Palabras clave: esclerosis múltiple, inicio tardío, diagnóstico diferencial.

Address: Ana Carvalho – Department of Neurology of Centro Hospitalar São João – Alameda Prof. Hernâni Monteiro 4200 319 Porto (Portugal) – Tel.: +351 225 512 100 – E-mail: a.teresa.carvalho@gmail.com

Multiple sclerosis (MS) is typically diagnosed in the third/fourth decade of life. Late onset multiple sclerosis (LOMS) defined as the first clinical presentation over 50 years[1] is unusual, the prevalence ranging between 2.7% and 12% according to different retrospective studies[2]. Nevertheless it is probably underestimated since LOMS is frequently misdiagnosed and there is a diagnostic delay ranging from 3 to 4.7 years[2]. As classically reported in MS beginning in younger ages, women are more affected than men, although in a highest ratio - 1.4:1[3] against 2:1[4]. Typical clinical presentation with motor symptoms (63-90% of patients) is described in the literature[2] although this is a non-consensual data, since there are some reports finding no differences between LOMS or young-onset initial symptoms[3]. Sensory symptoms are less common than usual and visual symptoms are rare[2]. The majority of LOMS patients seem to have a primary progressive disease course, ranging from 32% to 83% in different studies[1], in contrast with commonest relapsing-remitting course of younger patients. Regarding prognosis, a higher disability in LOMS in comparison with normal age of beginning was found in some studies[1]. In this study, we aim to describe the clinical and paraclinical characteristics of LOMS patients followed in our MS Clinic.

❑ Methods

Among our whole MS population (n=507) we retrospectively reviewed the clinical protocols of patients diagnosed with MS over 50 years. MS diagnosis was based on the revised McDonald criteria[5]. We analysed demographical (age and gender) as well as clinical data: clinical presentation, MS course, disease duration and neurological disability using the Expanded Disability Status Scale (EDSS)[6]. The disease severity was assessed using the Multiple Sclerosis Severity Score (MSSS), an algorithm that relates EDSS score to the distribution of disability in patients with comparable disease duration[7]. We also reviewed the paraclinical data, namely magnetic resonance image (MRI), cerebrospinal fluid (CSF) and visual evoked potentials (VEPs).

❑ Results

We identified 17 patients (3.35%) with LOMS (Table I). Women were more affected than men (10 female and 7 male patients, ratio 1.4:1). First symptoms began at the mean age of 55 years. Nine patients (52.9%) experienced the first symptoms between 50 and 54 years; 6 (35.3%) between 55 and 59 years and 2 (11.8%) after 60 years; the oldest patient had 69 years at the beginning of symptoms. Mean age at diagnosis was 58 years, (range 50-75). Mean disease duration until diagnosis, reflecting diagnosis delay, was 3.2 years (range 0-15). Motor symptoms were the commonest presentation, occurring in 8 patients (47%).

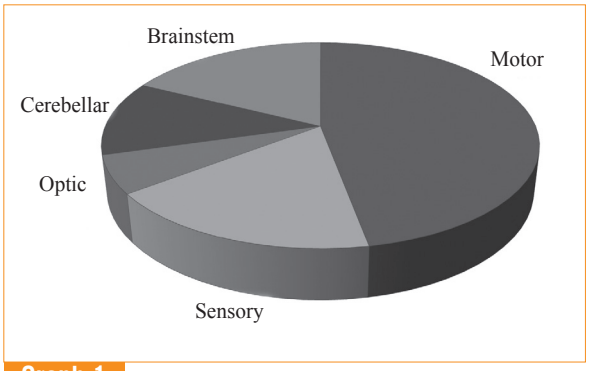
Regarding other symptoms, sensory occurred in 3 patients (17.6%), cerebellar in 2 (11.8%), brain-

Table I Description of LOMS patients

	Patient	Gender	Age of onset (years)	Diagnosis delay (years)	Presentation symptoms	Clinical form	Typical brain and/or spinal cord MRI	OCBs	VEPs	EDSS	MSSS
	1	F	69	6	Motor	PP	Yes	+	-	6	7.97
	2	M	52	0	Sensory	RR	Yes	+	-	1.5	2.87
	3	M	64	7	Motor	PP	Yes	n.p	-	6.5	8.63
	4	F	53	0	Sensory	RR	Yes	+	-	m.d	m.d
	5	F	56	0	Motor	CIS	Yes	-	n.p	3	7.27
	6	F	58	1	Motor	SP	Yes	+	+	7.5	9.88
	7	F	51	15	Brainstem	RR	Yes	+	+	m.d	m.d
	8	F	55	0	Brainstem	RR	Yes	n.p	n.p	0	0.35
	9	M	59	3	Motor	PP	Yes	+	n.p	6.5	9.32
	10	M	52	2	Optic neuritis	RR	Yes	-	+	1	0.71
	11	M	54	4	Cerebellar	PP	Yes	+	+	4	7.26
	12	F	51	1	Motor	SP	Yes	+	+	4.5	6.98
	13	M	50	3	Motor	SP	Yes	+	n.p	7	7.46
	14	M	50	0	Motor	SP	Yes	+	+	8.5	9.71
	15	F	55	1	Sensory	RR	Yes	n.p	+	2	4.13
	16	F	55	4	Brainstem	RR	Yes	+	-	2	2.64
	17	F	50	4	Cerebellar	SP	Yes	-	+	6	6.89
Mean value (if applicable)	-	-	55	3.2	-	-	-	-	-	4.4	6.14

CIS: Clinical Isolated Syndrome; EDSS: Expanded Disability Status Scale; F: female; M: male; m.d: missing data; MRI: Magnetic Resonance Image; MSSS: Multiple Sclerosis Severity Score; n.p: not performed; OCBs: Oligoclonal Bands; PP: Primary Progressive; RR: Relapse-Remitting; SP: Secondary Progressive; VEP: Visual Evoked Potentials.

stem in 3 (17.6%) and unilateral optic neuritis in 1 (5.9%) (Graph 1). Most patients had progressive forms (secondary and primary in 5 and 4 cases, respectively); relapsing-remitting course was seen in 7 patients and 1 patient had clinically isolated syndrome (Graph 2). Brain and spinal cord MRI, respectively, showed typical lesions in 100% and 82% patients at some point of disease evolution. CSF was analysed in 14 cases revealing oligoclonal bands (OCB) in 79%. VEPs were tested in 13 patients and they were positive in 8 (61.5%). The mean EDSS was 4.4 (range 0-8.5) and the mean progression index (MSSS) was 6.14 (range 0.35-9.88). First line treatment with immunomodulators was performed in 14 patients (13 - interferon beta; 1 - glatiramer acetate).



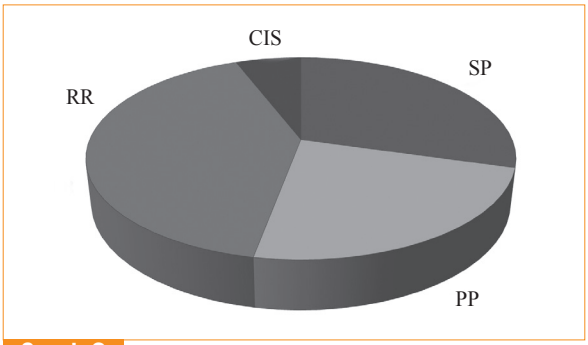
Graph 1 *Clinical presentation of LOMS patients.*

❑ Discussion

LOMS is an unusual and frequently misdiagnosed form of MS, which has been few addressed in the literature. Motor symptoms are the most typical presentation, sensory symptoms are less common than usually and visual symptoms are rare. Primary progressive disease course seems to be the commonest and prognosis is apparently worst than in younger ages. The recognized diagnosis delay may be explained by several factors: large number of conditions that mimic MS symptoms (e.g. stroke, cervical spondylotic myelopathy); atypical presentation, low

index of suspicion and high prevalence of white matter lesions with age. MRI, the most specific and sensitive examination tool for MS diagnosis, lacks some specificity in older patients due to the co-occurrence of microangiopathic lesions[1, 8]; in this sense, Barkhof criteria[5] seems be less specific in older patients than in young patients. The CSF analysis may help in order to increase the specificity of the diagnosis in suspect LOMS[9] and is useful to rule out other common neurological diseases in older patients.

In our series, the prevalence of LOMS fits the literature data and the female: male ratio (1.4:1) is exactly the same to that reported in the largest published series[3]. In addition, the highest occurrence of motor symptoms in presentation is in accordance with other studies[2], witch might be due to a higher tendency for spinal cord involvement in these patients, as suggested by Arias and colleagues[8]. We observed typical lesions in brain and spinal cord MRI at some point of disease evolution in almost all patients. In our patients OCB restricted to CSF were positive in 79% of assessed patients, a smaller value to that described in other series, which found that OCB occurred in LOMS and classic MS without differences[3]. The patients age and comorbidities may explain, in part, the severe evolution, measured by MSSS in our series.



Graph 2 *Clinical course of LOMS patients. CIS: clinical isolated syndrome; PP: primary progressive; RR: relapsing-remitting; SP: secondary progressive.*

In conclusion, the general characteristics of our LOMS population are similar to those elsewhere described, particularly as regards its low frequency in MS populations, female/male ratio, high occurrence of motor function involvement and severe evolution. We highlight the higher frequency of progressive forms and the greater progression index than the usually reported in MS starting at younger ages.

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