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Parkinsonism and multiple sclerosis – is there association?

Barbara Barun¹, Vesna V. Brinar¹, Ivana Zadro¹, Ivo Lušić², Dario Radović³, Mario Habek¹

From the:

¹Referral Center for Demyelinating Diseases of the Central Nervous System, University Department of Neurology, Zagreb School of Medicine and University Hospital Center, Zagreb, Croatia

²University Department of Neurology and ³Department of Nuclear Medicine, Split School of Medicine and University Hospital Center Split, Split, Croatia

Corresponding author:

Mario Habek, MD

University Department of Neurology

Zagreb School of Medicine

Kišpatićeva 12

HR-10000 Zagreb

Croatia

Phone: +38598883323; Fax: +38512421891; e-mail: mhabek@mef.hr

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Abstract

Association between multiple sclerosis (MS) and parkinsonism is rarely reported. We describe clinical, radiological and DAT scan findings in two patients presenting with parkinsonism. MRI revealed demyelinating lesions of the central nervous system consistent with MS in both patients. On the other hand, DAT scan findings were supportive of Parkinson's disease. There is still an open debate whether MS lesions can cause parkinsonism, or these are just coincidental findings of two different diseases in the same patient. Although there are cases of causal relationship between parkinsonism and MS, some literature reports and our observations suggest that Parkinson's disease and MS can coexist as two separate diseases in the same patient. It is possible that the symptoms of Parkinson's disease can be aggravated by MS plaques, explaining the favorable response to corticosteroids in some patients.

Key words: multiple sclerosis, Parkinson's disease, MRI, DAT scan

Introduction

Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system (CNS). MS plaques are characteristically found in the periventricular white matter supratentorially and the most common infratentorial locations are the surface of the pons, the cerebellar peduncles, and white matter regions adjacent to the fourth ventricle. As subcortical gray matter also contains myelinated fibers, demyelinating lesions can be found in the striatum, pallidum, thalamus, brainstem and cerebral cortex as well¹. Although demyelination in the basal ganglia is a hallmark of acute disseminated encephalomyelitis (ADEM)², symptoms due to deep gray matter damage can infrequently occur in MS patients. The most frequent movement disorders associated with multiple sclerosis are paroxysmal dystonias (tonic spasms), ballism/chorea, and palatal myoclonus, while parkinsonism associated with CNS demyelination appears to be a very rare finding³. There is still an open debate whether MS lesions can cause parkinsonian symptoms, or the reported cases are just coincidental findings of two different diseases in the same patient. We report on two patients with parkinsonism and demyelinating lesions of the CNS.

Case Reports

Case 1. In 2000, a 38-year-old patient with a history of meningitis at age 21 and two spontaneous abortions developed tremor in the left hand. Neurologic examination at that time revealed resting tremor and rigor with cogwheel phenomenon in the left hand. Because of her young age, MRI was performed and revealed multiple white matter hyperintensities without brainstem lesions. Spinal cord MRI revealed one lesion at C4 level (Fig. 1). Cerebrospinal fluid (CSF) findings, serum and CSF *Borrelia burgdorferi*, immunologic tests (ANF, anticardiolipin antibodies, ANCA)

and visual evoked potentials (VEP) were normal, and she was treated with intravenous corticosteroids with good recovery of the symptoms. Two years later (January 2002), during pregnancy, she developed resting tremor in her left arm and leg again. Neurologic examination revealed resting tremor in the left extremities with rigor, cogwheel phenomenon and reduced arm flexion. She had bradykinesia. Upon delivery, she experienced worsening of her symptoms. This time, along with corticosteroid treatment, therapy with levodopa was introduced, resulting in good recovery and almost complete reversal of neurological deficit. In 2006, exacerbation of her disease recurred; this time she developed diplopia along with extrapyramidal symptoms and characteristic parkinsonian gate. Repeat MRI, T2 and FLAIR sequences revealed a greater number of demyelinating lesions, however, without enhancement on gadolinium application. T1 sequence revealed one black hole. DAT scan was performed to show a low level of dopamine carrying protein in the right striatum, with normal findings on the left side (Fig. 3). These findings were consistent with unilateral Parkinson's disease (PD). The diagnosis was relapsing remitting multiple sclerosis and PD.

Case 2. In August 2000, a 53-year-old woman developed resting tremor and clumsiness in the right arm and leg. One year later, because of persistence of her symptoms, brain MRI was performed and revealed multiple supratentorial white matter hyperintensities (Fig. 1). CSF examination was negative for oligoclonal bands and corticosteroid therapy led to significant improvement of her symptoms.

Immunologic tests were negative and VEP were normal. In the next couple of years she had 4 new bouts of the symptoms, each time with good response to corticosteroid therapy. On control MRI in 2003, multiple white matter hyperintensities, were observed, mostly in both semioval centers and on the border of white and gray matter

(Fig. 2). Spinal cord MRI was normal. Her symptoms gradually progressed and she developed rigor of the left extremities. In April 2007 she started to develop forceful closure of the eyelids, neurological examination revealed blepharospasm along with marked rigor of all four extremities and resting tremor of the right hand. She had no eye movement abnormalities, no autonomic dysfunction, and postural reflexes were preserved. She also had signs of pyramidal lesion, with brisk reflexes of the right extremities and positive Babinski sign. Repeat brain MRI revealed new demyelinating lesions, without post contrast enhancement, and no brain stem or spinal cord lesions. DAT scan was performed to reveal very low levels of dopamine carrying protein in the caudate nucleus and putamen on the left side, and a low level of DAT in the left putamen with normal levels in the left caudate nucleus (Fig. 3). Levodopa therapy was started, with excellent recovery. The diagnosis of relapsing remitting multiple sclerosis and PD was confirmed.

Discussion

Nelson and Paulson proposed an interesting hypothesis that idiopathic PD may follow subclinical episodes of perivenous demyelination⁴. They suggest that the etiopathology of Lewy bodies (a hallmark of PD) may involve repeated perivenous demyelination of pigmented neurons that results in central chromatolysis, and that subclinical demyelinoclastic processes in time and space may result in PD. These perivenous demyelinations are a hallmark of ADEM, and there are many reported cases of postinfectious and postvaccinal parkinsonism (ADEM variants) that excellently responded to levodopa therapy³.

There are several case reports describing patients with parkinsonism and demyelinating lesions of MS^{3,5-11}. There are two main hypotheses that try to explain

this association. The first one is that it is purely accidental^{3,5,6}. The best documented case of coincidental MS and PD in the same patient is that reported by Valkovic *et al.*⁶. The authors base their conclusion on negative response of parkinsonian symptoms to immunosuppressive therapy or steroids, and findings of neuroimaging studies (MRI with absent lesions in the basal ganglia and a characteristic finding on DAT scan).

The other hypothesis is that demyelinating lesions can affect dopaminergic pathways, and thus cause parkinsonian features. It is supported by several case reports which bring into correlation demyelinating lesions and affection of dopaminergic system. Localization of the lesions can be in the nigrostriatal pathway⁷, globus pallidus⁸, or nucleus ruber⁹. Another supportive evidence of causal relationship is marked improvement of parkinsonism on corticosteroid therapy¹⁰. Some authors, on the other hand, describe patients with MS and PD, in which critically positioned MS plaques aggravate PD symptoms¹¹.

There are also cases of coexistent MS with other neurodegenerative diseases associated with parkinsonism. The most important one is pathologically proven coexistence of MS with multiple system atrophy (MSA), in which parkinsonian symptoms were due to MSA¹². There also are reports on MS in patients with spinocerebellar ataxia (SCA)¹³, and some studies have shown that allelic variants of the SCA 2 gene influence susceptibility to MS¹⁴.

Blepharospasm is an extremely rare symptom in MS¹⁵. Patients with blepharospasm and MS usually have brainstem lesions. It is interesting that our patient with blepharospasm had no brainstem lesions. However, it is known that MS symptoms do not always correlate well with demyelinating plaque location, as shown in patients with MS and cranial nerve palsies (Zadro *et al.*, this issue of CNN)¹⁶. On the other

hand, blepharospasm is also a very rare symptom of PD¹⁷, and only a minority of patients with idiopathic blepharospasm develop PD¹⁸. Patients with progressive supranuclear palsy (PSP) are more prone to develop blepharospasm in the course of the illness; however, our patient had no cognitive decline or vertical eye movement paresis, so the diagnosis of PSP was unlikely.

The diagnosis of relapsing remitting MS in both of our patients fulfilled the revised McDonald criteria¹⁹. On the other hand, DAT scan findings in both patients were consistent with PD, and both patients responded to levodopa therapy.

In conclusion, although there are cases of causal relationship between parkinsonism and MS, some of the reported cases and our two patients support the concept that PD and MS can coexist as two separate diseases in the same patient. It is possible that PD symptoms may be aggravated by MS plaques, explaining the good response to corticosteroids in some of the reported patients.

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Figures

Figure 1. Patient 1 MRIs: (a) brain MRI, T2 sequence; (b) brain MRI, T1 sequence; (c) spinal cord MRI; showing multiple supratentorial and cervical spinal cord lesions.

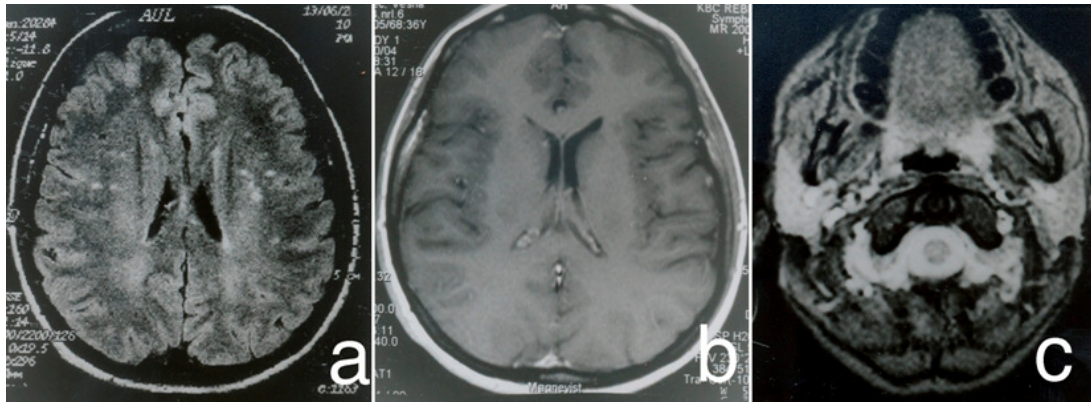


Figure 2. Patient 2 brain MRI: (a) T2 sequence; (b) T1 sequence; showing multiple demyelinating lesions.

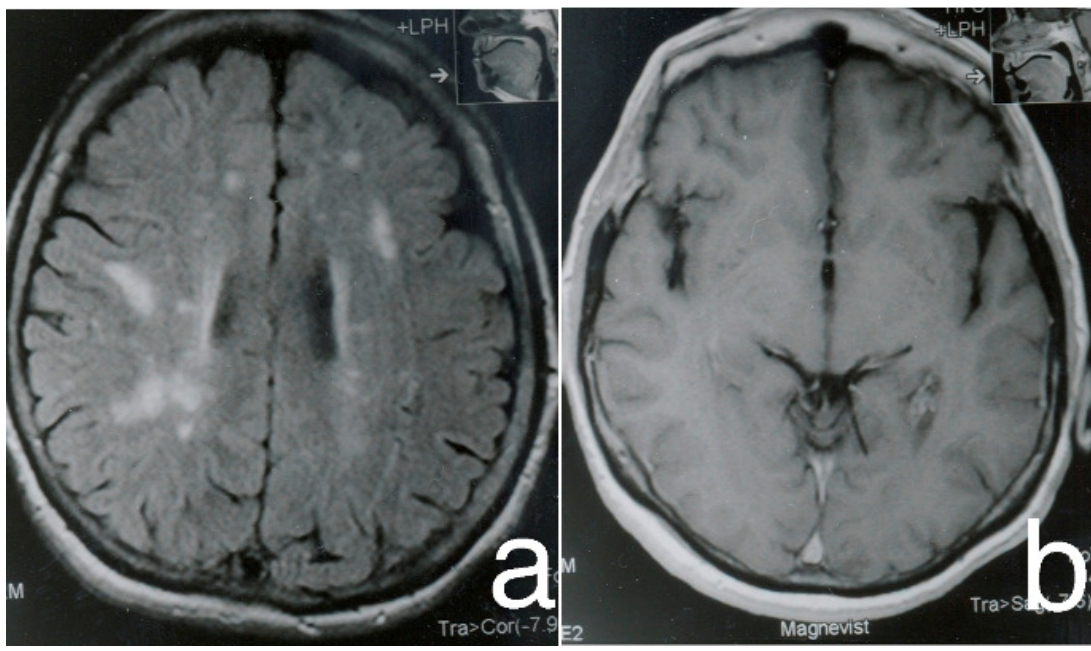


Figure 3. DAT scan findings: (a) patient 1 – note the low level of dopamine carrying protein in the right striatum; (b) patient 2 – note very low levels of DAT in the caudate nucleus and putamen on the left side, and a low level of DAT in the left putamen.

