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Case report

Multiple system atrophy masking multiple sclerosis

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ABSTRACT

Multiple system atrophy (MSA) and multiple sclerosis (MS) are progressive neurological disorders with overlapping clinical signs and symptoms. However, due to the course of the disease and the age of onset both disorders are rarely differential diagnosis for each other. We here report the remarkable association of the two diseases in one patient. As MSA dominated the clinical presentation, diagnosis and therapy of MS were delayed. We discuss the clinical symptoms in our patient and highlight the features that allow to differentiate both diseases.

1. Introduction

Multiple system atrophy (MSA) is a progressive neurodegenerative disorder characterized by parkinsonism, cerebellar and pyramidal signs, and dysautonomia. The diagnosis of MSA is based on clinical criteria and can be supported by neuroimaging. Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating disease with numerous clinical features that reflect the location of disseminated demyelinating lesions. The diagnosis requires evidence for temporal and spatial dissemination of lesions and is established based on clinical presentation, MRI, and CSF analysis.

2. Case report

A 66-year-old woman was referred to our hospital with a progressive akinetic-rigid syndrome associated with autonomic failure and dyspnoea. At the age of 55 she was starting to experience presyncopal episodes. A few years later she developed first urinary and then faecal incontinence. At the age of 61 she experienced left trigeminal neuralgia and weakness of the left arm that both gradually remitted followed by an episode of paraesthesia in the right arm and the right leg about 1 year later. In the following years she experienced a loss of fine motor skills and a progressive rigidity in both hands and rapid progressing difficulties to climb stairs. Abnormal blood pressure variations were noted for the first time. In 2005, aged 65, a parkinsonian syndrome was diagnosed at a local neurological clinic. A medication with levodopa up to 750 mg/d yielded no improvement. A neurogenic bladder dysfunction was diagnosed necessitating a suprapubic cystostomy. Upon discharge she was dependent on a walking frame. Within the following year she became severely impaired and required a wheelchair. Furthermore, she developed dysarthria and dysphagia and about 1 year prior to admission to our hospital she became dyspnoeic.

On admission, general examination showed a dyspnoeic patient with laryngeal stridor. Blood pressure (BP) was elevated supine with a marked drop in systolic BP by 40 mmHg and diastolic BP by 30 mmHg from lying to standing. Cranial nerve examination revealed hypometric saccades, bilateral saccadic pursuit, bilateral impaired suppression of the vestibulo-ocular reflex, left hemifacial hypoesthesia, reduced facial expression, high-pitched dysarthria, dysphagia, and tongue bradykinesia. On motor examination bradykinesia and cogwheel rigidity, Babinski's sign on the left, an exaggerated jaw jerk reflex, and positive palmomental reflexes bilaterally were observed. Additionally, there was left hemihypoesthesia, ataxic finger-to-nose test with intention tremor bilaterally, and marked bradydysdiadichokinesia. Stance and gait were not possible without assistance (see Video 1).

Extensive investigations including routine biochemistry, serological tests, cultures and polymerase chain reactions performed on blood and CSF, full-body CT scan, and cerebral CT angiography remained unremarkable. Examination of CSF revealed oligoclonal bands and elevated IgG and IgA indices. Furthermore, an intrathecal polyspecific antibody response was observed together with elevated varicella-zoster virus and measles antibody indices. Cerebral MRI showed bilateral periventricular T2-hyperintense lesions, marked supratentorial confluent leucoencephalopathy, diffuse brainstem T2-hyperintensities, and T2-hyperintense rims of the lateral putamina. There was mild supratentorial and cerebellar

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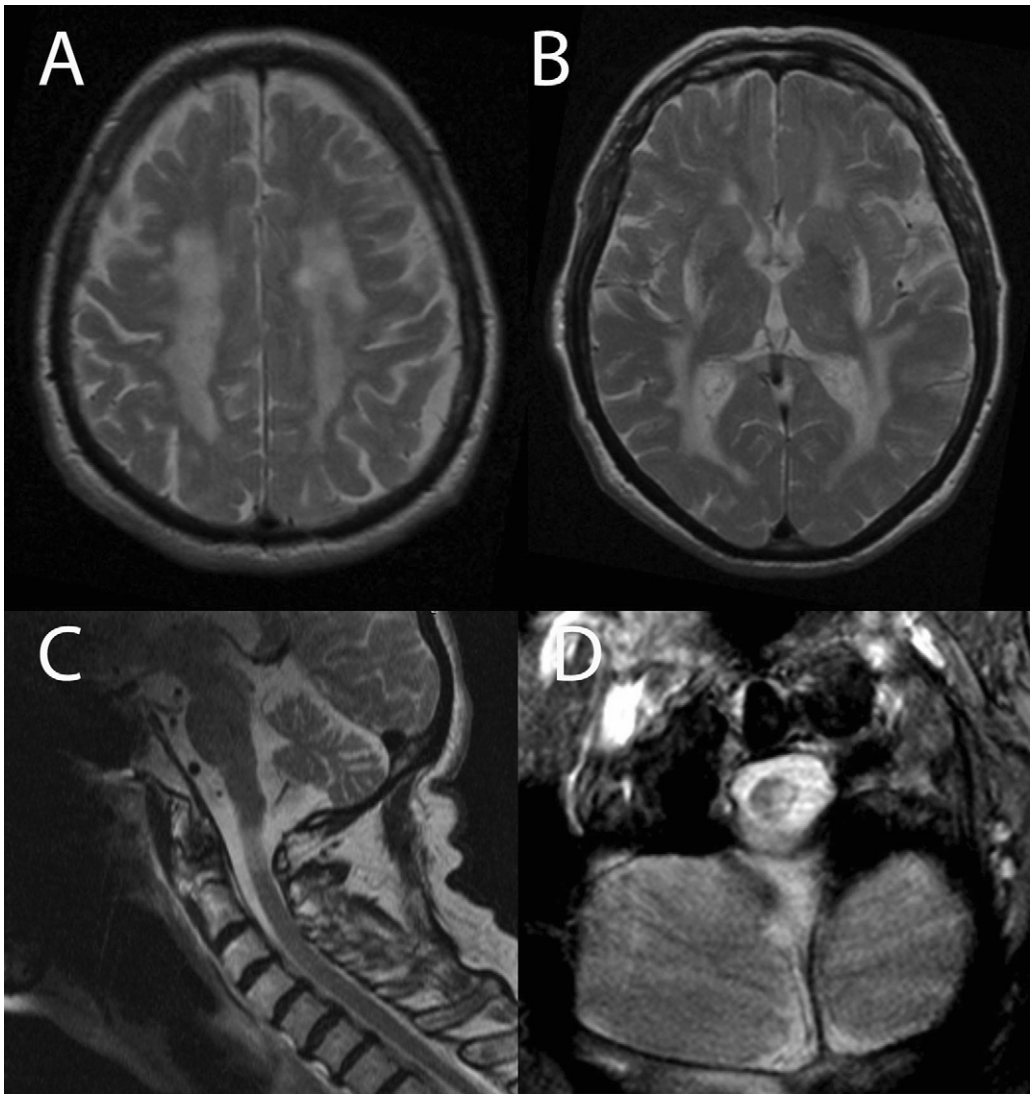

Fig. 1. (A) Axial T2 weighted MR image at the level of the semioval center depicting well defined, ovoid shaped lesions in addition to confluent leucoencephalopathy. (B) Axial T2 weighted MR image at the level of the basal ganglia shows the "putaminal rim sign" consisting of a T2 prolongation secondary to astrogliosis of the lateral putamen. (C and D) Paramedian sagittal T2 weighted MR image of the craniocervical junction demonstrates a well defined hyperintense lesion of the medulla oblongata and adjacent cervical spinal cord which is confined to the left hemicord on the axial slice.

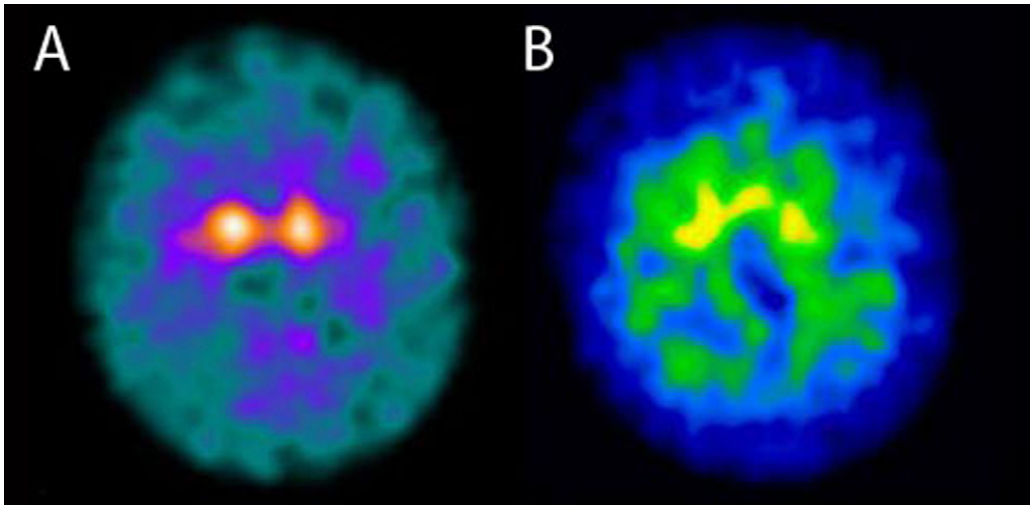

Fig. 2. (A) ^{123}I-FP-CIT SPECT reveals a significant bilateral decrease of the putaminal DAT binding. (B) ^{123}I-IBZM SPECT demonstrates severe deficiency of the D2 receptors in the whole striatum on both sides.

atrophy accompanied by a more pronounced atrophy of the brain stem and the middle cerebellar peduncle as well as the putamen (Fig. 1). The ^{123}I-FP-CIT SPECT demonstrated a significant bilateral decrease of the putaminal DAT binding, whereas the ^{123}I-IBZM SPECT showed a severe deficiency of D2 receptors in the whole striatum bilaterally (Fig. 2). Visually evoked potentials were normal, somatosensory evoked potentials showed affection of central somatosensory pathways. Anal sphincter electromyography revealed abundant pathologic spontaneous activity. A medication with levodopa up to 1000 mg/d followed by IV methylprednisolone yielded no improvement of symptoms.

3. Discussion

Our patient presented with a characteristic history and the major clinical signs of MSA, i.e. progressive parkinsonism with bradykinesia and cogwheel rigidity, cerebellar ataxia with bilateral intention tremor and marked dysdiadochokinesia, autonomic failure with urinary and faecal incontinence as well as pronounced orthostatic hypotension, and pyramidal signs [1]. Additionally, typical high-pitched dysarthria and dysphagia were observed and treatment with levodopa did not improve parkinsonism. Diagnosis of MSA was further supported by abnormal anal sphincter electromyography and characteristic SPECT findings [2]. According to the consensus statement for the diagnosis of MSA the diagnostic criteria for probable MSA were met [3].

However, our patient experienced symptoms not in line with MSA, especially several episodes of transient sensory deficits in different locations. At evaluation in our clinic a left sided hemihypoesthesia persisted with corresponding abnormal somatosensory evoked potentials. Furthermore, MRI revealed several well demarcated cerebral and spinal T2-hyperintense white matter plaques. The observed lesions met the revised McDonald criteria of multiple sclerosis for dissemination in space [4]. Taken together, the temporally disseminated clinical events and the appearance and distribution of the spinal and cerebral lesions were suggestive of MS. This diagnosis was further corroborated by CSF analysis that showed intrathecal immunoglobulin synthesis and polyspecific intrathecal antibody response against varicella-zoster and measles virus. The latter is a typical constellation in multiple sclerosis and is found in up to 89% of patients with definite multiple sclerosis [5]. Several symptoms of our patient cannot reliably be attributed to one of the disorders as both MSA and MS can be associated with these symptoms, e.g. ataxia, intention tremor, pyramidal signs, and ocular motor abnormalities.

The association of MSA and MS has been described only once previously [6]. The authors review the evidence for secondary parkinsonism in MS and conclude that MS hardly can mimic a "full-house" MSA. Due to the longer disease course prior to admission in our case (5 years vs. 11 years), we encountered a patient with nearly end-stage MSA. Indeed, it proved more difficult to diagnose MS as on clinical examination only sensory deficits clearly pointed to pathology beyond MSA. In contrast to the reported patient that suffered from primary progressive MS (PPMS) our patient developed relapsing-remitting MS (RRMS). The differentiation between these subtypes is essential as recent studies provide evidence for the heterogeneity of pathogenetic mechanisms underlying MS that are reflected in different clinical manifestations, e.g. PPMS and RRMS [7].

In summary, we present a patient with the exceptional association of MSA and relapsing MS. Although for both diseases an oligodendroglial pathology [8,9] and an associated neuroinflammatory response [7,10] have been proposed as major aetiological factors we assume a coincidence of MSA and MS in our patient. Due to the substantial overlap of clinical signs the differentiation between the two diseases can be challenging. Therefore, in patients with the suggested diagnoses of MSA or late-onset MS particular thorough clinical examination and further investigations, e.g. MRI and CSF, are needed to rule out alternative disease.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.clineuro.2009.08.015.

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