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Coexistence of MSA and PSP; A Diagnostic Challenge

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ABSTRACT

Progressive supranuclear palsy (PSP) is a neurodegenerative tauopathy characterized by Parkinsonism, vertical gaze palsy, and early falls. The neuropathology is characterized by neurofibrillary tangles, tufted astrocytes, and coiled bodies, but some brains show other pathologic processes. To investigate the frequency of a-synuclein pathology in PSP with immunohistochemistry and to report the clinical and pathological features of a case of PSP with concomitant Multiple system atrophy (MSA) (PSP/MSA), 290 cases of PSP were screened for a-synuclein pathology with immunohistochemistry. Double-labeling immunohistochemistry was performed on a case of PSP/MSA. Among the PSP cases screened for a-synuclein pathology, a single case of PSP/MSA was detected. The patient was an 86-year-old woman with clinical features consistent with PSP. She had no documented dysautonomia or cerebellar signs, and imaging studies were not diagnostic of MSA. Pathological examination showed s-immunoreactive neuronal and glial lesions consistent with PSP as well as a-synuclein immunoreactive glial cytoplasmic inclusions diagnostic of MSA. Double immunolabeling studies showed no co-localization of a-synuclein and s in most neuronal and glial lesions. Based upon the findings in this case, the neuropathologic changes of PSP and MSA are distinct and independent processes, but they can occasionally coexist.

Keywords: Progressive supranuclear palsy, Multiple system atrophy, Tau.

INTRODUCTION

Multiple system atrophy (MSA) is a rare neurodegenerative disease characterized by progressive autonomic failure and parkinsonian/cerebellar features. Motor features are characterized by rigidity, slowness of movement and tendency to fall in parkinsonian subtype but ataxia, wide based gait and uncoordinated limb movements predominate in cerebellar subtype. Progressive supranuclear palsy (PSP) is another neurodegenerative disease which is characterized by Parkinsonism, vertical gaze palsy, backward falls and cognitive dysfunction.

CASE

Our case is A 59 year old man who first presented with the chief complaints of dizziness and vertigo after standing up 5 years ago. Postural instability, imbalance and backward falls began unexpectedly and gradually progressed over 3 years. The patient cannot walk without assistance since 2017.He also suffers from erectile dysfunction, urinary incontinence, speech impairment cognitive dysfunction and decreased verbal fluency. He has usually talks or shouts during sleep and cannot maintain sleep. Drugs such as Leva-dopa, Rasagiline and Amantadine were prescribed for treatment but none of them were effective. Neurological examination revealed Vertical gaze palsy, backward falls, wide based gait, postural instability, spastic dysarthria, bradykinesia, rigidity and mild cognitive dysfunction. A MRI scan of the brain revealed “Hot cross bun sign” in Pons and “Hummingbird sign” in Midbrain which are compatible with MSA and PSP respectively.

RESULTS

In a screen of 290 cases of PSP, we found 31 cases with concurrent Lewy body disease and one case of concurrent MSA.

CASE REPORT OF PSP/MSA

This 84-year-old woman presented with a chief complaint of poor balance and deteriorating speech. She had neither family history of neurodegenerative disease nor history of neuroleptic drug intake. She had three children, one of whom had multiple sclerosis. She had balance problems and began falling unexpectedly at age 74. At age 79, she lost dexterity in the fingers, with difficulty doing up buttons, and her writing deteriorated. At age 81, she had drooling, slurred speech, and difficulties with swallowing. Poor balance gradually progressed over the years, and she required a walker for the last 2–3 years. Memory impairment developed in the last 1–2 years. Neither significant dysautonomia nor cerebellar signs were present. A magnetic resonance imaging (MRI) scan of the brain showed mild generalized atrophy and a left occipital lobe infarct. Neurological examination (at age 84) revealed blepharospasm, abnormal saccadic eye movements and restriction of vertical gaze, upgaze more impaired than downgaze. She had some non-sustained nystagmus in performing vertical eye movements. She had a right homonymous field defect and spoke with a strained, dysarthric, but intelligible voice. She had mild bradykinesia and rigidity in her extremities. She required a twohand assist to arise from a seated position and to walk. She died approximately 12 years after the onset of the disease. The patient was clinically diagnosed as having PSP.

DISCUSSION

Given the advanced age of most patients, it is not uncommon to find concurrent pathology in PSP, including Alzheimer type pathology, argyrophilic grain disease, Lewy body disease and vascular diseases. Rarely, mixed cases have features of PSP and another neurodegenerative disorder, such as Pick’s disease or

MSA [24]. To our best knowledge, there is only one other report in the literature of PSP/ MSA. Given that the prevalence of PSP is 5.3–6.4/ 100,000 persons and that of MSA is 3.0–4.4/100,00 persons, Takanashi and co-workers speculated the coexistence of PSP and MSA in the same patient must be extremely rare. The present study agrees with this conclusion, since we found only one case of MSA among almost 300 cases of PSP cases (0.3%). In contrast, the frequency of LBD in PSP was similar to that expected in a similarly aged cohort. In the PSP/MSA case reported by Takanashi and coworkers, the patient had a clinical syndrome consistent with MSA, including 6 years of severe cerebellar ataxia, autonomic failure, and akinetic-rigid Parkinsonism. Coexisting pathological features of PSP were not associated with overt clinical features of PSP. A MRI of the case showed marked atrophy of cerebellar vermis and the pontine base showed a high-intensity, ‘‘crisscross’’ sign typical of MSA on T2-weighted MRI. In contrast, the PSP/MSA case in this report had a clinical syndrome more fitting with PSP, including vertical supranuclear palsy, prominent postural instability with falls in the first year of disease onset, and dysarthria. The disease duration was 12 years, which is longer than usual for PSP and MSA. Except for the long disease duration, the present case met research criteria for PSP. The clinical features of typical PSP and MSA as well as those in the present case are summarized in Table 2. Of note was the absence of prominent cerebellar signs and dysautonomia in the present cases, which are characteristic features of MSA. The present case did not fulfill research criteria for MSA. The MRI findings also were not typical for MSA.

CONCLUSION

As both MSA and PSP diseases are rare diseases, so we speculate that coexistence of these disorders in a patient should be extremely rare, as only two cases of MSA and PSP coexistence have been reported. Although postmortem autopsy is required for definitive diagnosis of MSA and PSP, the symptoms and signs of our case are compatible with probable MSA and probable PSP according to their diagnostic criteria and we speculate that MSA has progressed before PSP in this case.