REM SLEEP BEHAVIOR DISORDER PRECEDEING OTHER ASPECTS OF SYNUCLEINOPATHIES BY UP TO HALF A CENTURY
DO Claassen, KA Josephs, JE Ahlskog, MH Silber, M Tippmann-Peikert, BF Boeve

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Background: Idiopathic REM sleep behavior disorder (RBD) may be the initial manifestation of synucleinopathies (Parkinson disease [PD], multiple system atrophy [MSA], or dementia with Lewy bodies [DLB]). Methods: We used the Mayo medical records linkage system to identify cases presenting from 2002 to 2006 meeting the criteria of idiopathic RBD at onset, plus at least 15 years between RBD and development of other neurodegenerative symptoms. All patients underwent evaluations by specialists in sleep medicine to confirm RBD, and behavioral neurology or movement disorders to confirm the subsequent neurodegenerative syndrome. Results: Clinical criteria were met by 27 patients who experienced isolated RBD for at least 15 years before evolving into PD, PD dementia (PDD), DLB, or MSA. The interval between RBD and subsequent neurologic syndrome ranged up to 50 years, with the median interval 25 years. At initial presentation, primary motor symptoms occurred in 13 patients: 9 with PD, 3 with PD and mild cognitive impairment (MCI), and 1 with PDD. Primary cognitive symptoms occurred in 13 patients: 10 with probable DLB and 3 with MCI. One patient presented with primary autonomic symptoms, diagnosed as MSA. At most recent follow-up, 63% of patients progressed to develop dementia (PDD or DLB). Concomitant autonomic dysfunction was confirmed in 74% of all patients. Conclusions: These cases illustrate that the α-synuclein pathogenic process may start decades before the first symptoms of PD, DLB, or MSA. A long-duration preclinical phase has important implications for epidemiologic studies and future interventions designed to slow or halt the neurodegenerative process.

Comment from Ryan J. Uitti, MD, FAAN, Associate Editor: A paper that documents the interrelationship of several movement disorders, further embellishing the compelling and ongoing story associated with synucleinopathy and clinical disorders.
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