Levodopa-induced motor fluctuations and dyskinesias in a young adult case of BPAN: are we missing Lewy bodies?

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Background: Beta-propeller protein-associated neurodegeneration (BPAN) is a neurological disorder characterized by progressive iron accumulation in the substantia nigra and in the globus pallidus, resulting in a wide array of symptoms including cognitive decline and movement disorders. Recent reports on BPAN patients have demonstrated widespread tau deposition, which might be suggestive of a tauopathy.
Case: This 34-year-old right-handed lady was referred for a 2-year history of progressive slowing of movement associated with episodes of â€œspasmsâ€• affecting the left leg. Over the months, she gradually developed clumsiness of the left limbs, cognitive decline and social isolation. She suffered from generalized seizures, which resolved with age. There was no family history of neurological disorders. On examination, she presented with generalized dystonia affecting the left limbs more than the right ones. Rapid alternating movements of the limbs were suggestive of bradykinesia. Gait was broad-based and severely affected by the dystonic posturing of the legs. Brain MRI disclosed bilateral hypointensity in the globus pallidus and in the substantia nigra on T2* sequences. SWI sequences confirmed iron accumulation. DaTSCAN brain images revealed a bilateral reduced uptake in the striatum. Genetic screening revealed a mutation in the WDR45 gene consistent with a diagnosis of BPAN. She then started levodopa treatment for her parkinsonism with a beneficial effect on motor function. Nevertheless, after a few months, she developed disabling motor fluctuations (wearing-off phenomenon) and dyskinesias.
Discussion: The accumulation of tau aggregates typically represents a neuropathological feature of patients with dementia. Conversely, the progressive accumulation of Î±-synuclein aggregates distinguishes Parkinsonâ€™s disease, which is characterized by troublesome levodopa-induced motor fluctuations. Interactions between tau and Î±-synuclein have been previously proposed as feed-forward loop essential for the development and spreading of neurodegeneration.
Conclusion: The observation of severe levodopa-induced motor complications in our case might suggest a new potential mechanism underlying BPAN. Further neuropathological investigations are needed to confirm our consideration.

Topic: Casi clinici
References:

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