

Acute-onset parkinsonism and confusion for West Nile Virus encephalitis

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Abstract

Introduction: When evaluating a patient with acute parkinsonism, several causes should be considered. From toxic-metabolic to infectious. Among virus, West Nile is a zoonosis which incidence has been increasing during the last years.

Methods: We report an elderly patient with new onset confusion, tremor and gait disorder after a viral prodrome. At physical exam, he had parkinsonism with impairment of delay recall without pyramidal, cerebellar or sensory deficits.

Results: MRI was unremarkable. CSF resulted positive for West Nile virus. Patient clinical course improved after seven months follow-up.

Conclusions: West Nile virus encephalitis is a cause of acute parkinsonism and the incidence of this zoonosis is trending up, specially, during summer and early autumn. It should be taken in consideration as a differential diagnosis when ordering CSF tests for acute parkinsonism.

Keywords

Parkinson disease secondary; encephalitis viruses; west nile virus.

Abbreviations

CBC: Complete blood count; BMP: Basic metabolic panel; HIV: Human Immunodeficiency Virus; HSV: Herpes virus; VZH: Varicella zoster; WNV: West nile virus; MRI: Magnetic resonance imaging.

Introduction

As part of a primary neurodegenerative disease or genetic disease, parkinsonism is insidious in onset

and slowly progressive. In contrast, when parkinsonism develops over days to weeks, a secondary cause should be considered. A review of the medication list, ruling out structural lesions, and careful examination are crucial [1].

Case Report

During summer, a 53-caucasian year-old right-handed male with no significant past medical history and not on medications presented to the Emergency Room of a tertiary academic medical center for evaluation of confusion and tremulousness in both arms. Patient had been in his usual state of health until two weeks prior to admission. He had developed fever, chills, headache, nausea, vomiting and diarrhea. He has not had contact with sick people. He had consulted at urgent care. They had performed CBC and BMP and chest x-ray. All the work-up had been non-actionable. He had not been prescribed any medications. These symptoms had resolved in about five days. About one week later, his wife noted him to be confused. For instance, he looked for his dog who had have died three years ago and he held the phone without knowing how to dial. Along with confusion, he developed new tremor in both arms. There was no associated headache or neck pain at that point. He denied recent travel, history of tick bite, history of head trauma, exposure to toxics or relevant family history. Patient smoked marijuana and he was a social drinker.

On neurological examination, he was oriented to person, place and time. Normal attention span and serial subtractions. He followed three step-commands appropriately. He scored 3 out of 5 in delayed recall. No cranial nerve or other ophthalmological abnormalities were noted. Cogwheel rigidity and mild bradykinesia were noted in four extremities. Tremor of 3-5 Hz was noted in all four extremities, predominant on the right arm and in the resting state; postural and action tremors were also present. Postural instability was present being evident in pull test; gait was shuffling. No cerebellar abnormal signs.

Brain MRI without contrast was normal. Complete blood count and comprehensive metabolic panel were unremarkable. Lumbar Puncture showed increased WBC (30 cells per field) with a lymphocytic pleocytosis (99%); protein was 69 mg/dl with normal glucose. CSF PCR of *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria Monocytogenes*, *Neisseria meningitidis*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, Cytomegalovirus, Enterovirus, HSV-1, HSV-2, HSV-6, Human Parechovirus, VZV and *C. neoformans/gatti* were negative. Serology for Lyme was negative. New York State Encephalitis Panel PCR in CSF (Lyme disease, Powassan virus, West Nile Virus (WNV), Eastern equine encephalitis virus and Saint Louis encephalitis virus) was performed. WNV IgM in CSF resulted positive and IgG negative. We ruled out autoimmune causes with CSF panel including LGI1, ANNA-2 and GAD65 antibodies.

Patient was discharged with diagnosis of WNV neuro-invasive disease. No medication was prescribed as symptoms were mild, and he completed physical therapy sessions.

At a two weeks follow-up, the patient's cognition normalized. After seven months, only the slight postural tremor and mild action tremor on the right arm persisted.

Discussion

Acute-onset parkinsonism could be caused by a) structural lesions, such as stroke or hematoma; b) intoxication by chemicals, such as carbon monoxide (more prevalent during winter) or manganese; c) side effects of medications, such as metoclopramide or neuroleptics; d) metabolic causes; e) infectious or autoimmune encephalitis, and lastly; f) psychogenic [1]. A full history taking, comprehensive examination and complementary studies such as lumbar puncture and imaging is warranted (Table 1).

Regarding metabolic causes, rapid correction of sodium can cause lesions in the basal ganglia causing acute parkinsonism [1], usually seen in an inpatient setting. Another differential diagnosis was autoimmune encephalitis related to oncological disease or not [2-4]. Paraneoplastic parkinsonism is rare but important differential diagnosis, specially in this group of age (late adulthood) [2]. It has been described in association with CRMP5, ANNA-2, and Ma2-antibodies [2]. Non-paraneoplastic encephalitis also can manifest with acute parkinsonism and patients have been found to be positive for LGI1, DPPX and GAD antibodies [2,3].

Prodrome with systemic symptoms (fever and gastrointestinal upset) pointed toward a viral etiology. Patient had confusion that localized a broader involvement of CNS. CSF showed lymphocytic pleocytosis which was compatible with CNS inflammation. Mainly influenza, Coxsackie, flaviviruses (Japanese encephalitis B, Saint Louis, WNV), herpes virus and HIV have been associated with acute parkinsonism [5-7].

Narrowing down to endemic diseases of New York state, WNV and Saint Louis virus should be checked and particularly during the summer and early autumn (the mosquito season).

WNV has caused seasonal increasing epidemic in the United States since 1999 [6,8]. It has caused a heightened awareness of emerging infections [9]. It was reported increase in incidence seen in Europe in 2018 [10]. Neuro-invasive disease was reported in 63% of patients with WNV infection during 2018 in the United States [11]. In a longitudinal study of patients with neuro-invasive disease, 45% presented with cognitive impairment and 35% presented with tremor [6,8]. In the majority, tremor persisted at follow-up [8]. WNV has been reported to be associated with a spectrum of movement disorders, for instance action tremor [12]. Our patient not only had resting tremor but also action tremor. Imaging studies may be normal [8].

The factors that predict either severity or long-term recovery of neurological function include age (older individuals did worse at follow-up examination) and immunosuppression [6,8,13]. Our patient was in late adulthood as possible factor for his tremor persistence.

Cellular factors altered in parkinsonism, such as alpha-synuclein, have been shown to play a role on WNV infection [14]. Treatment with L-dopa and amantadine significantly reduced the production of infectious virus in all cell types tested, but only amantadine reduced viral RNA levels. [14] Therefore, antiparkinsonian drugs could be therapeutic candidates for the development of antiviral strategies against WNV infection [14].

Tables: Acute-onset parkinsonism work-up overview.

Table 1: Approach to acute parkinsonism starting from history taking to more complex studies.

History	Medication history
	Toxic exposure
	History of head trauma
	Contact with sick people
	Family history
Physical exam	Complete neurological exam
	Psychiatric exam
	Ophthalmologic exam (slit lamp) *
Serum	Ionogram
	Liver function test
	HIV serology
Imaging	CT head or MRI brain
CSF	Chemistry, cell count and cytology
	PCR viral panel
	ELISA for endemic encephalitis including West Nile virus
	Consider autoimmune panel

*: to look for Kayser-Fleischer ring as a sign of Wilson disease

Conclusions

Parkinsonism developed during days/weeks can be diagnostically challenging. A methodic approach as we propose can help physician to sort out differential diagnosis. WNV is an emerging zoonosis that can cause neuro-invasive disease with parkinsonian features.

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