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CLINICAL VIGNETTE

Huntington's Disease-Associated Psychosis in a Patient Misdiagnosed with Tourette's Syndrome

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Case Report

A 43-year-old male with past medical history of Tourette's Syndrome was brought to the Emergency Department by his ex-wife due to odd behavior, auditory hallucinations and worsening aggression. According to his ex-wife, he had been diagnosed with Tourette's about ten years ago, possibly with symptoms onset five years prior. She described intermittent arm and leg jerking that had gradually worsened. The patient denied any childhood motor symptoms.

In the previous year, the patient's ex-wife reported onset of psychotic episodes. He had been hospitalized several times, most recently six months prior. During past admissions, he had been started on bztropine and risperidone. His ex-wife was unsure how regularly he took these medications and the patient himself was not able to confirm adherence. She felt that his behavior had deteriorated in recent months; he was acting out, behaving aggressively, and talking to himself. She was concerned about leaving him alone with their 8 year-old son, who lived with her and noted he had recently become homeless. He denied any tobacco, alcohol or drug use, which was confirmed by his ex-wife.

The patient could not provide any family history; with limited information from his ex-wife. She thought his mother had died in her mid-fifties of Parkinson's disease in a Costa Rican asylum. His maternal grandfather may also have died of Parkinson's at an unknown age.

Physical exam revealed a thin, unkempt male who was oriented to person, place, and month only. He was irritable, talked to himself frequently, and laughed inappropriately throughout the interview. He denied suicidal ideation, homicidal ideation, or auditory or visual hallucinations. His speech was tangential and insight and judgment were markedly impaired. His neurological exam was notable for continuous, large-amplitude movements of his bilateral upper extremities. He also had frequent, intermittent jerking of bilateral upper and lower

extremities. He had no abnormal facial movements. Cranial nerves II through XII were intact, without nystagmus. He had some evidence of tongue impersistence, though this was difficult to assess as patient also moved his tongue in and out voluntarily. Reflexes were 2+ bilateral patellar, biceps, and brachioradialis. He had no clonus or tremor. Romberg was negative and finger-to-nose was intact. The patient's gait was strikingly abnormal and notable for significant choreiform movements. His heel-to-toe gait was normal.

Clinical Course

The patient was admitted to the psychiatry service for management of his psychosis. Neurology was consulted to rule out an organic etiology of his presentation. Genetic testing for Huntington's was subsequently done during the admission and returned positive, with 48 CAG repeats. He was eventually discharged to an assisted living facility with planned follow-up at the movement disorders clinic.

Discussion

Huntington's Disease (HD) is an autosomal dominant neurodegenerative disorder characterized by CAG trinucleotide repeat expansion on the short arm of chromosome 4¹. The abnormal huntington protein leads to the degeneration of neurons in the caudate, putamen, and to lesser extent, the frontal cortex. At present, the exact mechanism of neuronal toxicity is unknown. The disorder is characterized by primarily choreiform movement disturbances, psychiatric symptoms and cognitive deterioration^{2,3}. This case presentation highlights the clinical features of a patient misdiagnosed with Tourette's and psychosis NOS who eventually tested positive for Huntington's Disease a decade after onset of his symptoms.

The patient's initial misdiagnosis of Tourette's Syndrome ultimately delayed the recognition of an association between the patient's movement disorder and his psychosis. The observation that Tourette's

typically presents in childhood or adolescence⁴ is a clue to an alternate diagnosis in a patient who denied motor symptoms prior to his late twenties/early thirties. His history is more consistent with the mean age of onset for Huntington's, between 35 and 45 years of age⁵. In retrospect, the maternal family history of early-onset "Parkinson's Disease" and a mother who died young in an asylum also hint at the true diagnosis.

There is limited research on the prevalence of psychopathology in Huntington's Disease. Studies of HD patients have reported a prevalence of psychotic symptoms from 20 to 76% [2,6]. Caine and Shoulson reported a point-prevalence of 37% depression and 27% psychosis in a 30-patient cohort. Folstein found a 41% lifetime prevalence of depression in a cohort of 88 HD patients². Studies have been limited by small sample size, variable assessment tools, lack of controls, and assessment at different disease stages^{2,3}. As a result, it is difficult to reliably estimate the true prevalence of psychiatric symptoms in Huntington's Disease.

Of particular interest in this case was the clinical implication for the patient's 8 year-old son. Huntington's Disease is characterized by anticipation, defined as an earlier age of onset or increased disease severity in successive generations. CAG repeats in the normal range (<35) are generally inherited in a stable fashion. However, mutant-range CAG repeats (>39) are unstable during intergenerational inheritance and can either expand or contract⁷. In HD, paternal transmission appears to be responsible for larger repeat CAG expansions than maternal transmission [1].

In a study of 337 HD transmissions, Aziz demonstrated that paternal transmission resulted in a significantly greater degree of offspring CAG expansion than maternal transmission ($p < 0.001$)⁷. This supports earlier findings by Kremer et al., who additionally found that offspring of affected mothers were more likely than offspring of affected fathers to have stable or reduced CAG repeat size⁸. Aziz also demonstrated that larger parental mutant CAG repeat size was associated with a greater degree of offspring CAG repeat expansion ($p < 0.001$)⁷.

The mechanism for parental gender effects on HD transmission is currently unknown. One theory considers the difference in cell division between oogenesis and spermatogenesis. While oogenesis is completed before birth, sperm undergo considerable post-pubertal cell division. This presents

opportunities for replication error and repair associated with replication⁹. Other authors postulate a difference in recombination events of autosomal genes between oogenesis and spermatogenesis. The relative fewer recombinational events in spermatogenesis compared to oogenesis may explain why the length of the mutant paternal allele plays a larger role in offspring CAG expansion⁷.

Although in retrospect this was a relatively classic presentation of Huntington's Disease, the lack of personal and family past medical history significantly delayed diagnosis. This case illustrates the challenges faced when evaluating a patient for the first time who either presents with late-stage disease or who has been previously misdiagnosed.

REFERENCES

1. **De Marchi N, Mennella R.** Huntington's disease and its association with psychopathology. *Harv Rev Psychiatry*. 2000 Jan-Feb;7(5):278-89. Review. PubMed PMID: 10689592.
2. **Naarding P, Kremer HP, Zitman FG.** Huntington's disease: a review of the literature on prevalence and treatment of neuropsychiatric phenomena. *Eur Psychiatry*. 2001 Dec;16(8):439-45. Review. PubMed PMID: 11777733.
3. **van Duijn E, Kingma EM, Timman R, Zitman FG, Tibben A, Roos RA, van der Mast RC.** Cross-sectional study on prevalences of psychiatric disorders in mutation carriers of Huntington's disease compared with mutation-negative first-degree relatives. *J Clin Psychiatry*. 2008 Nov;69(11):1804-10. Epub 2008 Nov 4. PubMed PMID: 19026253.
4. **Daroff RB, Fenichel GM, Jankovic J, Mazziotta JC.** *Bradley's Neurology in Clinical Practice*. 6th ed. Philadelphia:Saunders; 2012.
5. **Quinn N, Schrag A.** Huntington's disease and other choreas. *J Neurol*. 1998 Nov;245(11):709-16. Review. PubMed PMID: 9808238.
6. **van Duijn E, Kingma EM, van der Mast RC.** Psychopathology in verified Huntington's disease gene carriers. *J Neuropsychiatry Clin Neurosci*. 2007 Fall;19(4):441-8. Review. PubMed PMID: 18070848.
7. **Aziz NA, van Belzen MJ, Coops ID, Belfroid RD, Roos RA.** Parent-of-origin differences of mutant HTT CAG repeat instability in Huntington's disease. *Eur J Med Genet*. 2011 Jul-Aug;54(4):e413-8. doi: 10.1016/j.ejmg.2011.04.002. Epub 2011 Apr 23. PubMed PMID: 21540131.
8. **Kremer B, Almqvist E, Theilmann J, Spence N, Telenius H, Goldberg YP, Hayden MR.** Sex-dependent mechanisms for expansions and contractions of the CAG repeat on affected Huntington disease chromosomes. *Am J Hum Genet*. 1995 Aug;57(2):343-50. PubMed PMID: 7668260; PubMed Central PMCID: PMC1801544.
9. **Pearson CE.** Slipping while sleeping? Trinucleotide repeat expansions in germ cells. *Trends Mol Med*. 2003 Nov;9(11):490-5. Review. PubMed PMID: 14604827.

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