



Case Report

Deciphering the Neuropsychiatric Landscape of Huntington's Disease: Insights and Implications—A Case Report

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ABSTRACT

Huntington's disease (HD) is an autosomal dominant neurodegenerative illness with a specific phenomenology that includes chorea, incoordination, dystonia, behavioral difficulties, and cognitive decline. The most frequent cause of inherited chorea manifesting in adults is HD, which affects approximately 5 per 100,000 to 12 per 100,000 people. This case report describes the case of a 42-year-old woman from Assam who had been experiencing progressive and gradual onset choreiform movements of both upper limbs, affecting the fingers and face for the last two years, along with an unsteady gait and slurred speech and lack of personal care and hygiene. She also developed psychotic manifestations in the form of erotomanic delusions along with decreased sleep, restlessness, and disorganized behavior. A positive family history of dementia in their maternal grandmother and movement disorder in their paternal grandmother, along with the history of the death of her elder brother at birth, was present. The patient was admitted considering HD as a provisional diagnosis, and treatment with tablets tetrabenazine, olanzapine, risperidone, and lorazepam for her behavioral and movement symptoms was initiated. Her magnetic resonance imaging (MRI) brain report showed caudate atrophy. HD repeat expansion analysis that revealed full penetrance expansion of approximately 46 coronar angiogram (CAG) repeats in either allele was confirmatory of HD. There was an improvement in her symptoms seen in two follow-up visits to the outpatient department (OPD) after discharge except for reduced sleep; hence, melatonin 10 mg was added for it. Middle-aged patients presenting to psychiatrists with choreiform movement and psychiatric symptoms along with a positive family history should raise the suspicion of HD.

Keywords: Huntington's disease (HD), Psychiatric symptoms, CAG repeat, Anticipation, HD gene

INTRODUCTION

Huntington's disease (HD) is an autosomal dominant neurodegenerative illness with a specific phenomenology that includes chorea, incoordination, dystonia, behavioral difficulties, and cognitive decline.^[1] The most frequent cause of inherited chorea manifesting in adults is HD, which affects approximately 5 per 100,000 to 12 per 100,000 people.^[2]

Waters published the first clinical picture of the disease in 1842.^[3] George Huntington gave the illness the name Huntington's Chorea in 1872 and provided a detailed account of the clinical progression and symptoms.^[3] With the identification of both the disease's motor and non-motor signs and symptoms, the term "Huntington's disease" became widely used in the 1980s.^[3] Ten years after the development of molecular biology techniques, in 1983, a linkage on chromosome 4 was revealed, leading to the discovery of the HD gene.^[3] An unstable coronar angiogram (CAG) trinucleotide repeat expansion in exon 1 of the HD gene, formerly known as IT-15, on the short arm of chromosome 4 is the underlying genetic defect.^[3] At the N-terminus of the resulting mutant protein, "huntingtin," a polyglutamine strand of variable length is formed.^[1] Repeat

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lengths of 40 or longer indicate full penetration, which is characterized by increasing changes in cognitive, motor, and behavioral functions.^[2] Medium spiny neurons in the striatum are known to be lost due to nuclear aggregates created by mutant huntingtin protein, while the precise mechanism driving the degenerative modifications in HD remains unknown.^[2] Twenty-six or fewer CAG repeats are regarded as normal.^[2] Those with 36–39 CAG repeats are likely to have decreased penetrance, although they are nonetheless at risk for the illness.^[2] For individuals with 27–35 CAG repeats, the phenomenon of “anticipation” through paternal inheritance may pose a risk for extension beyond the HD range in the next generation.^[2] Although HD symptoms can develop at any age, they often do so in the third or fourth decade of life, and the average person continues to live for 15–20 years following the onset of symptoms.^[2] The age of motor onset and the number of CAG repeats are inversely correlated, but this only accounts for 50%–70% of the variation.^[2]

No treatment for the underlying neurodegeneration of HD is currently available.^[4] However, chorea may be effectively treated with tetrabenazine (now FDA-approved for use in HD), which blocks dopamine release through its action at the vesicular monoamine transporter 2.^[4] Low dosages (0.5–2.0 mg/day) of common high-potency antipsychotics like fluphenazine or haloperidol, other neuroleptics, benzodiazepines, or other dopamine-depleting medications like reserpine may help with chorea.^[4] For the management of psychotic symptoms, antipsychotics and benzodiazepines are considered useful adjuncts.^[4] Family education, along with a stimulating environment, is probably the greatest way to address apathy.^[4]

CASE REPORT

This case report describes the case of a 42-year-old woman from Assam admitted to the Department of Psychiatry, Gauhati Medical College and Hospital (GMCH), with chief complaints of decreased sleep, restlessness, irrelevant talk, poor personal care and hygiene, and abnormal involuntary movements of the upper limbs and face, along with an unsteady gait and slurred speech from last two years and increased from the last one month before admission.

Her symptoms were insidious in onset and the illness followed a progressive course. Her symptoms were noticed for the last two years by her maternal uncles only after she returned from Pune to live with them in Assam. Before this, they could just get information about her frequent change of jobs and residences from her neighbors in Pune as the patient herself used to keep very little contact with her family members. She was initially seen with symptoms of reduced sleep, remaining awake till late at night talking over the phone, being restless, pacing inside the house, lacking personal care

and hygiene, and disorganized behavior like littering her room by throwing away her things here and there and also not switching off electrical appliances like heaters. She also had abnormal involuntary movements of both upper limbs involving the fingers and the face occurring spontaneously at irregular intervals for a short duration of about a few seconds almost throughout the day except during sleep, along with an unsteady gait, tending to fall to either side of the body, and slurred speech which worsened over the past one month before admission. She was also observed talking irrelevantly about the former US attorney general's grandson being in love with her and that he would marry her because he had said this to her over phone chats previously. On asking further about him, she said that he is the rebirth of late former US Attorney General Bobby Kennedy and she was his wife in her previous life. She was seen by her family members spending time swinging a chain with a pointed locket like a pendulum, and on being asked would mention that she communicates through it with her late mother, also an angel by the name Lucifer, Jesus, and Bobby Kennedy's grandson. She was also hospitalized in 2022 for about four months for behavioral symptoms by a psychiatrist when her motor symptoms were hardly noticeable but with no improvement. Later, her motor symptoms became more pronounced and then seen by a neurologist who suspected her of having HD and started treatment with tablet tetrabenazine 25 mg and referred her to a psychiatrist for the behavioral disturbances. She was prescribed olanzapine 7.5 mg at bedtime by the attending psychiatrist. There was no history of fever, loss of consciousness, convulsions, head injury, other major medical illnesses, or indulgence in any addictive substance.

She had normal premorbid functioning. No history of any other major medical/psychiatric illness, seizure disorder, or head injury in the past. Positive family histories of forgetfulness suggestive of dementia in the maternal grandmother, movement disorder in the paternal grandmother, and history of death of her elder brother at birth were present.

On general examination, the patient was underweight with a BMI (Body Mass Index) of 16.26 kg/m². Her vitals were stable. On systemic examination, respiratory, cardiac, and gastrointestinal systems revealed no abnormalities. Cranial nerve assessment (CNS) examination revealed muscle wasting in both upper and lower limbs, exaggerated deep tendon reflexes, and choreiform movements of both upper limbs and face, along with an unsteady ataxic gait.

On mental status examination, she appeared untidy and unkempt with disheveled hair and clothes, had poor eye-to-eye contact, and an increase in psychomotor activity. She was found to have erotomanic delusions. Hallucination could not be elicited. Poor attention and concentration and impaired immediate and recent memory with grade 1 insight were found.

In investigations, routine blood tests, genetic analysis of CAG repeats, and magnetic resonance imaging (MRI) brain were done. Blood parameters showed deficient 1,25-dihydroxy cholecalciferol levels. MRI brain revealed caudate atrophy. She was admitted to the psychiatry ward, considering HD with behavioral abnormalities as a provisional diagnosis. The genetic analysis of CAG repeats showed 46 repeats indicating full penetrance and was confirmatory of the final diagnosis of HD.

She was managed with concomitant administration of tablets olanzapine 7.5 mg at bedtime, trihexyphenidyl 2 mg once daily, risperidone 3 mg at bedtime, lorazepam 2 mg twice daily, and tetrabenazine 25 mg once daily, along with intravenous (IV) fluids and vitamins as supportive treatment. Also, a cholecalciferol capsule was added for deficient 1,25-dihydroxy cholecalciferol levels. The abnormal jerky movements of limbs and face were seen to reduce in frequency and intensity, along with improvement in gait and speech within about ten days of admission. Delusion of erotomania and other behavioral disturbances also improved. The patient was discharged on 13/3/2024 after one month of hospitalization with improvement in symptoms and was given tablets tetrabenazine 25 mg, one twice daily; risperidone 4 mg + trihexyphenidyl 2 mg, one at bedtime; olanzapine 10 mg, one at bedtime; lorazepam 2 mg, one at bedtime; and cholecalciferol 60,000U, one capsule once weekly.

The patient came to the psychiatry outpatient department (OPD) for two follow-up visits within one month of discharge; she was maintaining well with improvement in her symptoms except for reduced sleep, therefore, melatonin 10 mg was added. There were no compliance issues or adverse events reported.

DISCUSSION

This case is a rare neurodegenerative disorder associated with psychiatric symptoms preceding the onset of movement disturbances with a positive family history that highlights the significance of ruling out the possibility of HD in the neurology and psychiatry OPD of any hospital setup. Most cases of HD that were documented included psychiatric symptoms, such as mania, depression, personality changes, apathy, irritability, and obsessive/compulsive behaviors,^[5] with a low rate of psychosis.^[5-7] We were interested in this case because before the motor symptoms appeared, the most obvious symptoms were the psychiatric symptoms with erotomaniac delusions and behavioral abnormalities being the key psychotic symptoms.

CONCLUSION

HD is characterized by disturbances in cognitive, motor, and psychiatric symptoms. Therefore, the prevalent and validating psychiatric components should be identified as early as possible during the disease course to effectively treat

the condition to enhance the quality of life and reduce the burden on caregivers.

Authors' contributions

DM- study conception and design, data analysis and review, PK- manuscript preparations, data collection, analysis and interpretation.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

Dr. Deepanjali Medhi is on the Editorial Board of the Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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