

# PROLONGED PSYCHOSIS BEFORE ONSET OF NEUROLOGICAL SYMPTOMS: AN ATYPICAL CLINICAL MANIFESTATION OF HUNTINGTON'S DISEASE

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## ABSTRACT

Huntington's disease (HD) is a rare, autosomal dominant, progressive neurodegenerative disorder. HD manifests with a triad of progressive motor, cognitive, and psychiatric symptoms. Our patient was a 39-years-old married female with over a nine-year history of psychotic symptoms. The patient was diagnosed and treated for schizophrenia. Over the last 2-3 years, the patient had a progressive decline in her Activities of Daily Living, instrumental activities of daily living, and psychotic symptoms. She developed slurred speech, gait disturbances, frequent falls, involuntary movements of the trunk and distal extremities, bowel and bladder incontinence, and severe weight loss. Her genetic test for Huntington's gene confirmed the diagnosis of HD. She was prescribed Olanzapine, fluoxetine, and clonazepam. Psychotic symptoms are rare in HD and usually appear well after the motor and cognitive symptoms. Our case highlights an unusual clinical presentation of HD, which can be diagnostically challenging and lead to diagnostic delays.

**KEY WORDS:** Huntington's Disease, Neurodegenerative disorder, psychosis

## INTRODUCTION

Huntington's disease (HD) is a rare and slowly progressing autosomal-dominant neurodegenerative disorder. The global prevalence of HD is 2.71 per 100,000. The prevalence ranges from 0.4 to 5.70 per 100,000 between Asia to Europe, North America, and Australia.<sup>1,2</sup> HD manifests with progressive cognitive, motor and psychiatric symptoms. Disease progression can be variable in individuals; 33-76% of HD patients can have psychiatric symptoms.<sup>3</sup> The most common psychiatric manifestations in HD include irritability (60%), aggression (40-60%), apathy (57%), depression (30%), anxiety (28%), and psychosis (4-12%).<sup>3,4</sup> Psychotic symptoms mimicking schizophrenia are rare in HD. Usually, these symptoms manifest well after the motor and cognitive symptoms.<sup>5,6</sup> We are sharing here an unusual and challenging presentation of HD. In our case, the psychotic symptoms preceded the motor and cognitive symptoms of HD.

## CASE PRESENTATION

Our patient was a 39-years-old female, married with three children. She presented to the psychiatry outpatient department along with her spouse. The patient presented with a nine-year history of sleep decline, paranoid feelings, self-mumbling,

restlessness, verbal anger along with physical outbursts of aggression, and decline in social participation. The patient was initially diagnosed as Schizophrenia. She received multiple antipsychotics and electroconvulsive therapies (ECTs) during her course of illness. In response to treatment, the patient had partial remission in symptoms.

In the past 3 years, the patient progressively declined in her Activities of Daily Living (ADLs) and was worsening in psychotic symptoms. She required assistance and supervision for eating, toileting, and personal care. She was unable to perform any of her prior social and occupational responsibilities, for example, domestic chores and managing the house hold. She developed slurred speech, decreased vocabulary with answers limited to few words, gait changes leading to falls and injuries, dance like movements in distal extremities progressing further to trunk. Patient also became stool and urine incontinent and had cachexia. Two of patient's family members had history of similar symptoms and died in their early 40s. Their cause of death was never established.

On mental state examination (MSE), the patient was restless and agitated, self-mumbling incoherently, appeared fearful and attempted to hit and bite people

near her. There was no verbal response to queries. The patient did not follow any commands. On examination the patient was hemodynamically stable and her personal hygiene was poor. Neurological examination was limited (due to non-cooperation). There was loss of muscle bulk, broad-based gait with choreiform movements.

For assessment and management of the above symptoms, inpatient psychiatry admission was given. For the evaluation of the neurological symptoms, we called a neurology consult. Her lab investigations showed presence of ASMA antibodies (Table 1), MRI brain showed involuntional changes typical of HD (Table 2 and Figure 1), and Huntington gene was positive which confirmed her diagnosis of HD. (Table 3)

The patient was managed on Olanzapine 20mg orally at night for psychotic and motor symptoms, fluoxetine 20mg orally in the morning for aggression and agitation,

and clonazepam 2mg/day orally in divided doses for sleep and motor symptoms. The neurology team did not add any further treatment. After dietician input, we started her on high calorie, protein-rich diet. The patient's agitation improved and her self-mumbling stopped. The family received details regarding the management and prognosis of HD with genetic counseling. Due to financial constraints, the family decided to provide her with informal nursing care at home after discharge.

At four and eight-week follow-up, the patient was less irritable, relaxed, and showed no signs of aggression. She responded to her name and followed commands partially, including shaking hands and making eye contact. Her choreiform movements also decreased. Like before, She required assistance in ADLs but showed interest in self-care (including bathing, toileting, and eating).

## Investigations

**Table 1: Blood Investigations**

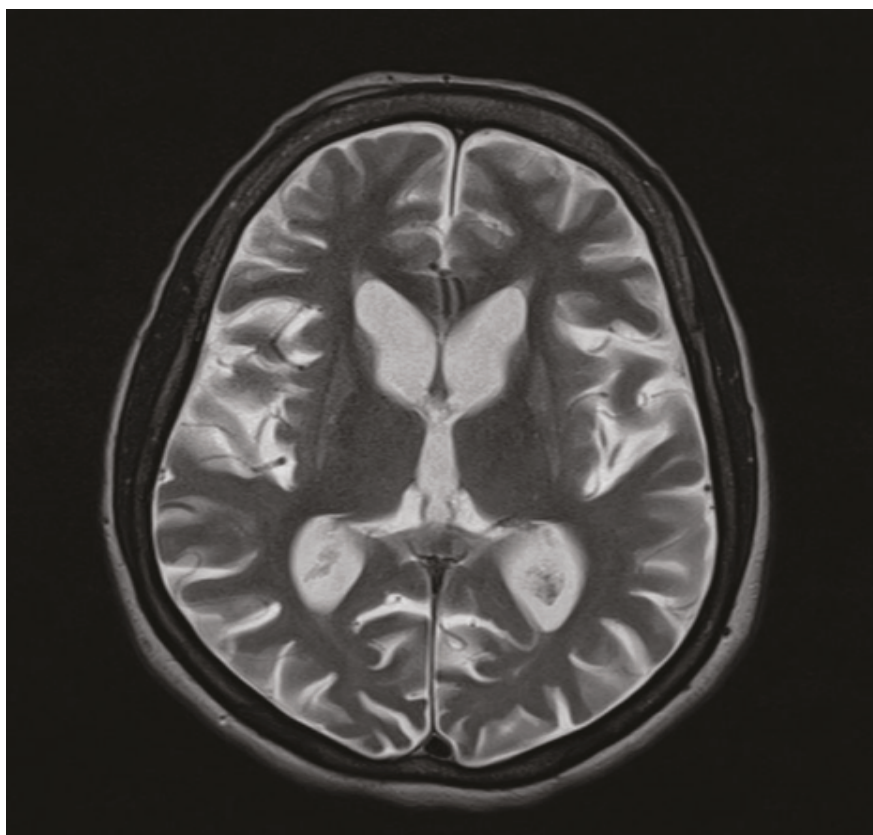
Investigations	Results	Reference range
Hemoglobin	<b>10.5 g/dL</b>	11-14.5 g/dL
Total leucocyte count	<b>11.5x10<sup>9</sup>/L</b>	4.6-10.8x10 <sup>9</sup> /L
Platelets	391x10 <sup>9</sup> /L	154-433x10 <sup>9</sup> /L
Sodium	142 mmol/L	136-145 mmol/L
Potassium	4.3 mmol/L	3.5-5.1 mmol/L
Chloride	108 mmol/L	98-107 mmol/L
Bicarbonate	27.2 mmol/L	20-31 mmol/L
Blood urea nitrogen	10 mg/dL	6-20 mg/dL
Creatinine	0.4 mg/dL	0.6-1.1 mg/dL
Total bilirubin	0.3 mg/dL	0.1-1.2 mg/dL
Direct bilirubin	0.1 mg/dL	0-0.2 mg/dL
Indirect bilirubin	0.2 mg/dL	0.1-0.8 mg/dL
Gamma-glutamyl transferase (GGT)	11 IU/L	Females: <38 IU/L
Alanine aminotransferase (ALT)	21 IU/L	Females: <35 IU/L
Aspartate aminotransferase (AST)	24 IU/L	Female: <31 IU/L
Alkaline phosphatase (AP)	108 IU/L	45-129 IU/L
Thyroid stimulating hormone (TSH)	1.75 uIU/ml	0.4-4.2 uIU/ml
Serum copper	109 ug/dL	Adult female: 80-155 ug/dL
Serum ceruloplasmin	0.36 g/L	Adults: 0.2-0.6g/L
Vitamin B12	410 pg/mL	>201 pg/mL acceptable
Serum Anti-nuclear antibody (ANA)	Negative	
Serum Anti-smooth muscle antibody (ASMA)	<b>Positive</b>	
Serum Anti-mitochondrial antibody (AMA)	Negative	

**Table 2: MRI brain**

MRI Brain	<ul style="list-style-type: none"><li>• Diffuse cerebral atrophy with bilateral caudate atrophy associated with dilatation of frontal horns of bilateral lateral ventricles.</li><li>• Bilaterally, Globus pallidus was not visible, along with atrophy of bilateral putamen.</li><li>• Overall appearance is highly raising the possibility of Huntington's disease.</li></ul>
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**Table 3: Molecular Genetics report**

Huntingtin gene (HTT)	The patient is heterozygous for one HTT normal allele with 17 CAG repeats and one expanded HTT allele with 49 CAG repeats. This finding is consistent with a diagnosis of Huntington's Disease.
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**Figure 1: MRI brain showing atrophy of bilateral putamen. Globus pallidus is not visualized.**

## DISCUSSION

HD is an autosomal-dominant disease, that usually presents with characteristic clinical manifestation. However, HD can present and evolve in an atypical manner during early to middle stage of HD. Therefore, HD can have a diverse range of initial symptoms.<sup>3</sup> In parkinsonism-predominant phenotype of HD, more neuropsychiatric manifestation and cognitive decline is noted than in chorea-predominant phenotype hence, a thorough physical examination and approach to history can help lead to the diagnosis of HD. Psychosis in HD is rare but reported in multiple case reports. In a study 11% of the patients had psychosis, out of whom psychotic symptoms started before the characteristic clinical symptoms of HD in a majority (55.3%) of the patients.<sup>7</sup> Other studies point that psychosis is usually seen well after characteristic motor and cognitive symptoms of HD is apparent.<sup>8</sup>

Our case discussed psychotic symptoms prior to onset of motor and cognitive features (pre-choreic stage). The existing evidence of pre-choreic psychosis is scarce and limited to case series and case reports. A case series mentions three family members who developed severe psychotic disorder between age 20-40 years, preceding chorea by three to nine years.<sup>6</sup> Another case of a 55-years old male with eight years history of psychosis progressing to HD is also reported.<sup>5</sup>

Our patient had psychotic symptoms for 6-years before other HD symptoms evolved. Patients with pre-choreic psychosis on antipsychotic treatment may develop tardive dyskinesia (TD). The occurrence of TD with motor symptoms of HD can make a diagnosis of HD difficult.<sup>4</sup> The same may have happened with our patient as her symptoms evolved.

Our patient had an atypical clinical presentation of HD. The atypical presentation was diagnostically challenging and lead to diagnostic delays. Untreated psychiatric symptoms of HD can be distressing to the patient as well as the caregiver. Treating psychiatric symptoms is vital

for improving the patient's quality of life in HD.<sup>9</sup> Lack of existing data of a rare condition like HD, with an unusual presentation, can undermine the possibility of neurodegenerative disorders. An in-depth approach to case presentation, history and physical examination can help revising the diagnosis with such challenging presentations.

At present, there is a lack of treatment guidelines for psychiatric symptoms in HD. There is supportive evidence for the use of antidepressants, antipsychotics, and clonazepam for choreiform movements. For agitation and irritability, evidence suggests antipsychotics and antidepressant use.<sup>4, 10-12</sup> There are also case reports on using various antipsychotics for the psychotic symptoms in HD.<sup>13-18</sup> A case report from India supported the use of clozapine and tetrabenazine with benzodiazepines after lack of response on two antipsychotics.<sup>19</sup>

Interestingly, our patient responded well to treatment better than before. There can be a few reasons for this. Firstly, there is a possibility of non-compliance due to lack of insight and possible forgetfulness due to the cognitive decline of the patient. Secondly, the patient received fluoxetine and clonazepam besides Olanzapine. We hypothesize that the drug regimen in combination improved the motor and psychiatric symptoms altogether. However, these outcomes are not generalizable as treatment guidelines based on this case report only. Our case builds to the current evidence on atypical HD cases and its management. Combining future researches to existing literature can help strengthen ways to adequate symptomatic management.

## CONCLUSION

Psychotic symptoms are rare in HD and usually appear well after the motor and cognitive symptoms, unlike this case. Our case highlights an unusual clinical presentation of HD, which can be diagnostically challenging and lead to diagnostic delays.

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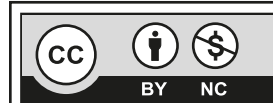
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Author's contribution:

**Marium Mansoor**; data collection, data analysis, manuscript writing, manuscript review

**Nida Rahman Khan**; manuscript writing, manuscript review

**Alviya Shafique**; manuscript writing



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