

# Psychosis in Huntington's Disease. a rare and Under-Investigated Psychiatric Manifestation

## Psychosis in Huntington's Disease: uma manifestação psiquiátrica rara e pouco investigada

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### Abstract

**Introduction:** Psychotic symptoms are among the least prevalent and under-investigated psychiatric manifestations (PM) of Huntington's disease (HD). **Case report:** We herein report a case of a 31-year-old male patient who presented PM with a predominance of negative symptoms, without any significant abnormal movement. HD was diagnosed based on positive DNA analysis and family history. HD imposes longitudinal follow-up through a multidisciplinary approach in order to improve the quality of life and prognosis. **Conclusion:** This case report highlights the importance of comprehending the PM in the initial presentation of HD so that the diagnosis is not delayed until the onset of motor symptoms.

**Keywords:** Huntington's Disease. Psychosis. Psychiatric Manifestation. Negative Symptoms.

### Resumo

**Introdução:** Os sintomas psicóticos estão entre as manifestações psiquiátricas (MP) menos prevalentes e pouco investigadas da doença de Huntington (DH). **Relato de caso:** Relatamos o caso de um paciente do sexo masculino, 31 anos, que apresentou MP com predomínio de sintomas negativos, sem qualquer movimento anormal significativo. A DH foi diagnosticada com base em uma análise de DNA positiva e na história familiar. A DH impõe um acompanhamento longitudinal por meio de uma abordagem multidisciplinar, a fim de melhorar a qualidade de vida e o prognóstico. **Conclusão:** Este relato de caso destaca a importância da compreensão das MPs na apresentação inicial da DH, para que o diagnóstico não seja atrasado até ao aparecimento dos sintomas motores.

**Palavras-chave:** Doença de Huntington. Psicose. Manifestação Psiquiátrica. Sintomas Negativos.

### INTRODUCTION

Huntington's disease (HD) is an autosomal dominant (AD) neurodegenerative disorder<sup>1-3</sup>. In 1993, an abnormal expansion of the CAG trinucleotide repeat ( $\geq 36$ ) was identified in the HTT gene, located in the short arm of chromosome 4, which encodes huntingtin, a cytoplasmic protein. If the number of repetitions is between 36-39, the disease has incomplete penetrance, but with  $\geq 40$  it is fully penetrant<sup>4,5</sup>. The worldwide prevalence of HD is estimated to be about 4-10/100,000 individuals<sup>5</sup>.

The clinical diagnosis of HD is supported by the presence of its classical motor signs, including chorea, combined with a family history suggestive of AD transmission. The diagnosis is confirmed through genetic testing to determine HTT CAG repeat length<sup>6</sup>. The mean age at onset of symptoms is 35-50 years<sup>12</sup> although it can occur at any age<sup>1,3</sup>.

Clinical presentation of HD is highly heterogeneous, usually comprising a triad of progressive motor, cognitive and

psychiatric symptoms<sup>1,7</sup>. The prevalence of psychiatric symptoms is significantly higher than in the general population and is associated with significant morbidity<sup>15</sup>. Cognitive manifestations may include deficits in declarative memory, procedural memory, verbal fluency, visuospatial skills, attention, and executive functions, among others<sup>8</sup>.

PM can develop gradually and are the first manifestation of HD in 31% of the cases. Although they can occur at any stage of the disease, they are often presented before the onset of motor symptoms and may precede them by a decade<sup>2,9,10</sup>. Mood disorders, personality changes, apathy, irritability, and aggressive behavior are the most common PM and will probably occur in every patient<sup>2,11</sup>. Psychotic symptoms occur in HD with an estimated prevalence of 3% to 11%. Psychosis can be very distressful for both individuals with HD and their caregivers. Management of HD requires a multidisciplinary approach, involving general practitioners, physiotherapists, neurologists,

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psychiatrists, occupational therapists, dieticians, and nurses<sup>12</sup>.

## CASE REPORT

We present the case of a 32-years-old Caucasian man, single, with no children, who completed high school and has been unemployed for 8 years. When he was 21 years old, he initiated psychiatric follow-up for depressive and anxiety symptoms and started treatment with sertraline 100 mg id. He showed very limited treatment compliance and abandoned psychiatric follow-up and medication within a month. Ten years later, he was brought to our emergency department (ER) with an order from the public health delegate. The patient's relatives reported that, for the last 8 years, he has had difficulty in seeking or maintaining a job, presenting severe social isolation, aggressive behavior towards his parents, and soliloquies. In the ER, the patient did not collaborate. He presented with blunted/inadequate affect. His speech was non-spontaneous, vague, and pseudo-intellectualized. He sometimes had unmotivated laughter, and delusions or hallucinations could not be excluded. He had no insight into his morbid condition.

In the psychiatric ward, as an inpatient, he spent most of the time in his room alone and did not participate in any group activities. The patient had a clinical presentation of psychotic syndrome with a predominance of negative symptoms. In fact, as an inpatient, the psychiatric evaluation showed a poor rapport and avoidance of eye contact, with blunted and sometimes inappropriate effects. His speech was vague, poor, and lacked vocal inflections, spontaneity, and flow of conversation. He presented anhedonia, avolia, and elementary auditory hallucinations. He denied delusions and had no insight into his morbid condition. In the Positive and Negative Syndrome Scale (PANSS), he scored 103 points out of 203 (43 of 49 in the negative symptoms subscale) and 95 points out of 120 in the Scale for the Assessment of Negative Symptoms (SANS). The patient's family history revealed that his father, paternal aunt, and paternal grandmother were diagnosed with HD. The patient's father has also been followed in psychiatry for several years with a diagnosis of psychosis secondary to HD, with multiple psychiatric hospitalizations. During this psychiatric hospitalization, the patient underwent a complete analytical evaluation that showed no relevant results. Drug screening in the urine was negative for benzodiazepines, opioids, cannabinoids, cocaine, and amphetamines. HIV, syphilis, hepatitis B and C serologies were negative. Electrocardiogram and Cranial Computed tomography (CT) scan were unremarkable. Cranial MRI showed: no atrophy of the head of the caudate nucleus; diffuse enlargement of the cortical grooves of the cerebral hemispheres, mainly in the parietal region, as well as the primary fissure and other grooves of the cerebellar hemispheres, in relation to the expected for the age group of the patient, a nonspecific finding. The neuropsychological evaluation showed cognitive deficits characteristic of HD (moderate commitment of sustained attention, episodic memory, deferred visual memory, executive functions, and verbal semantic fluency). The general physical examination was unremarkable. Neurological

examination revealed nonspecific, but possibly related changes, namely: tics (sniffing) and only partially suppressible head movements when testing ocular saccade initiation. No other neurological changes were present.

The patient was medicated with aripiprazole titrated to 20 mg and progressively became more cooperative. There were no episodes of psychomotor agitation and he denied auditory hallucinations. After a month as an inpatient, he was discharged clinically improved, scoring 49 points out of 203 in the PANSS (21 of 49 in the negative subscale) and 43 points out of 120 in the SANS. A suspected diagnosis of HD was made based on family history of HD, the clinical presentation of PM, cognitive deficits, personality problems, and gradual deterioration of the level of functioning. He eventually was submitted to genetic testing, which revealed a fully penetrant CAG pathogenic repeat expansion in the HTT gene (alleles: 46/ 27 CAG), initiating genetic follow-up. For the following 6 months, the patient has been clinically stable, maintained psychiatric follow-up, and eventually integrated an outpatient daily program that offered him a metacognitive training approach as well as support to help him restructure and maintain daily life routines and activities.

## DISCUSSION

This case report illustrates the significance of the occurrence of psychiatric and cognitive symptoms in the initial presentation of HD, which often occur before the onset of motor symptoms<sup>11</sup>. Our patient presented with PM associated with unspecific neurological changes, not allowing the diagnosis of HD according to currently accepted clinical diagnostic criteria. Nonetheless, considering the presence of a fully penetrant HTT mutation, significant psychiatric changes, and possibly related neurological changes, it is acceptable to consider that the patient has probably entered the prodromal phase of the disease. In a patient diagnosed with Huntington's disease based on positive DNA analysis and family history, the PM is probably related to the neurodegenerative process. The emergence of specific motor changes would allow a clinical diagnosis. It is difficult to evaluate the beginning and evolution of symptoms, nevertheless, it is possible to assess a loss of functionality. For the last 8 years, he has been unemployed, has shown severe social isolation and aggressive behavior towards his parents. The patient has a clinical presentation of a psychotic syndrome with a predominance of negative symptoms. As a differential diagnosis, according to the complementary diagnostic tests and clinical records, we ruled out acute organic psychosis and Substance/Medication-Induced Psychotic Disorder. Simple Schizophrenia, due to the predominance of negative symptoms, could not be ruled out. However, an underlying medical condition was present. Even considering that it is difficult to retrospectively clarify the nosological diagnosis, the psychotic syndrome (secondary to HD) fulfills the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) criteria for Psychotic Disorder Due to Another Medical Condition (HD) and

### 3 Psychosis in Huntington's Disease

Other mental disorders due to brain damage and dysfunction and physical disease (HD), respectively<sup>13,14</sup>.

Psychotic symptoms are one of the least prevalent PM of HD<sup>2</sup>. Delusions and, to a lesser extent, hallucinations are more common in advanced stages, particularly of a paranoid and persecutory nature<sup>10</sup>. Psychotic symptoms do not show a specific pattern and, in some of the patients, psychosis has peculiar presentations, like the ones in this case report. The loss of functionality may suggest appearance and accumulation of negative symptoms and can delay HD recognition. Psychotic disorders can develop gradually, initially having a higher prevalence of adjustment reactions or personality disorder<sup>12</sup>. Psychotic symptoms have been under-investigated and research

is needed to elucidate the characteristics of HD patients presented with psychosis<sup>15</sup>. It is relevant to highlight that scientific literature is insufficient regarding the clinical evolution of these patients and longitudinal follow-up will further clarify the diagnosis, response to treatment, and progression of the illness. As described in the literature and illustrated by this case report, PM that often occurs before the onset of motor symptoms is variable in the course of the disease. Thus, it is relevant to study this population of patients in order to apply to neuropsychological tests, qualifying an intervention in earlier stages. This way, we will be able to provide more appropriate treatment strategies to improve the quality of life and prognosis of these patients.

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