Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Huntington's Disease and Psychosis

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DOI: https://doi.org/10.36347/sjmcr.2025.v13i07.050 | **Received:** 18.01.2025 | **Accepted:** 22.02.2025 | **Published:** 26.07.2025

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Abstract **Case Report**

Huntington's disease (HD) is a rare, autosomal dominant neurodegenerative disorder caused by a CAG trinucleotide repeat expansion in the huntingtin (HTT) gene on chromosome 4. It leads to the production of a toxic protein variant, causing neuronal dysfunction and cell death, primarily in the striatum. The disease is characterized by a triad of motor impairments (chorea, dystonia, bradykinesia), cognitive decline (executive dysfunction, memory loss), and psychiatric symptoms (depression, irritability, psychosis). A case study of a 56-year-old woman with HD revealed severe psychiatric symptoms, including persecutory delusions, aggression, and hallucinations. Initial misdiagnosis as schizophrenia delayed proper management. Brain MRI confirmed HD-related atrophy, leading to appropriate treatment with quetiapine, which improved symptoms, though full remission was not achieved. Diagnosis relies on genetic testing, neuroimaging, and clinical evaluation. Management is multidisciplinary, involving neurologists, psychiatrists, and therapists. While no cure exists, treatments target symptom relief. Tetrabenazine is used for chorea, while SSRIs and antipsychotics help manage psychiatric symptoms. Further research is needed to develop disease-modifying therapies and improve patients' quality of life.

Keywords: Huntington's disease, psychosis, a neurodegenerative disease, therapeutic approaches.

INTRODUCTION

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder characterized by motor impairments, cognitive decline, and psychopathological alterations [1]. HD is caused by an expansion of the cytosine-adenine-guanine (CAG) trinucleotide repeat in the huntingtin (HTT) gene located on chromosome 4, leading to the production of a toxic variant of the eponymous protein, which results in polyglutamine aggregate formation and, subsequently, neuronal dysfunction and cell death, particularly in the striatum [2, 3]. Hyperkinetic movement disorders with prominent chorea are typically present in the early stages of the disease [1, 4]. As the disease progresses, additional motor deficits become more evident, leading to dystonia or tics accompanied by rigidity, bradykinesia, and postural instability [5]. Furthermore, cognitive decline can manifest many years before the onset of motor symptoms, in the form of impaired executive, visuospatial, and short-term memory functions. (1) Behavioral changes in HD can mimic the behavioral variant of frontotemporal dementia (bv-FTD) [6]. Psychopathological alterations such as apathy, disinhibition, irritability, and depressive symptoms are well-known characteristics of the disease [1, 9]. Psychosis is less common [9-11]. In the context of HD, psychosis is a poorly defined term, most often referring to hallucinations and delusions.

CASE PRESENTATION

To explore this link, we report the case of a 56-year-old female patient, married and mother of three children, admitted to the women's emergency hospital unit at Ar-razi Hospital in Salé by her family. Over the past four years, the patient had experienced episodes marked by behavioral disturbances, including hetero-aggressiveness and agitation, with verbalization of persecutory, mystical-religious, and bewitchment-related delusional statements. Her condition had been tolerated by her family for six years.

The current episode began three months ago, with increasing instability. She became aggressive towards her daughters and sister, attempted to flee the family home but was prevented by her daughters, which

provoked agitation and property destruction. She also attempted to attack her daughter with a bladed weapon.

The patient was hospitalized at our facility at the request of a third party in accordance with the Mental Health Dahir in Morocco. Her medical history included psychiatric follow-up for approximately 10 years and hospitalization at HAS in April 2024. She had been menopausal for around 10 years.

Upon psychiatric examination at admission, the patient exhibited abnormal hand movements with whole-body swaying. She became irritable and agitated upon seeing her husband, which exacerbated her movements. She was of thin build, with stable vital signs. Her facial expressions were mobile, and contact with her was easy. Her basic mental functions appeared preserved; she was alert, attentive, and well-oriented in time and space, with intact memory and normal speech flow and continuity.

She exhibited a poorly systematized persecutory delusion centered on her husband, along with intuitive and interpretative mechanisms of bewitchment, reported with low affective charge. She did not report perceptual disturbances but displayed attitudes suggesting their presence, such as a listening posture. Her mood was neither sad nor euphoric, with blunted affect. Her judgment was impaired, insight was negative, sleep was disturbed, and appetite was preserved.

Physical examination was unremarkable. A diagnosis of schizophrenia was made based on the presence of delusional syndrome, hallucinatory syndrome, and impaired judgment and insight. A complete biological workup and ECG were requested, both of which returned unremarkable.

Brain MRI showed bilateral atrophy of the lenticular and caudate nuclei, leading to enlargement of the frontal horns of the lateral ventricles with a decreased FH/CC ratio, bilateral striatal atrophy, and diffuse cortico-subcortical atrophy inconsistent with age, findings compatible with Huntington's disease.

The patient was started on quetiapine 50 mg with dose escalation. Psychotic symptoms gradually improved during her hospital stay, with stabilization of her mental state and resolution of auditory hallucinations. Although there was a significant improvement in persecutory and bewitchment delusions, residual symptoms persisted, and complete remission was not achieved.

The patient was discharged after four weeks of hospitalization and received outpatient care with follow-up at our psychiatric hospital, Ar-razi in Salé. The evolution was marked by good therapeutic adherence, both in psychiatric and neurological follow-up for HD management.

DISCUSSION

Huntington's disease (HD), also known as Huntington's chorea, is a rare neurodegenerative disorder caused by a trinucleotide repeat expansion, characterized by the loss of GABAergic neurons in the basal ganglia [1]. HD follows an autosomal dominant inheritance pattern and affects approximately 1 to 7 individuals per million [1, 2]. The condition exhibits full penetrance and is controlled by a gene located on the short arm of chromosome 4. The nucleotide triplet expansion leads to CAG repeat elongation on chromosome 4. In juvenile-onset cases, the disease is characterized by more than 60 repeats [8].

Clinically, HD presents as a triad of motor deficits, cognitive decline, and psychiatric disturbances. Motor symptoms include chorea (jerky, involuntary movements), dystonia (sustained muscle contractions), and voluntary movement impairments. Psychiatric manifestations, such as irritability, anxiety, and depression, often precede motor symptoms. Additional features include rigidity (Westphal variant), dementia, and emotional disturbances [9, 10].

Juvenile-onset HD manifests in childhood or adolescence with rapid progression, whereas late-onset cases occur later in life and may be milder. Each phenotype requires tailored management approaches to address specific symptoms and needs.

The diagnostic process for HD involves neuroanatomical imaging techniques, including CT and MRI scans. It is essential to recognize that radiological findings in HD vary among individuals and throughout the disease course. There is often a correlation between the extent and location of brain changes and clinical symptoms. Radiological assessment, combined with clinical evaluation, genetic testing, and other diagnostic measures, plays a crucial role in diagnosing and monitoring HD.

A multidisciplinary care approach involving neurologists, psychiatrists, physiotherapists, and social workers is essential.

Psychopathological abnormalities, including depressive episodes, frequently precede the development of neurological symptoms in HD patients [17]. Psychotic symptoms in HD are rare and challenging due to inconsistent data, often demonstrating treatment resistance [18-20].

In our HD patient, the psychotic symptoms presented were considered unusual. Literature describes tardive dyskinesia resembling HD motor symptoms, which was excluded through genetic testing [21].

Our case highlights the immense value of neuroimaging techniques in patients presenting with

psychotic and executive dysfunction alongside movement disorder symptoms.

HD often has a familial component, and its impact on family members can be profound. Education and support for family members, both emotionally and practically, are critical.

Current therapeutic approaches primarily focus on symptom management rather than addressing the underlying cause of the disease. Current treatment strategies aim to alleviate physical, cognitive, and psychiatric symptoms to improve overall quality of life [5-10].

There is no consensus or available drug developed to slow HD progression. Treatment focuses solely on symptom relief. Tetrabenazine is the only approved drug for managing choreiform movements in HD. Clinical trials evaluating cholinesterase inhibitors, commonly used for cognitive deficits in Alzheimer's disease, have largely shown unfavorable results in HD. Atypical antipsychotics are preferred for psychosis management due to their reduced extrapyramidal side effects. Treatment of depression often involves selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). Paramedical interventions, including speech therapy, rehabilitation, nursing, and social support, are essential in HD care [11-14].

CONCLUSION

In summary, Huntington's disease (HD) is a complex neurodegenerative disorder with no treatment to halt its progression. Symptom management relies on a multidisciplinary approach, including pharmacological treatments for motor and psychiatric symptoms. The impact on families is significant, requiring support. Further research is needed to better understand the disease and develop more effective treatments while improving patients' quality of life.

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