Dissociative amnesia with fuge features in a patient with Huntington's disease

Disocijativna amnezija s obilježjima fuge kod bolesnika s Huntingtonovom bolešću

Ante Štefić, Vanja Đuričić, Valentin Kordić, Sara Đuričić, Maristela Šakić, Melita Jukić*

Summary

Huntington's disease is a severe, incurable neurological disease characterised by motor, cognitive, and psychological symptoms. This paper presents the case of a Huntington's disease patient with dissociative symptoms. Clinical characteristics, genetic background, diagnostics, and guidelines for treating Huntington's disease are shown in the paper. We emphasised the importance of knowing the genetic basis and testing the descendants of the patients. We highlighted the difference between behavioural perseveration as a common psychomotor disorder in these patients and symptoms of obsessive-compulsive disorders.

Dissociative disorders may occur under extreme mental stress and exhaustion, such as when dealing with a severe incurable illness. These disorders are not typical psychopathological phenomena for Huntington's disease, but conditions of hopelessness and despair after facing a severe diagnosis may lead to dissociative symptoms. Dissociative disorders as indicators of exhaustion of mental functioning require caution, especially given their high frequency of occurrence with suicidality as extreme exhaustion of mental functioning.

So far, treatment of Huntington's disease is only symptomatic, emphasising the relaxation of motor choreatic movements and heterogeneous mental disorders. Antipsychotics that reduce choreatic movements but also affect psychotic symptoms, behavioural perseverations and mood stabilisation are used primarily to relieve symptoms.

As it is a progressive disease that ends in severe motor deficit, dementia and death, treating these patients with a multidisciplinary team that includes neurological, psychiatric and palliative care, physical therapy, nursing, and social care is necessary. Psychotherapeutic and sociotherapeutic approaches make it easier for patients and their families to cope with this severe disease. Genetic testing of the offspring is desirable to determine the potential carrying of the mutated gene and its transmission to subsequent generations in which the disease appears earlier.

Key words: Huntington’s disease, dissociative amnesia, chorea, antipsychotics, behavioural perseverations

Sažetak

Huntingtonova bolest je teška, neizlječiva, neurološka bolest, karakterizirana motoričkim, kognitivnim i psihičkim simptomima. Ovaj rad je prikaz slučaja bolesnika s Huntingtonovom bolešću kod kojega su se razvili disocijativni simptomi. U radu su prikazane kliničke značajke, genetska podloga, dijagnostika i smjernice za liječenje Huntingtonove bolesti. Naglasili smo važnost poznavanja genetske osnove tectestiranja potomaka oboljelih. Istakli smo razliku između bihevioralnih perseveracija kao čestog poremećaja psihomotorike kod ovih bolesnika i simptoma opsesivno-kompulzivnih poremećaja.

* Nacionalna memorijalna bolnica „Dr. Juraj Njavo“, Vukovar, Hrvatska (Ante Štefić, dr.med.; Vanja Đuričić, dr.med.; doc.dr.sc. Melita Jukić, dr.med.); Klinički bolnički centar Osijek, Osijek, Hrvatska ( Valentīn Kordić, dr.med.); Medicinski fakultet Osijek, Osijek, Hrvatska (Sara Đuričić, studentica medicine); Specijalna bolnica za psihijatriju i paliativnu skrb „Svete Rafael“, Šumetlica, Hrvatska ( Maristela Šakić, dr.med.)

Correspondence address/Adresa za dopisivanje: Ante Štefić, dr.med., Nacionalna memorijalna bolnica „Dr Juraj Njavo“, Županijska 35, 32 000 Vukovar, Hrvatska E-mail: ante.stefic@gmail.com

Received/Primljeno 2023-05-28; Revised/Ispravljeno 2023-07-20; Accepted/Prihvaćeno 2023-10-05
U stanjima izraženog psihičkog stresa i iscrpljenosti, kao što je suočavanje s teškom neizlječivom boleću, mogu se javiti disocijativni poremećaji. Ovi poremećaji nisu tipični psihopatološki fenomeni za Huntingtonovu bolest, ali stanja beznada i očaja nakon suočavanja s teškom dijagnozom, mogu dovesti do pojave disocijativnih simptoma. Disocijativni poremećaji kao pokazatelji iscrpljenosti mentalnog funkcioniranja zahtijevaju oprez, posebice s obzirom na njihovu visoku učestalost javljanja sa suicidalnošću kao krajnjim iscrpljenjem psihičkog funkcioniranja.

Liječenje Huntingtonove bolesti za sada je samo simptomatsko s naglaskom na ublažavanje motoričkih poremećaja, te heterogenih psihičkih smetnji. Za ublažavanje simptoma koriste se u prvom redu antipsihotici koji reduciraju koreatske pokrete, ali imaju djelovanje i na psihičke simptome, bihevioralne perseveracije, te stabilizaciju raspoloženja.

Kako se radi o progresivnoj bolesti koja završava teškim motoričkim deficitom, demencijom i smrtnim ishodom, kod ovih bolesnika liječenje je nužno pružiti s multidisiplinarnim timom koji uključuje neurološku, psihijatrijsku i socijalnu skrb.

Psihoterapijski i socioterapijski pristupi olakšavaju nošenje oboljelih i njihovih obitelji s ovom teškom boleću. Psihijatrijska i socijalni pristupi olakšavaju nošenje oboljelih i njihovih obitelji s ovom teškom boleću. Pozaljeno je genetsko testiranje putemaka, kako bi se utvrdilo potencijalno nošenje mutirana gena i prijenos na sljedeće generacije kod kojih se bolest javlja u sve ranijoj dobi.

Ključne riječi: Huntingtonova bolest, disocijativna amnezija, korea, antipsihotici, bihevioralne perseveracije

Introduction

Huntington’s disease (HD), also called Huntington’s chorea, is a neurological and mental disorder inherited in an autosomal dominant manner. It is characterised by a range of motor, psychological, and cognitive impairments. The motor abnormalities are a loss of coordination and disorganised, uncontrollable motions called chorea that become more obvious as the disease progresses. HD patients often have mental problems that differ across individuals and can be very upsetting. HD is characterised by the degradation of neurons in the striatum and, as the disease advances, in the cerebral cortex, which results with dementia. Cortical atrophy progresses from the posterior to the anterior regions. This spatially selective degeneration may explain the clinical heterogeneity of neurological and mental symptoms of HD.

Patients with HD often have heart failure, muscular atrophy, and weight loss as additional symptoms. Symptoms usually occur between the ages of 30 and 50. However, they may occur at any age. Life expectancy is lowered due to complications such as pneumonia, cardiovascular diseases, and injury from falls. The disease lasts about 20 years from the diagnosis and ends with death.

In populations of European origin, the prevalence of HD ranges from 10 to 14 per 100,000 people. In Croatia has a lower prevalence, at 4.46 per 100 000 residents. It is a very rare disease in Asia with a prevalence of less than 1 per 100 000 people and most commonly sporadic as a new mutation without a family history. Men and women around the world are equally affected.

The huntingtin gene (HTT) is located on chromosome 4 and contains the genetic information for the transcription of the protein huntingtin. Huntingtin is widely expressed in the cytoplasm of neurons and their vesicle membranes, especially in large striatal and cortical neurons.

The disease is typically inherited from a parent whose HTT has been changed. The new mutation is to blame in up to 10% of cases. Wild-type alleles have up to 35 cytosine-adenine-guanine (CAG) repeats, while HD patients have 36 and more repeats. HD can be inherited through the maternal and paternal germlines, but it manifests more often and earlier when inherited through the paternal germline. As the disease passes through generations, symptoms may manifest at younger ages as the number of CAG repeats increases. The amplification of the CAG repeats in the gene responsible for encoding the huntingtin protein produces an aberrant mutant protein that damages brain cells through various mechanisms. In these patients, CAG repeats are unstable and expand when transmitted along the germline, resulting in a decrease in the age of onset with each generation. This phenomenon is known as anticipation.

Meiotic division in males and females differs. During spermatogenesis, the number of CAG repeats increases, while during oogenesis, there are almost equal increases and decreases. It is a reason why the earlier onset of HD is frequently inherited through the male germline.

Variations of symptoms can be seen in HD patients’ motor, cognitive, and mental characteristics. Chorea, characterised by short, uncontrollable, exaggerated, and semi-purposeful movements, is one of the most conspicuous symptoms. It progresses from sporadic, low-
amplitude facial and extremity twitches to continuous, large-amplitude body movements. Dystonia can affect writing, eating, and balancing. It often causes persistent muscular contractions that induce unusual postures such as torticollis and opisthotonos. Intercurrent diseases, stress, and worry can rapidly worsen motor symptoms.\(^15\)

HD deteriorates cognitive, perceptive, and emotional functions. A wide range of mental symptoms in HD includes anxiety, depression, apathy, obsessive-compulsive disorders (OCD), suicidality, disinhibition, irritability, psychosis, and cognitive, behavioural, and sexual disorders. Cognitive and behavioural problems can manifest up to 15 years before motor abnormalities and significantly diminish life quality.\(^6\)

Impaired emotional functions often include anxiety, depression and apathy, whose prevalence ranges from 38% to 73%.\(^16\) Less regular is OCD, ranging from 10% to 52%.\(^17\) Behavioural perseverations, however, might be mistakenly identified as OCD and can affect up to 75% of patients with HD.\(^18\) The difference between OCD and behavioural perseveration is that the will does not control behavioural perseveration. In contrast, the patient can control actions in OCD despite internal tension.\(^17\) Psychotic symptoms are less common, with prevalence ranging from 3% to 11%.\(^19\) Sexual dysfunctions in HD are prevalent, 85% of men and up to 75% of women report having significant sexual problems\(^20\), with the majority exhibiting symptoms of a hypoactive sexual condition, but paraphilia and increased sexual desire were also observed.\(^21\) The suicide risk is highest when premanifest patients develop disease and lose independence. 20–30% of HD patients report having suicidal thoughts at some point, and 7–10% commit suicide.\(^22\)

Dissociative disorders are not usual in patients with Huntington’s disease, but various forms of dissociative disorders may occur. A transient or permanent interruption of the continuity of standard integration of consciousness and other mental functions such as perception, attention, memory, movement and behaviour control characterises these disorders. Although dissociative conditions are recorded in brain damage and under the influence of anaesthetics, they are thought to arise due to several biological and psychosocial factors. These disorders usually do not have an organic cause but occur in mental exhaustion due to psychological trauma as a primary etiological factor. The psychological explanation says that their purpose is to defend the conscious mind against an unacceptable idea, considering that more than 70% of patients with dissociative disorder attempt suicide and often self-harm behaviour.\(^23\)

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), dissociative disorders include depersonalisation/derealisation disorder, dissociative fugue, dissociative amnesia, and dissociative identity disorder. The tenth revision of the International Classification of Diseases (ICD-10) classifies dissociative disorders with conversion disorders and distinguishes amnesia from fugue. Dissociative amnesia is the inability to recall the event immediately before and after the traumatic event, and dissociative fugue contains all forms of dissociative amnesia but also includes leaving home or the workplace, during which the patient maintains self-care and makes simple social contacts. Such a journey does not fit the schedule and the patient’s plans. A clear line between dissociative amnesia and fugue cannot be established. These two entities are probably part of the continuum. Conditions of severe stress, hopelessness, and despair in serious and incurable diseases can trigger dissociative reactions.\(^24\)

Despite the limited data available, several published studies have estimated that 0.2% of the general population experiences dissociative amnesia and a fugue state during life.\(^25\) This phenomenon is most prevalent in the third and fourth decades of life, with an identical frequency among both genders.\(^23\)

HD is a severe, neurodegenerative disease, and no specific disease-modifying medications are currently available. The only cure is symptomatic. The goal of treatment for chorea is to lower its severity to make it more tolerable. First-line therapies for motor difficulties include approved tetrabenazine and antipsychotics. The specific mechanism of action of tetrabenazine needs to be clarified. It is thought that inhibiting the vesicular monoamine transporter by tetrabenazine leads to a reduction of the uptake of monoamines into synaptic vesicles and a consequent lack of monoamines in presynaptic nerve terminals, including dopamine, which might cause the anti-chorea effect.\(^26\)

Antipsychotics used in treating psychotic conditions have the unwanted property of blocking the nigrostriatal pathway, consequently causing the development of extrapyramidal movements. To treat choreatic movements, the unwanted property of antipsychotics in treating psychotic symptoms is used to reduce the activity of dopaminergic D2 receptors in the nigrostriatal pathway.\(^27\) Antipsychotics with strong D2 antagonistic properties, like the first-generation antipsychotic haloperidol, effectively stop choreatic movements. However, it has unwanted adverse side effects on muscarine, histamine, and adrenergic receptors, resulting in hyposalivation,
obstipation, sedation, hypotension, and neurotoxicity. 

Nowadays, the first-choice antipsychotics for HD patients are newer second-generation antipsychotics with strong D2 antagonistic properties, like risperidone and olanzapine. They effectively reduce chorea and psychotic symptoms while having fewer unwanted side effects.

Various agents have been studied for treating different symptoms, but the benefit of some of them remains unclear. Compared to motor HD symptoms, mental symptoms are more susceptible to treatment. 

Psychiatric symptoms, frequently distressing for patients, are commonly addressed with conventional pharmacological therapies for patients without HD. Antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs) are commonly prescribed for treating depression, anxiety, and OCD. In addition to controlling unwanted choreatic movements, antipsychotics are used for psychotic symptoms like delusions and hallucinations. However, they can help with psychotic-depressive symptoms, expressed OCD and behavioural perseverations. Trials of memantine and cholinesterase inhibitors used to treat cognitive difficulties in Alzheimer’s disease have been unsatisfactory in HD. The loss of cognitive ability is progressive, and dementia is unavoidable. The modern HD patient’s treatment team often includes allied health professionals from neurology, psychiatry, palliative care, physiotherapy, nursing, and social care.

Case Report

The emergency psychiatric clinic received a patient from police officers. The patient was found alone in a car in a cornfield, where he had been for two days. The mother with whom he lives reported him missing after he said he would have a cup of coffee in town but failed to return as promised for lunchtime. The patient sat in the car for two days and did not eat or drink anything during that time. He said it was chilly, but he ignored it. He did not know why he had not gotten out of the car or sought help.

The patient was a 41-year-old man, divorced for two years, and the father of two daughters. The daughters lived with his ex-wife. He had recently been diagnosed with Huntington's disease and had been living with his mother since then. The mother took care of his therapy (haloperidol of 2mg in the morning and evening, mirtazapine of 15 mg in the evening, and alprazolam of 0.25 mg as needed in cases of tension). She said that he did not take a more significant amount than usual. The patient denied the consumption of alcohol and other illicit psychoactive substances. He said that he was upset and saddened before leaving home after having gotten a call from his daughters, saying they would not visit him.

The patient was partially time-oriented when arriving at the emergency psychiatric clinic; he thought the date was two days earlier. He was in a lowered mood and congruent affective state. His thought flow was slowed down, punctuated with occasional blocks of thought but without delusions or hallucinations. There were not any destructive or suicidal ideas or urges. During the examination, he was repeatedly sitting on the floor, even though he could not explain why he was doing it, and it was not under his control. He had expressed involuntary choreatic movements of both hands.

From the medical record, he was known to have received treatment for anxiety and depressive disorders for the previous three years, had a decreased libido, and was under pressure due to frustrating circumstances related to divorce for the last two years. He had occasional involuntary hand twitches, and a neurologist performed magnetic resonance of the brain, which showed basal ganglion atrophy. After that, a genome analysis confirmed that the reason for brain damage was the Huntington's disease. In addition to mental disorders and proven Huntington's disease with 48 CAG repeats, he had no other diseases.

The family had no psychiatric history. He had a mother of 72 years, his father had died at the age of 65 from colon cancer, and his older sister was healthy at age 45.

A laboratory examination of red and differential blood counts and basic biochemical parameters revealed that all required parameters were within the reference interval.

Mirtazapine was replaced with fluvoxamine (100 mg in the evening), resulting in fewer behavioural perseverations. Haloperidol was replaced with risperidone (1 mg in the morning and evening), to which he responded favourably by reducing involuntary movements; alprazolam 0.5 mg was continued as needed. He got psychotherapeutic and socio-therapeutic support in accordance with his capacities. Despite the treatment, the amnesia for the time of two days when he had been alone in the car was persistent.

Discussion

We decided to show a rare occurrence of dissociative amnesia with features of dissociative fugue in a patient with a rare disease such as HD.
Dissociative disorders are not characteristic of HD, but the despair in which this patient found himself may cause this reaction. Even minor frustrations in patients with these severe illnesses who face feelings of hopelessness can also lead to the development of suicidal behaviour. In this case, although the patient denied suicidal ideation and urges upon arrival. We cannot safely rule out their occasional existence, especially considering the high suicidal rate in HD patients.  

In the European Union, a prevalence of 1 per 2000 inhabitants is used to define rare diseases, so HD in Croatia, with a prevalence of 4.6 per 100,000 inhabitants, meets the criteria of rare diseases.  

Due to the rare occurrence of this disease, we wanted to gather information about its aetiology, clinical picture, diagnostics, and treatment. The aetiology of this disease is quite clear. The underlying cause of the disease is a genetic mutation in the number of CAG repeats, whose number in each subsequent generation increases and thus manifests the disease at an earlier age. Since this patient has a living mother who is elderly and does not have this disease, it is not possible that he inherited HTT from his mother. It is unlikely but possible that he inherited it from his father due to the phenomenon of anticipation in this disease, who never had symptoms of HD and died of cancer at a relatively older age than the patient was at the time of getting the diagnosis of HD. This patient is most likely to have a rare occurrence of a new mutation that causes HD in less than 10% of cases. More than 40 CAG repeats result in the complete penetration of the disease by age 65, so the occurrence of a manifest disease at approximately 40 years of age, which is also the most common age at which this disease manifests, is not surprising with 48 repeats. Testing patients' daughters for the possible expectation of disease symptoms and transmission to subsequent generations is crucial.  

Since there is not any specific treatment that would change the course of the disease, we relied on symptomatic treatment. To treat motor symptoms, we opted for risperidone as a second-generation antipsychotic because it has fewer side effects than first-generation antipsychotics. Considering that fluvoxamine also blocks enzymes involved in the elimination of risperidone, which leads to a rise in its concentration, lower doses of risperidone were sufficient, even though higher doses of antipsychotics are usually needed to stop chorea than to treat psychotic disorders. The combined activity of risperidone and fluvoxamine also reduced disease-specific behavioural perseverations, occasionally misclassified as OCD. It is necessary to consider the presence of depressive and anxious symptoms in these patients because they may have a biological basis in brain damage. Additionally, the extended period of unrecognised prodromal symptoms can lead to impaired social functioning, cognitive difficulties, and sexual disorders, increasing the burden on these patients.  

**Conclusion**  

HD is a genetic neurodegenerative disease of unusual occurrence at an earlier age as it passes through generations of offspring and requires good knowledge of the genetic basis, biological characteristics, and course of the disease. Motor symptoms characterise this disease, but since it is a degenerative disease, various psychological symptoms and comorbidities of mental disorders often develop depending on the affected brain structures and gene penetration. Among common symptoms such as behavioural perseverations, psychotic symptoms, mood disorders, and impaired sexual and cognitive functions, dissociative disorders may occur based on psychological grounds of exhaustion and hopelessness. Dissociative disorders as indicators of exhaustion of mental functioning during severe stressful conditions require caution, especially considering the high frequency of suicidality in patients with HD, which might result from the fatigue of these patients to cope with the difficulties and despair that this disease brings.  

It is essential to distinguish the symptoms of HD into different categories and to approach each symptom with a characteristic treatment. The choice drugs for motor symptoms without the availability of tetrabenazine, with which we have no experience, are newer antipsychotics with expressed D2 effects, such as risperidone and olanzapine. These antipsychotics also treat other less common mental disorders in these patients, such as psychotic symptoms, psychotic depressive disorders, and very common behavioural perseverations. Various antidepressants are also helpful in treating depressive and anxiety symptoms, OCD, and behavioural perseveration. It is essential to comprehend the relationship between different psychiatric drugs and their synergistic effects in treating the various symptoms of HD.  

The psychotherapeutic and socio-therapeutic approaches make it easier to carry patients and their families with this severe disease, where genetic testing of descendants is desirable to identify the potential carrying of a mutated gene.
References


