

*Ante Ivkovic, Marina Titlic, Tade Tadic, Ivana Erceg,
Anton Marovic, Dragan Primorac*

Choroba Huntingtona. Opis przypadku

Split University Hospital, Laboratory for clinical and forensic genetics
dr. D. Primorac
Split University Hospital, Department of Neurology
prof. dr J. Lusic

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Summary

Huntington's disease, Case report – Huntington's disease (HD) is a chronic neurodegenerative disorder, characterized by the following triad of clinical hallmarks: chorea, cognitive impairment and behavior disorders [8]. In 1993 the gene responsible for HD, whose mutation results in HD, was identified and mapped on the chromosome 4p16.3 [6]. The mutation is a characteristic expansion of a CAG nucleotide triplet. In this paper we present a 36-years-old female patient with HD who was submitted to a complete diagnostic procedure including genetic testing. Her pedigree was reconstructed using available medical documentation and tracing other members of her family.

Streszczenie

Choroba Huntingtona (Huntington's Disease – HD) jest przewlekłą zwyrodnieniową chorobą neurologiczną cechującą się triadą objawów: ruchami płasawicznymi, obniżeniem funkcji poznawczych i zaburzeniami zachowania. W roku 1993 wykryto gen, którego mutacja jest odpowiedzialna za rozwój HD i zlokalizowano go w miejscu 4p16.3. Wykryta mutacja ma charakter dynamiczny i polega na zwiększeniu liczby powtórzeń trypletu nukleotydu CAG. W pracy przedstawiono przypadek chorej lat 36, z objawami HD, którą przyjęto do Kliniki Neurologicznej Uniwersytetu w Splicie, w celu pełnego

przebudania, włącznie z oceną genetyczną. W przypadku tym udało się, na podstawie dokumentacji medycznej, odworzyć drzewo genealogiczne i uzyskać dane dotyczące innych członków rodziny.

Introduction

Huntington's disease (HD) was originally described by George Huntington in 1972. HD is an inherited, degenerative brain disorder and has population frequency of 5–7/100 000 [8]. HD is characterized by behavioural and cognitive disturbances and chorea. Usually HD starts in the third or fourth decade, but there is a wide range of onset, from childhood to older age. There is also a correlation between the CAG repeat number and age of onset of the disease [9]. At the beginning HD may be unrecognized by the patient and family due to slowly progressive nature of the illness. There are frequent, irregular, flicking movements of any limb or body and facial grimacing frequent symptoms. The gait is poorly coordinated, choreic with hypokinesia and bradykinesia [11]. Emotional instability is presented through a broad spectrum of symptoms, such as anhedonia, apathy, irritability and depression with common suicidal thoughts. Typically, the duration of the disease is about 15 years, but also shows differences from case to case. The onset before 20 years (juvenile HD), shows rapid progression with typical duration of 8 years, commonly associated with seizures. Progression of the disease leads to dementia and significant impairment of motor skills, psychiatric alterations, chorea, and, consequently, the patient becomes dependent on nursing care until death. Genetically HD is characterized by mutation on the gene IT-15 (huntingtin) localized on the chromosome 4p16.3 which codes for the protein huntingtin. The mutation is a characteristic expansion of a nucleotide triplet CAG repeat [5, 7]. The CAG repeat codes for a long polyglutamine domain in an expressed protein. The function of this protein is still unknown and it is believed that mutation causes gain-of-function. The DNA repeat expansion ranging from 35 to 95 repeats in the affected person. In the diagnosis clinical findings and MRI [2] usually help, but genetic testing is the only way to establish an accurate diagnosis of Huntington's disease. The purpose of this article is to present a case of a 36-years-old female patient, misdiagnosed and erroneously treated for 10 years until genetic testing has become available and revealed the characteristic mutation of the IT-15 gene.

Case report

We examined a 36-years-old female patient in the terminal phase of HD who had complete diagnostic elaboration including genetic testing. We constructed

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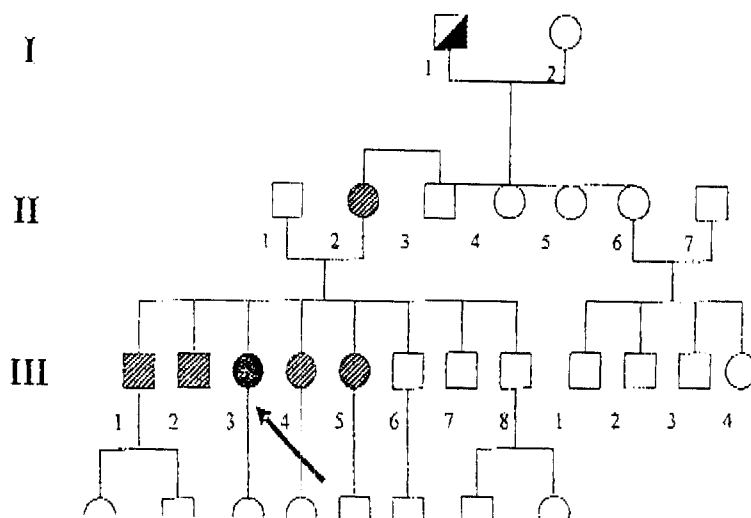
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her family tree (fig. 1) using available medical documentation and tracing other members of her family. HD started to appear at the age of 25-26 years, at first with inadequate behaviour, uncontrolled social inhibitory mechanisms and in the meantime she started to be depressive and withdrawn in her own world. All social contacts with her family became inappropriate and somehow she was excluded from the society. After two years the first clumsy movements became apparent and the patient was again repulsed by her society. At that time she was diagnosed as having psychosis. Three years ago for the first time the diagnosis of Huntington's chorea according to clinical symptoms was considered, although in that time she did not undergo any diagnostic procedures to confirm that diagnosis. Meanwhile, HD progressed and now, 10 years after the first symptoms appeared, the patient is in the terminal phase of the disease, requiring nursing care in a specialized institution. She came to the Department of Neurology, Split University Hospital, for supplementary observation. On admission, she was well hydrated and had good respiration but motionless, and peripheral blood analysis showed correct results. Urine analysis revealed urine infection, which was successfully treated with antibiotics. MRI of the head showed dilatation of ventricles due to an extensive brain atrophy and prominent atrophy of caudate nucleus (fig. 2). Neurological findings: she exhibited inability to walk, paresis of upward gaze, facial grimacing, mastication muscles and tongue were in constant motion, akinesia, incontinence, speech was monotonous, hardly articulated, Babinski sign on both legs and clonus of triceps surae muscle were positive. Muscular rigidity and ratchet-like cogwheel quality of wrists and elbow joints were present. All these findings made genetic testing of our patient rational. Genetic testing revealed 56 CAG triplet repeats, a characteristic genetic field on the gene responsible for HD. Family history has shown that Huntington like symptoms already had appeared in her family. Our patient had two sisters, which had shown identical progress of the disease, first with inadequate behaviour, then with uncontrolled movements. All of them had at least one child and they were healthy, with normal, healthy development for their age. Furthermore, two of the patient's five brothers became ill at the age of 30 years (fig. 1). At the beginning they manifested weakness during movements but they did not have any psychiatric problems. But later on one of them had depression and committed suicide, while another one died soon in the terminal phase of disease. One of them had two children and they have normal healthy development for their age. The mother of our patient had similar symptoms and died at the age of 40. Further family examination has shown that mother's father had symptoms more like Parkinson's disease including uncontrolled head movement and hand tremor. Unfortunately, we were unable to perform genetic testing of these

are some studies that have shown a linear correlation between the number of CAG repeats and consequent degree of the atrophy in the striatum [7]. In our patient MRI has also shown a prominent atrophy of nucleus caudatus and these changes are thought to contribute in psychic alterations in HD patients [4]. Another study did not show significant differences with respect to the size of CAG expansion and distinct psychiatric phenotype found in HD patient [10]. The purpose of this paper is to direct attention to a regular diagnosis of HD using besides MRI and clinical findings, genetic testing to circumvent the possibility of errors in the HD patient treatment as it was in our case. There are a number of neurological and psychiatric disorders with similar beginning symptoms and those symptoms are usually masked by the use of various drugs prescribed by various physicians and it is very hard then to establish HD diagnosis. Today when genetic testing is available in confirming the diagnosis of HD, these patients can receive palliative treatment for alleviation of symptoms under control

of a nurse in the terminal phase of the disease at home or in a special institution. A positive diagnosis, in time, will help these patients to get better quality of life in the future. There is still present an open, ethical question in determining the presence of the disease in people who do not have manifestations of the disease, but have positive genetic testing (CAG triplet length more than 35.5) and a positive family history. There are still many unanswered questions about screening members of family affected with HD, which have to be solved in future.



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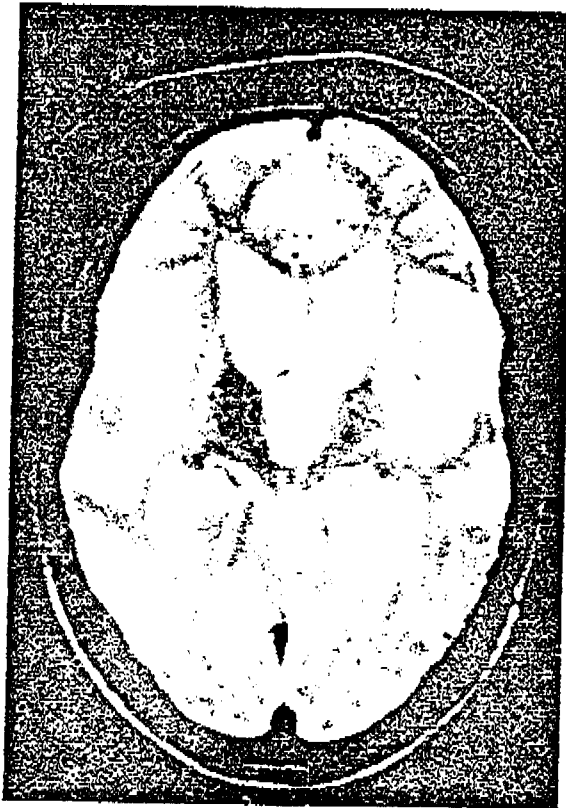


Fig. 2: MRI glôwy. Obraz T2-zależny, w płaszczyźnie osiowej wykazuje zmiany zanikowe mózgu z poszerzeniem rowków kory i szczeliny Sylwiusza. Komora trzecia jest umiarkowanie poszerzona. Zmiany zanikowe obejmują jądra ogoniaste i putamen – obustronnie

Ryc. 2: MRI scan. MRI, T2-weighted axial picture reveals atrophic changes of cerebrum with broad cortical sulci and a broad Sylvian fissure. The third and lateral ventricles are remarkably dilated. There are atrophic changes of the nucleus caudatus and putamen bilaterally.

Piśmiennictwo

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Ivana Erceg, M.D.

Laboratory for clinical and forensic genetics

Split University Hospital

Spinciceva 1

21000 Split

Croatia

Tel: +385 21 556 672

Fax: +385 21 389 510

e-mail: ivana.ercog@st.hinet.hr

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