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Complicated symptomatology and diagnosis of Creuzfeld-Jakob disease on a basis of clinical case

Marta Jurga

4th Military Teaching Hospital, Rudolfa Weigla 5, 50-981 Wroclaw, Poland

ORCID: 0009-0002-9359-8525

https://orcid.org/0009-0002-9359-8525

E-mail: marta.jurga9@gmail.com

Katarzyna Kuśmierczyk

District Medical Center in Grójec, Piotra Skargi 10, 05-600 Grójec, Poland

ORCID: 0009-0005-2768-0362

https://orcid.org/0009-0005-2768-0362

E-mail: kusmierczyk.kasia@gmail.com

Patrycja Karkos

Lower Silesian Oncology Center in Wrocław, Plac Ludwika Hirszfelda 12, 53-413 Wrocław, Poland

ORCID: 0009-0005-7491-5638

https://orcid.org/0009-0005-7491-5638

E-mail: karkos.patrycja@gmail.com

Hanna Gruszczyńska

Minsk Mazowiecki District Hospital, Szpitalna 37, 05-300 Mińsk Mazowiecki, Poland

ORCID: 0009-0007-2784-5168

https://orcid.org/0009-0007-2784-5168

E-mail: hangruszczynska@gmail.com

Natalia Kuderska

4th Military Teaching Hospital, Rudolfa Weigla 5, 50-981 Wroclaw, Poland

ORCID: 0009-0005-7274-9218

https://orcid.org/0009-0005-7274-9218

E-mail: natkuderska@gmail.com

Kacper Jurga

4th Military Teaching Hospital, Rudolfa Weigla 5, 50-981 Wroclaw, 4th Military Teaching Hospital, Rudolfa Weigla 5, 50-981 Wroclaw

ORCID: 0009-0005-5774-542X

https://orcid.org/0009-0005-5774-542X

E-mail: kacper.jurga123@gmail.com

Ewa Okowińska

University Teaching Hospital in Wroclaw 50-556 Wrocław, ul.Borowska 213, University Teaching Hospital in Wroclaw 50-556 Wrocław, ul.Borowska 213

ORCID: 0009-0006-7105-5940

https://orcid.org/0009-0006-7105-5940

E-mail: ewa.okowinska1@wp.pl

Aleksandra Cieślik

Lower Silesian Oncology Center in Wrocław, Plac Ludwika Hirszfelda 12, 53-413 Wrocław, Poland

ORCID: 0009-0003-0770-334X

https://orcid.org/0009-0003-0770-334X

E-mail: acieslik01@gmail.com

Klaudia Wojtyła

4th Military Teaching Hospital, Rudolfa Weigla 5, 50-981 Wroclaw

ORCID: 0009-0004-1609-5638

https://orcid.org/0009-0004-1609-5638

E-mail: klaudiawojtyla29@gmail.com

Jakub Lambrinow

University Teaching Hospital in Wroclaw 50-556 Wrocław, ul.Borowska 213, University Teaching Hospital in Wroclaw 50-556 Wrocław, ul.Borowska 213

ORCID: 0000-0002-6619-4640

https://orcid.org/0000-0002-6619-4640

E-mail: klambrinow@gmail.com

Abstract

Creutzfeldt-Jakob disease (CJD) is a rare condition. In this study we describe the diagnosis of the disease in a 73-year-old female, presenting dementia. Diagnostic tests unveiled characteristic features of CJD. The diagnosis of CJD was confirmed. It is important to always take into consideration the diagnosis of CJD in the diagnostic process of dementia.

Purpose: The aim of this scientific paper is to present symptoms and diagnostic methods of Creutzfeldt-Jakob disease based on a clinical case.

Review Methods: We conducted our study as a literature review based on information gathered from PubMed, Embase, Google Scholar using combinations of the following. As a part of study, we also present a case description from our materials from clinical practice.

Keywords: Creutzfeldt-Jakob disease; prion disease; progressive dementia; cognitive deficit

Introduction

Creutzfeldt-Jakob disease is a rare neurological disease from the group of prion diseases [1]. Prion diseases are very unusual, with an annual mortality rate of approximately one to two per million. Creutzfeldt-Jakob disease is considered as the most common prion disease in humans. It was first described in 1920 by German neurologist Hans Gerhard Creutzfeldt, and later by Alfons Maria Jakob. Depending on the etiology, Creutzfeldt-Jakob disease can be divided into four forms: sporadic, familial, iatrogenic, and variant CJD [2]. In the presented case, we will be discussing the sporadic form of the disease, the most common form of CJD (85%–90%) [3]. Sporadic Creutzfeldt-Jakob disease (sCJD) poses significant diagnostic challenges due to its complex clinical and neuropathological characteristics. This neurodegenerative condition is fatal and causes rapidly progressive dementia [4]. The occurrence is estimated as 1.5 to 2 cases per million people annually and the disease typically manifests in individuals between the ages of 55 and 75 [5,6]. The underlying cause of the disease is the process of abnormal folding of the cellular prion protein (PrPC) into a misfolded

form known as PrPSc and its accumulation in neurons [7]. Interestingly, the disease is classified as an infection, yet no activation of the immune system is observed [1]. In the course of Creutzfeld-Jakob disease, characteristic neuropathological changes include the presence of spongiform changes in the gray matter, hypertrophic astrocytosis, neuronal loss and deposition of prion protein (PrP) [4,8].

Case presentation

A 73-year-old patient with a history of hypertension, atrial fibrillation and adrenal adenoma was transferred by the emergency medical team to the Department of Neurology for diagnosis of visual disturbances, weakness of the right limbs and speech disorder that had been progressing for about a month. In the interview, the patient's family reported long-term sleep disturbances and dizziness. On admission, neurological examination revealed qualitative disturbances of consciousness, motor aphasia and right-sided extrapyramidal syndrome. A wide panel of diagnostic tests were performed at the Department. MRI of the brain showed subcortical atrophy with moderate secondary dilatation of the ventricular system. The EEG examination was abnormal with generalized and paroxysmal slow activity. Cerebrospinal fluid was collected for examination. Normal cytosis and slightly increased protein concentration were described in the fluid. The patient was consulted by an ophthalmologist - ophthalmological examination did not reveal any causes of visual disturbances.

The patient received treatment, but an increasing cognitive impairment was observed. An attempt was also made to perform a neuropsychological test. The test showed the presence of global cognitive deficits, including the processes of perception, thinking, attention, memory, language functions, speech and executive functions. During the patient's further stay, myoclonus of the upper limbs and deep cortical visual disturbances were observed in the patient - another ophthalmological examination revealed the lack of light sensation on both sides, as well as ataxia of the trunk and limbs, which prevented verticalization. Considering the entire clinical picture, a sporadic form of Creutzfeldt-Jakob disease was suspected. Therefore, the cerebrospinal fluid was sent for testing for the presence of 14-3-3 protein. The result was confirmed as positive, so a diagnosis of sporadic Creutzfeldt-Jakob disease was settled.

Discussion

Symptomatology

The prevalence of Creutzfeldt-Jakob neurodegenerative disease is low, at one-two cases per million population per year [5,9]. The diagnosis of Creutzfeldt-Jakob disease often leads to death within a short time after diagnosis. The most common causes of death are infection and cardiac or respiratory failure [10,11].

The pathogenesis of sCJD is marked by the accumulation of PrPSc, which has been classified into at least six distinct phenotypes. This heterogeneity is attributed to the varying structural forms of PrPSc, which result in different clinical presentations and neuropathological features [12,13]. In addition, the disease progresses rapidly with the onset of severe neurological symptoms. This can lead to a critical deterioration in the patient's condition and daily functioning. The most often observed symptoms are personality changes, especially with depressive characteristics, sleep disorder and weight loss [14]. Patients with Creutzfeldt-Jakob disease also present with non-specific symptoms in the early stages of the disease, which can be confused with other curable diseases [15].

Diagnostic process

Currently, definitive diagnosis of sCJD requires brain tissue analysis to identify the presence of PrPSc, the only reliable biomarker available [7]. Clinical diagnosis, however, is often complicated and relies on a combination of clinical symptoms, imaging techniques, and laboratory tests that serve as surrogate biomarkers [8]. Recent advances, particularly with the introduction of the ultrasensitive Real-Time Quaking-Induced Conversion (RT-QuIC) assay, have revolutionized diagnostic capabilities. This assay has allowed for the detection of PrPSc in various peripheral tissues of sCJD patients, sometimes pre-dating clinical symptoms, offering a compelling progression in the early diagnosis of the disease [6,16,17]. Significant diagnostic values of the method caused an inclusion of the CSF RT-QuIC test in the diagnostic criteria for sCJD by the World Health Organization (WHO). However, despite its advantages, it's important to note that only a limited number of specialized laboratories have

adopted RT-QuIC technology [18,19]. In diagnostic imaging, brain lesions may be confused with epileptic status, although there are minor differences between the imaging of these two conditions [20]. For all these reasons, Creutzfeldt-Jakob disease should be considered in the diagnostic process in patients with non-specific, rapidly progressive neurological symptoms, especially in the presence of rapidly progressive dementia [10,11]. Including the possibility of Creutzfeldt-Jakob disease in the early stages of diagnostic process can speed up the diagnosis and save patients time spent in hospital for further tests and, because of the possibility of misdiagnosis, even overmedication, which seems unnecessary at least in view of the lack of causal treatment in Creutzfeldt-Jakob disease.

Conclusions

Despite its rare occurrence, Creutzfeldt-Jakob disease should be considered in the diagnostic process in patients presenting with rapidly progressive dementia with myoclonus and other less specific symptoms such as sleep disturbance, speech disorder and limb weakness, as presented in this case study. Consideration of a possible Creutzfeldt-Jakob presentation can speed up the diagnostic pathway, especially with access to the new diagnostic tool RT-QuIC assay and give patients with Creutzfeldt-Jakob disease the chance to improve their quality of life during their limited lifetimes, in addition to preventing over-medication and early palliative care.

DISCLOSURE

Author`s contribution:

Conceptualization: Marta Jurga

Methodology: Patrycja Karkos

Check: Marta Jurga

Formal analysis: Ewa Okowińska

Investigation: Kacper Jurga

Resources: Aleksandra Cieślik

Data curation: Katarzyna Kuśmierczyk

Writing - rough preparation: Jakub Lambrinow

Writing - review and editing: Hanna Gruszczyńska, Klaudia Wojtyła

Visualization: Natalia Kuderska, Hanna Gruszczyńska

Supervision: Klaudia Wojtyła

Project administration: Natalia Kuderska

All authors have read and agreed with the published version of the manuscript.

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According to our ethics review board, ethics approval is not necessary for a case report; therefore, ethical approval is not required for this case report in accordance with local guidelines. All procedures performed in this study were in accordance with the ethical standards of the Institutional and/or National Research Committee(s) and with the Helsinki Declaration. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Informed Consent Statement

Informed consent was obtained for the patient photos and information used in the paper.

Data Availability Statement

All the data generated or analyzed during this case report are included in this article. Further inquiries can be directed to the corresponding author.

Acknowledgments

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

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