CREUTZFELDT-JAKOB DISEASE (CLINICAL CASE)

Oros M.M., Lutz V.V., Bulecza B.A.

Uzhhorod National University, Uzhhorod, Ukraine

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ABSTRACT

Background. Creutzfeldt-Jakob Disease (CJD) is a rare neurodegenerative disorder belonging to the group of transmissible spongiform encephalopathies caused by prion agents. Despite numerous studies, early diagnosis of CJD remains challenging due to the non-specific nature of symptoms in the initial stages and their similarity to other rapidly progressive dementias and psychiatric disorders.

Aim. To present a clinical case of the sporadic form of Creutzfeldt-Jakob disease with an emphasis on diagnostic difficulties and possibilities for confirming the diagnosis.

Materials and Methods. A 47-year-old female patient with progressive cognitive impairment, cerebellar ataxia, and extrapyramidal disorders was examined. Neurological assessment included evaluation of the level of consciousness, motor functions, and coordination. Laboratory investigations comprised ElectroEncephaloGraphy (EEG), Magnetic Resonance Imaging (MRI) of the brain, and cerebrospinal fluid analysis for specific biomarkers, particularly the 14-3-3 protein, which is an important marker for confirming the diagnosis of CJD.

Research Ethics. The patient was included in the study after providing informed consent. The study was conducted in full compliance with existing international and national bioethical standards and regulations (the Nuremberg Code and the WMA Declaration of Helsinki, 1964–2024) regarding ethical principles for medical research involving human subjects.

Results. The patient demonstrated characteristic clinical manifestations, including rapidly progressive dementia complicated by pronounced cerebellar ataxia and coordination disturbances. MRI findings revealed atrophic changes in the basal ganglia and cerebellum, which are typical of CJD. EEG showed periodic sharp-wave complexes, the main diagnostic criterion for this disease. Cerebrospinal fluid analysis revealed an elevated level of 14-3-3 protein, which further confirmed the diagnosis of CJD.

Conclusions. Considering the characteristic clinical manifestations, EEG and MRI changes, and the presence of the specific 14-3-3 protein in cerebrospinal fluid, the diagnosis of CJD was confirmed *in vivo*. Identification of these changes is a key step for timely confirmation of the diagnosis and determination of further patient management strategies. Given the rapid progression of CJD and the absence of etiotropic therapy, neuro-palliative care represents an essential component of management, enabling symptom relief and improvement of the patient's quality of life during disease progression.

Keywords: *electroencephalography, magnetic resonance imaging, 14-3-3 protein, cerebrospinal fluid, neuro-palliative care.*

Introduction

Creutzfeldt-Jakob Disease (CJD) is a neurodegenerative disorder that is presumably caused by a slow infectious agent, or a prion. The main clinical manifestations of CJD include dementia, pyramidal and extrapyramidal disorders, cerebellar dysfunction, myoclonus, cognitive impairment, and loss of personal identity. The course of the disease is characterized by rapid progression: the patient's condition deteriorates to a vegetative state, with the development of coma and subsequent death within several months [1–5].

From an epidemiological perspective, the incidence of CJD is approximately 1–2 cases per million population per year [6]. At the same time, improvements in surveillance systems and increased

Corresponding Author:
Oros Mykhailo M. – DMedSc, Professor, Head of the Department of Neurology, Neurosurgery and Psychiatry, State Higher Educational Institution "Uzhhorod National University", Ukraine.
✉ 27 Andriia Novak str., Uzhhorod, 88000, Ukraine.
E-mail: kaf-neurology@uzhnu.edu.ua

awareness among healthcare professionals contribute to more timely detection of the disease. According to a recent cohort analysis in the United States, diagnostic delays, frequent misdiagnoses, and significant healthcare resource expenditures remain pressing issues, highlighting the importance of establishing specialized centers and prion disease registries [7].

One of the main difficulties is early and accurate diagnosis. Initial clinical manifestations are often non-specific and may mimic other forms of rapidly progressive dementia, parkinsonism, or psychiatric disorders. In recent years, cases have been described in which parkinsonism was the initial manifestation of sporadic CJD [1]. Although EEG and MRI remain the main diagnostic tools, their sensitivity in the early stages of the disease is limited. Recent studies emphasize the need to combine EEG data, diffusion-weighted MRI, and cerebrospinal fluid biomarkers, while simultaneously excluding potentially treatable conditions that may mimic CJD [2].

Aim of a study was to present a clinical case of Creutzfeldt-Jakob Disease, in which the diagnosis was confirmed by clinical manifestations, typical ElectroencEphaloGraphy (EEG) findings, characteristic Magnetic Resonance Imaging (MRI) features, and neuropathological signs.

Materials and Methods

The study was carried out using methods of clinical observation, laboratory and instrumental diagnostic methods, and a comparative method.

Research Ethics

The patient was included in the study after providing informed consent. The study was conducted in full compliance with existing international and national bioethical standards and regulations (the Nuremberg Code and the WMA Declaration of Helsinki, 1964–2024) regarding ethical principles for medical research involving human subjects.

Results

A 47-year-old female patient (M.) was admitted to a neurological hospital with complaints of pain in the elbow joints, which she associated with a tick bite, progressively worsening coordination disturbances, cognitive impairment, general weakness, low mood, and depressive symptoms.

From the medical history, it is known that approximately one year prior to examination the patient had been bitten by a tick. Laboratory tests revealed high titers of IgM and IgG antibodies to Borrelia burgdorferi. The patient was treated by an infectious disease specialist and completed a 28- day course of doxycycline and ceftriaxone. Despite therapy, her condition gradually worsened, with increasing cognitive impairment and ataxia. Further treatment at the place of residence was ineffective, after which the patient was referred to a neurologist for further management.

According to the life history, the patient is married, has one child, and has worked as a laboratory scientist in a clinical diagnostic laboratory of a district hospital for 24 years. She has no harmful habits.

On neurological examination, the pupils were of normal size with preserved light reaction (D=S, where D – Dexter, S – Sinister, that is, the reflex is equally pronounced on both sides); bilateral weakness of convergence was noted; horizontal low-amplitude nystagmus; flattening of the right nasolabial fold; moderate dysarthria.

Deep tendon reflexes were increased, more pronounced on the right (D>S); Babinski and Rossolimo pathological reflexes were positive bilaterally. Muscle strength and tone in the lower limbs were reduced, with preserved sensation. In the Romberg position, marked ataxia was observed; gait was ataxic; during the finger-to-nose test, bilateral dysmetria was noted.

Brain MRI revealed bilateral pathological changes in the basal ganglia and thalamus, as well as atrophic processes of the cerebral cortex and cerebellum. Differential diagnosis was recommended between a neurodegenerative process (including CJD) and metabolic disorders of the subcortical gray matter. Microangiopathy corresponded to grade 2 according to the Fazekas scale.

EEG demonstrated a pattern typical of CJD-periodic sharp-wave complexes.

Routine blood and urine analyses showed no pathological changes.

Biochemical blood analysis revealed values within physiological limits, except for increased alanine aminotransferase activity (72.6 U/L) and decreased serum ionized calcium level (1.15 mmol/L; normal range 2.15–2.5 mmol/L).

Thyroid-stimulating hormone, vitamin B12, and folic acid levels were within normal ranges.

Cerebrospinal fluid analysis showed that it was clear; protein level was 0.114 g/L, glucose 4.31 mmol/L; cytosis consisted of single neutrophils, 0–1 lymphocyte per field of view, and 1–2 erythrocytes. The cerebrospinal fluid test for 14-3-3 protein was positive.

DNA of cytomegalovirus and Epstein-Barr virus, as well as antibodies to the NMDA receptor (NR1 subunit), were not detected.

The patient received palliative care and symptomatic treatment, including sertraline and analgesics as needed.

Discussion

CJD remains one of the most severe neurodegenerative disorders due to its rapid progression, diagnostic complexity, and lack of effective therapy. Current research focuses on improving diagnostic accuracy, studying molecular heterogeneity, and integrating neuro-palliative care; however, many significant challenges remain unresolved.

During diagnosis, other causes of rapidly progressive dementia must be excluded. Alzheimer's disease, frontotemporal dementia, and dementia with Lewy bodies may clinically mimic CJD, especially in cases of atypically rapid progression. However, these disorders typically progress over months or years, and their MRI and cerebrospinal fluid biomarker profiles differ significantly. In Alzheimer's disease, amyloid and tau biomarkers (CSF Aβ42, p-tau) are informative, whereas dementia with Lewy bodies is characterized by visual hallucinations and fluctuations in attention [8; 9].

Autoimmune encephalitis is currently considered one of the most important differential diagnoses, particularly given its potential reversibility. Syndromes such as encephalitis associated with antibodies to NMDA receptors, LGI1, CASPR2, or GABA-B receptors may present with psychiatric symptoms, seizures, and movement disorders, closely resembling CJD. Unlike prion diseases, autoimmune encephalitis is characterized by inflammatory changes in cerebrospinal fluid, involvement of the medial temporal lobes on MRI, and a positive response to immunotherapy [10]. Importantly, misdiagnosis of autoimmune encephalitis as CJD has been repeatedly reported in the literature [11].

Vascular causes, including multi-infarct dementia, cerebral amyloid angiopathy, or vasculitis, may present subacutely with multifocal neurological symptoms. In such cases, MRI usually reveals ischemic or hemorrhagic lesions that do not correspond to the typical CJD pattern of cortical ribboning or basal ganglia hyperintensity [12]. Assessment of inflammatory markers and cerebral angiography help exclude primary central nervous system vasculitis.

Thus, the differential diagnosis of CJD encompasses a wide spectrum of neurodegenerative, autoimmune, and vascular pathologies. Decisive importance is attributed to characteristic MRI and EEG findings, specific cerebrospinal fluid biomarkers, and – most importantly – the potential reversibility of autoimmune and paraneoplastic processes. Therefore, a systematic and multidisciplinary diagnostic approach is essential for timely diagnosis of prion disease and exclusion of potentially treatable alternatives.

Given the inevitably fatal course, neuro-palliative care is now recognized as a key component of patient management. Recently proposed clinical guidelines emphasize the importance of early integration of palliative services to alleviate symptoms, reduce psychosocial burden, and support caregivers [3]. This is particularly relevant given the extremely rapid progression of the disease.

Therapeutic approaches remain experimental. Clinical trials involving the monoclonal antibody PRN100 have demonstrated its safety and ability to cross the blood-brain barrier; however, they have not shown a significant effect on patient survival [4]. Therefore, the mainstay of treatment remains symptomatic therapy aimed at controlling myoclonus, seizures, and agitation. There is an urgent need to develop new clinical trial design models adapted to rare, rapidly progressive diseases [5].

Conclusions

Thus, CJD remains a fatal neurodegenerative prion disorder with diverse clinical manifestations and rapid progression, creating significant diagnostic and therapeutic challenges. The presented clinical case highlights the importance of considering CJD in the differential diagnosis of rapidly progressive dementias and movement disorders, particularly when initial symptoms may mimic autoimmune, infectious, or vascular processes.

Detection of characteristic MRI and EEG changes, as well as the presence of specific cerebrospinal fluid biomarkers, particularly the 14-3-3 protein, are key criteria for confirming the diagnosis *in vivo*.

Given the absence of etiotropic treatment, early recognition of the disease is crucial not only for improving diagnostic accuracy but also for timely initiation of neuro-palliative care, genetic counseling (when indicated), and provision of psychosocial support to the patient's family.

Despite emerging molecular discoveries and promising experimental therapies, CJD remains a diagnosis of exclusion, underscoring the necessity of comprehensive evaluation to rule out potentially treatable conditions.

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Authors' Contributions

Contribution / Authors	A	B	C	D	E	F
Oros M.M.	+	+	+	+	+	+
Lutz V.V.			+			+
Bulecza B.A.			+			+

Notes: A – concept; B – design; C – data collection; D – statistical processing and interpretation of data;
E – writing or critical editing of the article;
F – approval of the final version for publication and agreement to be responsible for all aspects of the work.

Declarations

Conflict of interest is absent.

All authors have given their consent to the publication of the article, to the processing and publication of their personal data.

The authors of the manuscript state that in the process of conducting research, preparing, and editing this manuscript, they did not use any generative AI tools or services to perform any of the tasks listed in the Generative AI Delegation Taxonomy (GAIDeT, 2025). All stages of work (from the development of the research concept to the final editing) were carried out without the involvement of generative artificial intelligence, exclusively by the authors.

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