CLINICAL CASE

CONTENTS

Creutzfeldt – Jakob disease: clinical cases

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ABSTRACT
A 68 y.o. woman delivered to the emergency department with severe speech impairment in a somnolent state - 13 points Glasgow Coma Scale. Her relatives described a clinical manifestation: rapidly progressive dementia, visual disturbances, abnormal gait and coordination, retrograde amnesia. A 67 y. o. man delivered to the emergency department with headache, vertigo, abnormal gait and coordination, progressive extremities weakness, disorientation, memory and concentration impairment. His relatives told about extremely rapidly progression of symptoms during last three months. First clinical case presents a Heidenhain variant, second case – Brownell - Oppenheimer variant.

KEY WORDS: rapidly progressive dementia, prion disease, diagnostic criteria in vivo

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INTRODUCTION

Creutzfeldt - Jakob disease (CJD) is a transmissible spongiform encephalopathy that manifests as a rapidly progressive dementia. There are four types of CJD: sporadic, variant, familial, iatrogenic. It is not very common disease, but nowadays the molecular basis of prion propagation and the pathogenesis of illness are well understood. All human prion diseases have similar pathomorphological features – spongiform degeneration of the gray matter, gliosis, neuronal loss, and deposits of insoluble prion protein (PrP^{Sc}) [1]. There are strict and recognizable clinical features and imaging patterns on magnetic resonance (MR) imaging helping a neurologist to be confident in diagnosis. In this article, we described two clinical cases of CJD observed in St. Panteleimon Hospital during 2023 year.

CASE REPORT

1 CASE

A 68 y.o. woman delivered to the emergency department with severe speech impairment in a somnolent state - 13 points Glasgow Coma Scale. Her relatives described a clinical manifestation: rapidly progressive dementia, visual disturbances, abnormal gait and coordination, retrograde amnesia. According to the patient`s history, she had coronary artery disease, II stage of an essential arterial hypertension, and also complicated professional anamnesis – patient worked with a fresh meat of domestic animals. General examination was performed in emergency department: BP 160/100 mm Hg, heart tones were rhythmic.

Neurological examination showed horizontal nystagmus with a right side gaze fixation, facial asymmetry, left side tongue deviation, extrapyramidal signs, tendon and periosteal reflexes D>S, subcortical signs. Active movements in upper and lower extremities were restricted due to muscle rigidity. The patient had abnormal bilateral foot signs – Babinski, Strumpel. Romberg`s test wasn`t performed due to her somnolence.

MRI findings: cortical hyperintensity in right frontal, temporal and occipital lobes (DWI), hyperintensity in right nucleus caudatus, putamen and thalamus (fig. 1). Cerebral microangiopathy signs also were presented. EEG investigation demonstrated periodic sharp wave complexes in the left parieto-temporal lobe.

2 CASE

A 67 y. o. man delivered to the emergency department with headache, vertigo, abnormal gait and coordination, progressive extremities weakness, disorientation, memory and concentration impairment. His relatives told about extremely rapidly progression of symptoms during last

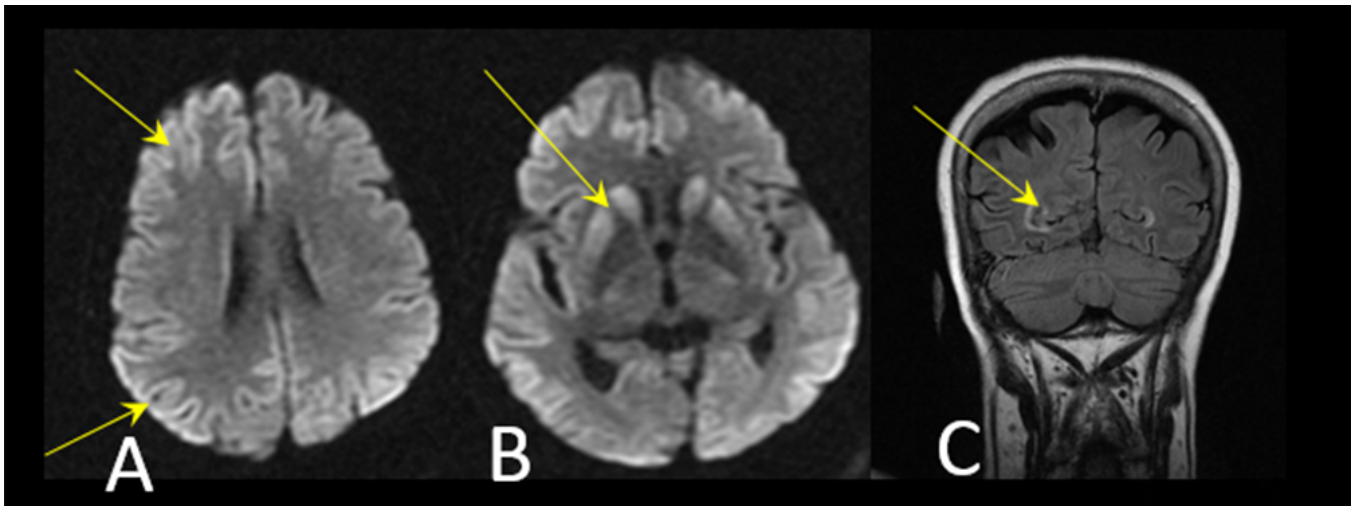

Fig. 1. MRI findings: A - cortical hyperintensity (DWI), B and C - hyperintensity in right nucleus caudatus, putamen and thalamus (DWI, FLAIR).

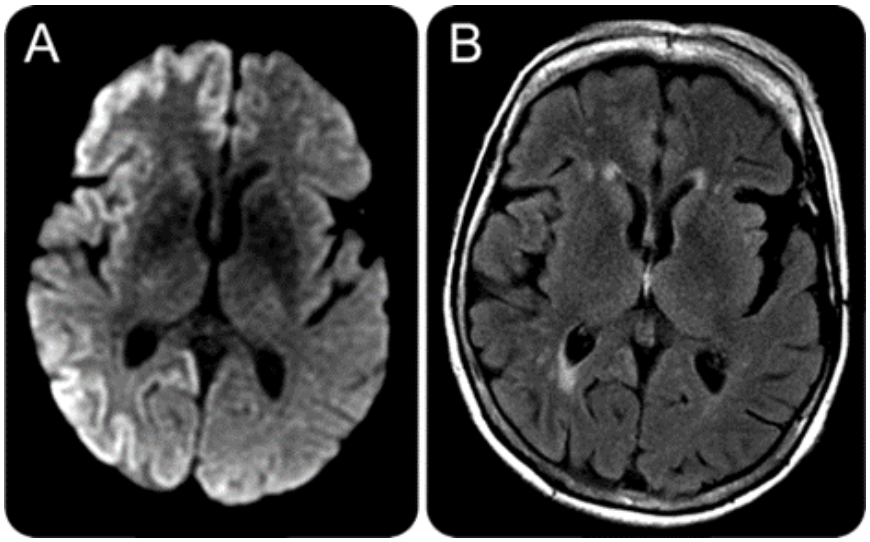

Fig. 2. The axial diffusion-weighted image (A) showed restricted diffusion throughout the cortical ribbon of the right hemisphere. There was corresponding decreased signal on the apparent diffusion coefficient map. The changes were not easily seen on the fluid-attenuated inversion recovery sequence (B).

three months. A patient had coronary artery disease, II stage of an essential arterial hypertension, and also complicated professional anamnesis – he worked with a fresh meat of domestic animals. General examination was performed in emergency department: BP 160/90 mm Hg, heart tones were rhythmic.

Neurological status: conscious - 15 points Glasgow Coma Scale, periodic time and place disorientation, horizontal nystagmus, cerebellar ataxia, left side pyramidal signs. The Romberg`s test showed ataxia. The patient performed a finger-to-nose test unsatisfactory. Tendon and periosteal reflexes D=S. Active movements in upper and lower extremities without any restrictions.

MRI findings: cortical hyperintensity in frontal, temporal, parietal and occipital lobes bilaterally, mostly on the left hemisphere without damage of basal ganglia (DWI). A small vessel disease and degenerative cortical changes were detected in T2 scans.

Diagnosis of CJD remains a challenge because of the large variability of the clinical symptoms especially in its early stages of disease. The Centers for Disease Control and Prevention (CDC) listed recognizable clinical features and paraclinical tests to supplement the replicable diagnostic criteria in vivo (table 1).

There is a high diagnostic accuracy of CSF real-time quaking-induced conversion but identified inflammatory brain disease as a potential source of (rare) false-positive results, indicating thorough consideration of this condition in the differential diagnosis of Creutzfeldt-Jakob disease [3].

Nowadays there are typical MR imaging patterns in sporadic CJD such as cortical and basal ganglia involvement with hyperintensity at DWI in the insula and cingulate (limbic lobe), involvement of the superior frontal gyri and the cortical areas near the midline [4]. The perirolandic area is usually spared. In 2020, a study investigating a large cohort with 770 patients with definite sporadic Creutzfeldt - Jakob disease applied an improved diagnostic index showing 92% sensitivity and 97% specifici [5].

Table 1. The CDC`s diagnostic criteria of CJD [2].

Diagnosis	Definite	Probable	Possible
Sporadic CJD	Diagnosed by standard neuropathological techniques; and/or immunocytochemically; and/or Western blot confirmed protease-resistant PrP; and/or presence of scrapie-associated fibrils.	Neuropsychiatric disorder plus positive RT-QuIC in cerebrospinal fluid (CSF) or other tissues OR Rapidly progressive dementia; and at least two out of the following four clinical features: myoclonus; visual or cerebellar signs; pyramidal/extrapyramidal signs; akinetic mutism. AND a positive result on at least one of the following laboratory tests: a typical EEG (periodic sharp wave complexes) during an illness of any duration; a positive 14-3-3 CSF assay in patients with a disease duration of less than 2 years; High signal in caudate/putamen on magnetic resonance imaging (MRI) brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR). AND without routine investigations indicating an alternative diagnosis.	Progressive dementia; and at least two out of the following four clinical features: myoclonus; visual or cerebellar signs; pyramidal/ extrapyramidal signs; akinetic mutism AND the absence of a positive result for any of the four tests above that would classify a case as "probable" AND duration of illness less than two years AND without routine investigations indicating an alternative diagnosis.
Iatrogenic CJD	Progressive cerebellar syndrome in a recipient of human cadaveric-derived pituitary hormone; or sporadic CJD with a recognized exposure risk, e.g., antecedent neurosurgery with dura mater implantation.		
Familial CJD	Definite or probable CJD plus definite or probable CJD in a first degree relative; and/or Neuropsychiatric disorder plus disease-specific PrP gene mutation.		

Table 2. Clinical subtypes of CJD [6]

Features	Subtypes		
	Heidenhain	**Brownell-Oppenheimer**	**Stern**
Symptoms and signs at onset	Isolated visual symptoms: poor vision; disturbed perception of colors or structures; optical distortions and hallucinations. All without any ocular disease. May also occur in genetic CJD.	Isolated cerebellar ataxia	Presenile dementia and sleep disturbances: inability to initiate and maintain sleep; frequent arousals; enacted dreams. Younger age at onset than the other groups.
Molecular genetic correlation	Most are MM-MV1 type. Rare cases due to MM 2C and MM 2C+1.	VV2	MM2 C*
Paraclinical tests	EEG: PSWCs. CSF analysis: t-tau and 14-3-3 protein levels increased.	EEG: absence of PSWCs. CSF analysis: 14-3-3 protein levels not elevated.	EEG: absence of PSWCs CSF analysis: 14-3-3 protein levels not elevated in most cases.
Imaging	80% show occipitoparietal hyperintensity at DWI or FLAIR	Cerebellar atrophy. Increased ADC ± BG and cortical findings at DWI	Hypoperfusion or hypometabolism at SPECT and PET No signal intensity alterations at DWI

Note: BG = basal ganglia, C = cortical, DWI = diffusion-weighted imaging, PET = positron emission tomography, PSWCs = periodic sharp wave complexes, SPECT = single photon emission computed tomography.
* This variant (MM2 thalamic) is virtually indistinguishable from fatal familial insomnia.

It is important to remember about mimicking disorders such as severe hypoxic ischemic encephalopathy, hypoglycaemia, autoimmune-mediated encephalopathy, encephalitis, hyperammonemia, mitochondrial disorders, extrapontine osmotic demyelination, thalamic abnormalities [6]. Their MR imaging features can mimic CJD imaiging patterns, especially a cortical ribbon sign (fig. 2), [7].

There are three main clinical subtypes of CJD: Heidenhain, Brownell - Oppenheimer, Stern (table 2), [6].

CONCLUSIONS

Described clinical cases correspond to the criteria of possible CJD according to CDC's Diagnostic Criteria for Creutzfeldt - Jakob Disease (2018). First clinical case presents a Heidenhain variant, second case - Brownell-Oppenheimer variant. The most recommended approaches to in vivo diagnosis of CJD are strict application of diagnostic criteria, careful interpretation of neurovisualization, EEG.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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