

Creutzfeldt-Jakob disease mimicking Lewy body dementia – a case report

Marta Nesteruk¹, Tomasz Nesteruk², Marzena Ułamek-Kozioł^{3,4},
Anna Holak-Puczyńska², Małgorzata Dorobek¹

¹ Department of Neurology, Central Clinical Hospital of the Ministry of Interior, Warsaw

² Department of Radiology, Central Clinical Hospital of the Ministry of Interior, Warsaw

³ First Department of Neurology, Institute of Psychiatry and Neurology, Warsaw

⁴ Laboratory of Ischemic and Neurodegenerative Brain Research,

Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw

Summary

Lewy body dementia and Creutzfeldt-Jakob disease are recognized on the basis of certain diagnostic criteria. However, common symptoms such as: dementia, extrapyramidal syndrome, psychotic disorders may cause difficulty to make the correct diagnosis especially in the early stage of the disease. Each of these diseases may have atypical onset. The further course and the appearance of other symptoms indicate a proper diagnosis. Electroencephalogram and examination of 14-3-3 proteins in cerebrospinal fluid are helpful in the differential diagnosis.

We present a case of a 66-year-old patient initially suspected of Lewy body dementia. On admission, psychomotor retardation, dysarthria, upper extremities dysmetria, extrapyramidal tension in the upper limbs, lower extremities ataxia, slow gait and unstable Romberg test were present. Mini-Mental State Examination (MMSE) score was 24/30. On neuropsychological assessment early stage of dementia was diagnosed. Anxiety-depressive symptoms were observed with periodic visual-auditory components. After less than 3 weeks there was a deterioration of neurological state. Dysarthria and lower limbs ataxia were increased, ataxia of the trunk appeared and psychomotor retardation got worse. There was significant progression of cognitive impairment, therefore complete neuropsychological examination was impossible to perform. MMSE score was 12/30 (12 points less than three months earlier). The course of the disease and additional tests results confirmed the diagnosis of sporadic Creutzfeldt-Jakob disease.

Key words: Creutzfeldt-Jakob disease, Lewy body dementia, progressive dementia

Introduction

Sporadic Creutzfeldt-Jakob disease (sCJD) most frequently affects patients aged 60–70 with inconsiderable predominance of females [1]. The disease lasts about 6–12 months. It usually begins with nonspecific symptoms such as depression, sleep disorders and weight loss [1, 2]. Dementia is present in the majority of patients. Many patients develop psychotic disorders, one of the most common are visual hallucinations. Further in the course of the disease pyramidal and extrapyramidal symptoms, myoclonus and cerebellar symptoms appear. Diagnostic criteria of probable sCJD include:

- (1) progressive dementia;
- (2) confirmation of at least 2 of 4 symptoms:
 - myoclonus,
 - visual or cerebellar symptoms,
 - pyramidal or extrapyramidal symptoms,
 - akinetic mutism;
- (3) Characteristic changes in electroencephalogram (EEG) or the presence of 14-3-3 proteins in cerebrospinal fluid (CSF);
- (4) Duration of illness less than 2 years.

If there are no changes in the EEG and the result of the 14-3-3 proteins is negative but the other criteria are met, possible sCJD is recognized. The 14-3-3 proteins are positive for 95% of patients with sCJD [1]. Periodic sharp and slow wave complexes (observed in 60–70% of patients) are typical electroencephalographic grafoelements, usually registered after 12 weeks of the disease onset [1, 2].

Lewy body dementia (LBD) most often affects patients aged 50–80 [3, 4]. The disease usually lasts 3–7 years [2]. Criteria for diagnosis of probable LBD include: dementia and at least 2 of 3 core symptoms:

- recurrent visual hallucinations,
- fluctuating cognitive disorders,
- parkinsonism [5].

If the patient has dementia and one of the three core symptoms, possible DLB is recognized.

Case report

A 66-year-old woman with hypertension and persistent atrial fibrillation was admitted to the Department of Neurology because of dizziness with imbalance increasing for several months. The patient experienced several falls. Memory disorders appeared and the speech became blurred. A few weeks before admission, the patient experienced

visual and auditory hallucinations; with proper execution judgment. The patient was hospitalized a month earlier in the Internal Medicine Department due to the transient left limbs numbness with dizziness and balance disorders. Transient ischemic attack was diagnosed.

On admission, psychomotor retardation, dysarthria, upper extremities dysmetria, extrapyramidal tension in the upper limbs, lower extremities ataxia, slow gait, and unstable Romberg test were present.

Magnetic resonance imaging (MRI) revealed cortical atrophy in the frontal and temporal lobes, without signs of ischemia and focal lesions (Figure 1).

Diagnosis was supplemented with cerebrospinal fluid examination, obtaining a clear fluid. CSF examination revealed cytos 3 cells/ μ l, protein 47.2 mg/dl, glucose 66 mg/dl, *Borrelia burgdorferi* antibodies were negative. CSF was also examined for 14-3-3 proteins, β -amyloid and tau proteins.

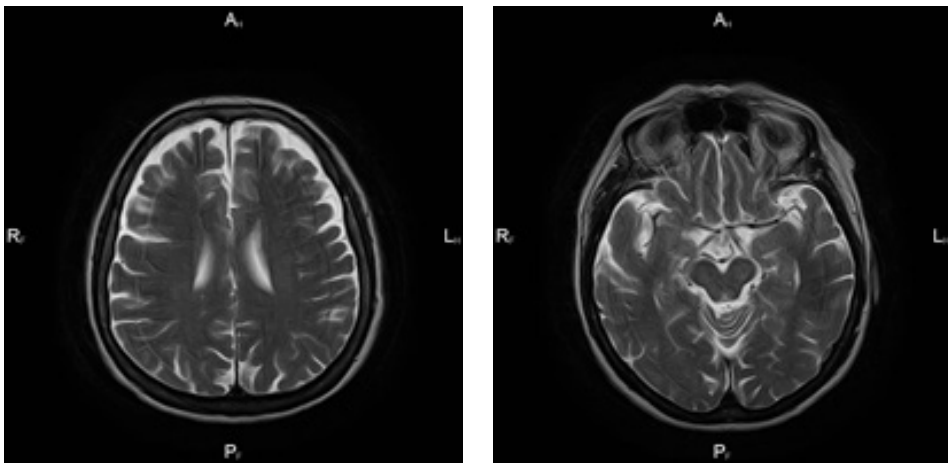


Figure 1. T2-weighted images; cortical atrophy of the temporal and frontal lobes

Groups and a series of slow waves with a slight left sided prevalence, against the background of the preserved basic activity in both temporal regions, were registered in EEG.

The Mini-Mental State Examination (MMSE) score was 24. On neuropsychological assessment early stage of dementia was diagnosed (deficits of executive functions accompanied by deficits of attention and episodic memory). Anxiety-depressive

symptoms were observed with periodic visual-auditory components. Antidepressant treatment was modified (mianserin and tianeptine) by a psychiatrist.

During hospitalization the patient had physiotherapy, with improvement, although the symptoms were fluctuating, with periodic exacerbation of imbalance. The suspicion of Lewy body dementia was made (rivastigmine treatment was started). The patient, in good general condition, was transferred to the Neurological Rehabilitation Department for further motor rehabilitation. After less than 3 weeks of rehabilitation, the patient returned to the Department of Neurology due to deterioration of neurological state. Dysarthria and lower limbs ataxia were increased, ataxia of trunk appeared and psychomotor retardation got worse. There was a significant progression of cognitive impairment (therefore complete neuropsychological examination was impossible to perform). The MMSE score decreased from 24 to 12. There were no new lesions in brain MRI. A positive result of the 14-3-3 proteins was obtained (determined during the previous hospitalization). Moreover pathologically elevated tau proteins concentration in CSF were obtained: total tau protein over 2,261.9 pg/ml (cut-off for our laboratory above 277) and phosphorylated tau protein 82.8 pg/ml (cut-off for our laboratory above 55). Value of β -amyloid was normal, high. In control EEG, changes in both temporal regions with marked left sided prevalence were registered in the form of groups and a series of slow waves which were in the left hemisphere periodically accompanied by low voltage sharp waves. The patient fulfilled the criteria of probable Creutzfeldt-Jakob disease (fast progressive dementia, present cerebellar and extrapyramidal symptoms, duration of illness less than 2 years, positive result of 14-3-3 proteins in CSF). There was no family history of CJD. Rivastigmine treatment was withdrawn. The patient was discharged in a stable condition under the care of her family.

After about 2 months, the patient was admitted to the Gastroenterological Department due to dysphagia. On admission the patient was unable to walk, conscious but without logical verbal contact. Laboratory tests revealed elevated inflammatory parameters, electrolyte abnormalities, elevated aminotransferases, and elevated renal function parameters – hypoproteinemia and hypoalbuminemia. The patient received intravenous liquids and electrolytes supplementation. The patient died after a few days of hospitalization.

Discussion

At the beginning of the disease, the differentiation between CJD and DLB can cause difficulties because of several common symptoms: dementia, extrapyramidal syndrome, psychotic disorders (most often visual hallucinations). All these symptoms were present in the described patient, however, during the first hospitalization, it was not possible to diagnose rapidly progressive dementia because at that time only early

stage of dementia was diagnosed. We already considered the possibility of sCJD, that is why the CSF was sent to estimate 14-3-3 proteins. After less than 3 weeks the patient became severely demented. The MMSE result decreased rapidly from 24 to 12 points. In the meantime positive result of 14-3-3 proteins in CSF became available. At that stage we could diagnose sCJD.

Myoclonus as well as akinetic mutism can appear in both these diseases [2]. The further course of the disease and the results of additional tests indicate a higher probability of CJD or DLB [6, 7]. Not only EEG and assessment of 14-3-3 proteins in CSF are important, but also MR images of the brain [2, 8, 9]. Some authors even recommend inclusion of characteristic MRI lesions in the diagnostic criteria for sCJD – detection of either hyperintensity in the basal ganglia (both in the caudate nucleus and the putamen) or in at least two cortical regions [9]. However, in our patient ‘radiological criteria’ were not met.

Sometimes histopathological examination shows a different result despite meeting the criteria for probable CJD. It is important to take into account Alzheimer’s or LBD’s etiology, especially when the result of 14-3-3 proteins is negative or when CSF is not tested [10]. Elevated total tau protein could be a parameter confirming CJD, as was in the case of our patient [11, 12].

It is also important that CJD-specific EEG changes can also occur in LBD, but without meeting the other criteria CJD cannot be recognized [13]. Due to the similarity of some clinical symptoms, there are also cases where CJD is found to be LBD [4, 6, 8, 14] or sometimes Alzheimer’s disease (AD) [15]. There may also be cases where, apart from the histopathological changes typical of CJD, Lewy bodies are present (as well as argyrophilic grains and AD-specific changes) [16].

It is estimated that about 30% of CJD cases are atypical [1]. Sometimes, the disease may manifest with isolated psychiatric symptoms such as anxiety [17], which is related to the introduction of anxiolytic therapy which always proves ineffective.

Conclusions

Differentiating CJD from LBD can cause significant diagnostic difficulties especially in the early stages of the disease because all symptoms are not present at the same moment, and many symptoms are common for both diseases. Diagnostic vigilance and periodic assessment of the patient are very important to avoid mistake.

References

1. Krasnianski A, Meissner B, Heinemann U, Zerr I. *Clinical findings and diagnostic tests in Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease*. *Folia Neuropathol.* 2004; 42(Suppl B): 24–38.
2. Tartaglia MC, Johnson DY, Thai JN, Cattaruzza T, Wong K, Garcia P et al. *Clinical overlap between Jakob-Creutzfeldt disease and Lewy body disease*. *Can. J. Neurol. Sci.* 2012; 39(3): 304–310.
3. Ransmayr G. *Dementia with Lewy bodies: Prevalence, clinical spectrum and natural history*. *J. Neural. Transm. Suppl.* 2000; 60: 303–314.
4. Saint-Aubert L, Pariente J, Dumas H, Payoux P, Brandel JP, Puel M et al. *Case report of Lewy body disease mimicking Creutzfeldt-Jakob disease in a 44-year-old man*. *BMC Neurol.* 2016; 16: 122. Doi: 10.1186/s12883-016-0643-y.
5. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H et al. *Diagnosis and management of dementia with Lewy bodies: Third report of the DLB Consortium*. *Neurology.* 2005; 65(12): 1863–1872. Doi: 10.1212/01.wnl.0000187889.17253.b1.
6. Plessis du DG, Larner AJ. *Phenotypic similarities causing clinical misdiagnosis of pathologically confirmed sporadic Creutzfeldt-Jakob disease as dementia with Lewy bodies*. *Clin. Neurol. Neurosurg.* 2008; 110(2): 194–197.
7. Marin LF, Felício AC, Bichuetti DB, Santos WA, Borges LR, Buainain RP et al. *Clinical findings in Creutzfeldt-Jakob disease mimicking dementia with Lewy bodies*. *Arq. Neuropsiquiatr.* 2008; 66(3B): 741–743.
8. Tsvigoulis G, Bonakis A, Papatthanasiou MA, Chondrogianni M, Papageorgiou SG, Voumvourakis K et al. *Magnetic resonance imaging reveals Creutzfeldt-Jakob disease in a patient with apparent dementia with Lewy bodies*. *J. Neurol. Sci.* 2014; 340(1–2): 130–132. Doi: 10.1016/j.jns.2014.03.010.
9. Zerr I, Kallenberg K, Summers DM, Romero C, Taratuto A, Heinemann U et al. *Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease*. *Brain.* 2009; 132(Pt 10):2659–2668. Doi: 10.1093/brain/awp191. Erratum in: *Brain.* 2012; 135(Pt 4): 1335.
10. Krvavica A, Morović M, Mrden A, Mislov D, Duka-Glavor K, Ivanac K et al. *Alzheimer and Lewy body pathology or Creutzfeldt-Jakob disease*. *Coll. Antropol.* 2014; 38(2): 701–704.
11. Dupiereux I, Zorzi W, Quadrio I, Perret-Liaudet A, Kovacs GG, Heinen E et al. *Creutzfeldt-Jakob, Parkinson, Lewy body dementia and Alzheimer diseases: From diagnosis to therapy*. *Cent. Nerv. Syst. Agents Med. Chem.* 2009; 9(1): 2–11.
12. Jacquin A, Deramecourt V, Bakchine S, Maurage CA, Pasquier F. *Unusual features of Creutzfeldt-Jakob disease followed-up in a memory clinic*. *J. Neurol.* 2014; 261(4): 696–701. Doi: 10.1007/s00415-014-7246-6.
13. Doran M, Larner AJ. *EEG findings in dementia with Lewy bodies causing diagnostic confusion with sporadic Creutzfeldt-Jakob disease*. *Eur. J. Neurol.* 2004; 11(12): 838–841.
14. Ukai K, Matsuo K, Nakamura R, Sobue G, Kosaka K, Shibayama H et al. *A case of dementia with Lewy bodies that temporarily showed symptoms similar to Creutzfeldt-Jakob disease*. *Psychogeriatrics.* 2010; 10(4): 201–205.
15. Tschampa HJ, Neumann M, Zerr I, Henkel K, Schröter A, Schulz-Schaeffer WJ et al. *Patients with Alzheimer's disease and dementia with Lewy bodies mistaken for Creutzfeldt-Jakob disease*. *J. Neurol. Neurosurg. Psychiatry.* 2001; 71(1): 33–39.
16. Fernández-Vega I, Ruiz-Ojeda J, Juste RA, Geijo M, Zarranz JJ, Sánchez Menoyo JL et al. *Coexistence of mixed phenotype Creutzfeldt-Jakob disease, Lewy body disease and argyrophilic*

grain disease plus histological features of possible Alzheimer's disease: A multi-protein disorder in an autopsy case. Neuropathology. 2015; 35(1): 56–63. Doi: 10.1111/neup.12150.

17. Liu W, Lu Y, Zhong G, Jiang B, Pan Z. *Clinical and MRI evaluation of anxiety as the first symptom of sporadic Creutzfeldt-Jakob disease: A case report.* Exp. Ther. Med. 2016; 11(4): 1513–1515.

Address: Marta Nesteruk
Central Clinical Hospital of the Ministry of Interior
Department of Neurology
02-507 Warszawa, Wołoska Street 137
e-mail: msuchcicka@gmail.com