Rapidly progressive dementia with psychosis caused by CJD

Georgios Mousailidis MD, MSc, Carlo Lazzari MD, Shafalica Bhan-Kotwal MD, MSc, Ahmed Shoka MD

Rapidly progressive dementias are conditions that typically cause dementia over weeks or months. They are a particular challenge for psychiatrists and neurologists as the differential diagnosis is often different from the more typical, slowly progressive dementias. Early and accurate diagnosis is essential, as many of the aetiologies are treatable. Creutzfeldt-Jakob Disease (CJD) is a very rare, progressive and lethal illness caused by prions. Here, the authors present a case of CJD that manifested itself as rapidly progressive dementia, with psychosis, without any neurological signs and symptoms initially.

The term ‘rapidly progressive dementia’ (RPD) encompasses a heterogeneous group of medical conditions that cause progressive cognitive impairment, leading to functional disability or death within a short period of time, usually less than 24 months. Creutzfeldt-Jakob disease (CJD) represents an important cause of RPD. However, many patients with RPD may present with other diagnoses, mainly non-prion neurodegenerative (np-ND) diseases like Alzheimer’s disease (AD) and dementia with Lewy bodies (DLB) or non-neurodegenerative (non-ND) treatable conditions.

Clinical diagnosis of RPD is based on an extensive work-up that includes brain magnetic resonance imaging (MRI), electroencephalography (EEG) and blood and cerebrospinal fluid (CSF) studies, often requiring the determination of metabolic, infectious and autoimmune test panels. Dementia signs in general (ICD-10) include ‘loss of the ability to think, remember, learn, make decisions, and solve problems’. More specifically, dementia affects memory, language, vision, cognition, attention, self-care, emotions and personality.

CJD is considered a transmissible spongiform encephalopathy (or prion disease), which can cause dementia among other symptoms. There are four main types of CJD: 1. Sporadic CJD (sCJD) with prevalent cognitive deterioration and myoclonus. The precise cause of sCJD is unclear, but it has been suggested that a normal brain protein changes (‘misfolds’) and turns into a prion. 2. Familial CJD (fCJD) with autosomal dominance inheritance and with a duration of five to eleven years characterised by insomnia, dementia and autonomic symptoms. 3. Iatrogenic CJD (iCJD) caused by therapy with growth hormone, corneal transplantations and use of dural grafts, and finally 4. Variant CJD (vCJD) from consumption of contaminated beef and characterised by young age of onset and behavioural, psychological and sensory symptoms.

We will present a case of CJD that manifested as rapidly progressive dementia, with psychosis, without any neurological signs and symptoms initially.

Presentation
A 55-year-old white British man was referred to general adult psychiatric services due to a sudden deterioration of his mental health. He previously lived abroad for seven years in a rural area of southern Europe. The person under investigation was never in contact with mental health services before. He used to be a heavy user of alcohol but stopped drinking some years ago. There was negative family history for dementia and acquired diseases and negative history for cranial traumas. At some point his family reported that he had gone missing for approximately one month. At this time his family was contacted by one of his friends who was very concerned about his mental state. He agreed to put him on a plane home to the UK, and his family would meet him at the airport. When his family met him, they found that he had been severely neglected and had lost weight. He was reviewed by a GP who found that he was dehydrated and low in folic acid; there was nothing else of concern around his physical health. His family mentioned that at this time he was very muddled, he was hearing voices and hallucinating. He reported that his neighbour had been contaminating his water with blood.

Following his assessment, he was admitted to our general adult psychiatric ward as he was very vulnerable and had no capacity or insight into his mental illness. His Mini
Mental State Examination (MMSE) on admission was remarkably low, scoring 10/30 even with some help and prompting. On the ward, he showed evidence of psychosis, responding to visual and auditory hallucinations. He was having conversations with his own image in the mirror and there were bouts of disinhibited behaviour, suggestive of frontal lobe syndrome (FLS). At the same time, he showed marked cognitive deficits with a complete cancellation of recent and remote memory, with time, place and person disorientation. Furthermore, his cognitive functions showed marked and severe impairment of attention, concentration with lack of judgement and abstract thinking. He also had word finding difficulties, severe reduction in verbal fluency with poverty of speech and progressive mutism, which occurred some months later. Occasionally his mood was very low and he was unable to do simple everyday tasks or take care of himself. As the time progressed he could not initiate tasks without prompting, requiring help with his food and dressing. The diagnostic criteria for dementia according to ICD-10 were all satisfied.

On admission his cranial nerve examination was normal. Muscle strength, tone and bulk as well as reflexes, coordination, sensory function and gait were normal as well. No abnormal movements were recorded and no extrapyramidal symptoms were observed. His ECG was normal sinus rhythm with a slight intraventricular conduction delay, the QTc was 436ms and the heart rate was 59 beats per minute. His modified early warning (MEW) score was always within the normal ranges of ‘0’ indicating no major concerns in his cardiorespiratory, neurological and metabolic systems. After almost six months of the disease’s onset he started having some myoclonic jerks. Later on he developed a profound ataxic gait and started leaning to the left.

An EEG, done a few days after admission, was non-specific and showed subclinical diffused epileptogenic spikes in the brain. For this reason, he was started on carbamazepine 100mg twice daily. A short course of sertraline was introduced to reduce possible depression, but was stopped due to increased disinhibition, which was improved after sertraline discontinuation. Additionally, in order to reduce the psychotic symptoms, he was prescribed risperidone 2mg twice daily. This medication appeared to control the psychotic symptoms well.

**Investigation**

Biochemical investigations included: anti-N-methyl-D-aspartate (anti-NMDA) antibodies, tests for malaria, syphilis, human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), lymphocyte subpopulations, autoantibodies, rheumatoid factor, full blood count, and complete blood biochemistry, which were all normal.

Brain CT scan showed atrophic changes in the occipital and parietal lobes. A positron emission tomography (PET) scan showed a diffuse pattern of hypometabolism bilaterally affecting frontal, temporal, parietal and occipital lobes with temporal regions more affected (not supporting an acute illness). MRI showed a diffused cortical atrophy and extensive cortical ribboning. EEG reported non-specific widespread encephalopathy with moderately frequent sharp waves and ill-defined component over the anterior and temporal regions of both hemisphere, particularly over the right temporal region. The final EEG diagnosis indicated a non-specific encephalopathy with potential epileptogenic foci.

**Discussion**

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)\(^\text{12}\) the rapidly declining memory, attenuating execution of tasks, and growing difficulty in activities of daily living (ADL) performance could be noted in the patient just within a four-month interval are typical symptoms and signs of dementia. Neurodegenerative disorders, such as Alzheimer’s disease, usually cause slowly progressive dementia. Different disorders, such as infectious, neoplastic, metabolic, autoimmune and vascular conditions can provoke rapidly progressive dementia.\(^\text{13}\)

Based on the morbidity history and observations in our psychiatric ward, we concluded that the main diagnosis for the patient was dementia rather than delirium. The patient’s cognitive function declined dramatically in just a few months, and it did not favour a primary degenerative disease, such as dementia of the Alzheimer’s type. In the clinical case investigated, a team of specialists coordinated their efforts to speculate on symptoms, causes, and needed investigations.

Typical investigations when sCJD is suspected, include EEG, which can show episodic sharp-wave complexes; CSF examination, which shows proteins like 14-3-3, S100b and neurone-specific enolase\(^\text{14,15}\) and brain MRI techniques, which have altered the diagnostic approach in sCJD to a considerable degree. Early in the disease course, fluid attenuation inversion recovery (FLAIR) and diffusion weighted imaging (DWI) sequences demonstrate hypersignals in the striatum (caudate and putamen) and thalamus as well as ‘cortical ribboning’
(hypersignal delineating the cortex) in the parietal, temporal and frontal cortices. MRI with these sequences (DWI being more sensitive than FLAIR) is highly sensitive and specific (92 and 94%, respectively) for the diagnosis of sCJD. Moreover, PET can show a generalised hypometabolism due to diffuse atrophy of the brain. The diagnosis of sCJD is based on the World Health Organization (WHO) clinical diagnostic criteria, which have been updated in 2009 to include the aforementioned typical MRI findings. However, a definitive diagnosis of sCJD can be made only after the demonstration of prions in the brain. Clinical criteria for probable sCJD require the existence of dementia with a progressive course and at least two of the following: pyramidal and/or extrapyramidal symptoms; visual or cerebellar symptoms, myoclonus; ataxia, dysesthesia or a movement disorder, appear later. Only rarely does the EEG in vCJD show the periodic sharp waves that characterise sCJD. vCJD is characterised by the presence of the pulvinar sign on the MRI (hyperintensity of the pulvinar relative to the anterior putamen). Definitive diagnosis of vCJD requires demonstration of prions in the tonsillar tissue.

Overall, sCJD has been characterised by prominent neurological symptoms, while vCJD is described as primarily psychiatric in presentation and course. In this case the patient presented initially with rapid onset dementia, with psychotic symptoms. Only after almost six months of the disease’s onset, he started having some myoclonic jerks. Later on he developed profound ataxic gait and started leaning to the left. We suspected that the most probable diagnosis for this patient was sCJD as the patient had dementia, positive MRI findings for sCJD and progressively he developed myoclonus and mutism. His ataxic gait could have been the result of a cerebellar deficit. There was no history of an iatrogenic exposure to the CJD agent. In view of his initial symptoms of rapidly progressive dementia with psychosis, this would primarily favor vCJD as the most likely diagnosis. However, it was felt this would be highly unlikely due to the patient’s age and that the pulvinar sign not being present on the patient’s MRI.

Conclusion
The evaluation of a patient with a RPD can be challenging and time consuming. Therefore, it is important to have a structured approach to the diagnostic evaluation. Diagnosis of many forms of human prion diseases and distinction from other RPD has become easier and more accurate because of the more common use of imaging techniques, mainly MRI. This case illustrates the importance of thorough evaluation on patients with rapidly progressive dementia without any neurological signs. Therefore, when assessing patients showing early rapid deterioration of cognitive function, with psychosis not associated with neurological symptoms, the general psychiatrist should not assume a diagnosis of primary degenerative dementia such as Alzheimer’s disease or frontotemporal dementia. Brain CT scan and other imaging examinations, such as brain MRI should also be arranged for more comprehensive evaluation.

Declaration of interests
No conflicts of interest were declared.

Dr Mousaidis is CT2 Doctor in Training. Dr Lazzari is Specialist Registrar in Psychiatry. Dr Bhan-Kotwal is Consultant Old Age Psychiatrist, and Dr Shoka is Consultant Psychiatrist; all at The Lodge, Essex Partnership University NHS Foundation Trust.
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References