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The different faces of Creutzfeldt-Jacob Disease CJD in psychiatry

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ABSTRACT

Objective: Creutzfeldt-Jacob Disease (CJD) is a rapidly progressive spongiform disease of the central nervous system. Psychiatric symptoms, though considered rare, can be the presenting symptoms of CJD and impose diagnosis difficulties. We reviewed prospectively our database to identify the frequency of psychiatric symptoms as identifying symptoms among our community.
Methods: We included all patients in Sheba Medical Center who were diagnosed with CJD between the years 2006 and 2012. Data were collected retrospectively.
Results: Twenty-three patients with CJD were admitted to our hospital during this 6-year period. Among them, 10 (44%) were diagnosed first as "psychiatric patients" due to psychiatric presenting symptoms.
Conclusion: In our series, the frequency of misleading psychiatric symptom was 44%. Clinicians should therefore include CJD in their differential diagnoses of new onset dementia, particularly when associated psychosis and depression symptoms persist and worsen, despite standard psychiatric treatments.

Initially described in 1921, Creutzfeldt-Jakob Disease (CJD) is a rare, rapidly progressive spongiform neurodegenerative brain disease [1]. The case rate is 1–2 per million annually, and symptoms usually start around the age of 60 [2]. The latency period can last years, but time from onset of symptoms to death is typically less than a year [3]. Classic features include dementia, ataxia and myoclonus, but can initially present with nonspecific psychiatric symptomatology such as fatigue, anxiety or a change in personality in about one third of cases [4].

Four categories of CJD have been described [5]:

- Sporadic CJD, (sCJD) – spontaneous protein transformation or somatic gene mutation, responsible for 85% of the cases.
- Hereditary/Familial CJD – due to familial mutations which runs in families, responsible for 15% of cases.
- Acquired CJD – (less than 1% of cases) caused by contact with infected tissue. This human-to-human prion transmission happens either by ingestion of human brain in cannibalistic rituals (kuru) or might happen during a medical procedure (e.g., dural graft implants). This type is now extremely rare.
- Variant CJD – caused by ingestion of meat products from animals with bovine spongiform encephalopathy (BSE). This subtype has received increased media attention due to concerns regarding BSE or mad cow disease, which have been found in US and Canadian cattle populations.

Initial presentation of sCJD can be severe depression, psychotic states or other "psychiatric" presentation, but is considered uncommon [2]. A review of 126 cases of CJD over a 25-year period [6], found six who were hospitalized for symptoms of depression during their course of disease. One misdiagnosed as psychosis have been documented in several case reports [7–10]. Our study explores the frequency of psychiatric symptoms as presenting symptoms in our hospital, serving mainly Jewish community, in the center of Israel.

1. Methods

1.1. Subjects

This study was an institutional review board (IRB)-approved retrospective medical record review of all patients (23) diagnosed with CJD found in Tel Hashomer hospital, between the years 2006 and 2012. This record system includes inpatients admitted to the hospital. The subjects were identified using encoded diagnosis of CJD (Fig. 1).

1.2. Inclusion criteria

The criteria used for inclusion of the patients as positive for CJD were taken from those of the Center For Disease Control And Prevention diagnostic criteria for CJD [11] (2010) and the World Health Organization criteria [12] (1998) (for the cases diagnosed prior to 2010). We included in the review only the patients who meet the criteria for definite or probable CJD. Definite cases were diagnosed by standard neuropathological techniques; and/or immunocytochemically; and/or Western blot confirmed protease-resistant PrP (protein resistant perion protein); and/or presence of scrapie-associated fibrils. Probable cases were diagnosed by rapidly progressive dementia; and at least two out of the following four clinical features: myoclonus, visual or cerebellar

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signs, pyramidal/extrapyramidal signs, akinetic mutism and a positive result on at least one of the following laboratory tests: (a) a typical Electroencephalography (EEG) (periodic sharp wave complexes) during an illness of any duration; (b) a positive 14-3-3 cerebrospinal fluid (CSF) assay in patients with a disease duration of less than 2 years; and (c) magnetic resonance imaging (MRI) high signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging or fluid-attenuated inversion recovery and without routine investigations indicating an alternative diagnosis.

1.3. Exclusion criteria

Patients were excluded if they did not have adequate documentation to meet criteria for definite or probable CJD. Patients with possible CJD were excluded. No neuropathological verification was available in any of the excluded possible cases.

1.4. Data collection

Each subject included in this study had their medical record comprehensively reviewed. Due to the retrospective and chart review nature of this study, it was not possible to use a formal, objective psychiatric assessment. However, when neuropsychiatric symptoms were noted, they were categorized as psychotic symptoms, depressive symptoms, anxiety symptoms, behavioral dyscontrol/agitation, sleep disturbances or other. The categorization and timing of symptoms were based on the available notes as documented by the treating teams and family members.

In addition to categorization of the observed manifestation, treatments offered to the patients during the course of illness were documented.

The medications were classified as anxiolytics/hypnotics, anticonvulsants/mood stabilizers, antidepressants, antipsychotics or other treatment interventions noted.

Prodromal or presenting symptoms were defined as the clinical signs and symptoms that led the patient to seek medical attention and were retrospectively recognized as the initial manifestations of the disease course.

2. Results

2.1. Subjects

Twenty-three patients with CJD (probable or definite) were admitted to our hospital during the years 2006–2012. Among them, 10 (44%) were diagnosed first with psychiatric disease. Six of the cases (26%) had positive family history of CJD. The rest, 7 patients (30%) were admitted for evaluation, which found out CJD. Overall, the majority of the patients (44%) were diagnosed with "psychiatry disease," or referred for a psychiatrist evaluation, prior to the diagnosis of CJD.

3. Case reports

3.1. Psychosis

A. H. is a 59-year-old female, Libyan origin, married and the mother of four children. Family genetic is significant for sister suffering from schizophrenia.

Recent (3 months prior to her admission) history is significant for a diagnosis of psychosis, developed after the age of 58, which was treated with antipsychotic (Thioridazin). Simultaneously, extrapyramidal signs appeared and difficulties in memory. When she became mutistic and stopped eating and drinking, a diagnosis of catatonic schizophrenia was made, and she was admitted to a psychiatric department by forced administration and treated with electroconvulsive therapy (ECT) due to diagnosis of catatonic schizophrenia, with no improvement. Parallel to the treatment in the psychiatric ward, she was examined repeatedly by neurologist consultant, due to the atypical presentation (i.e., severe extrapyramidal signs and memory decline in late onset psychosis), and an lumbar pancture (LP) and MRI was made. The MRI findings demonstrated a characteristic picture of CJD, sporadic type.

I. L. is a 52-year-old female, married and the mother of four children, worked as an advertising director until recently. Three months prior to her admission, for the first time in her life, a confusional and psychotic state developed. She was brought to the Emergency Room (ER) due to changes in appetite and sleep. In the ER, she demonstrated signs of acute psychosis (whisper instead of talking since she was sure someone was listening, and tried to make her daughter leave home since she was sure her daughter was against her). She was admitted in the psychiatric ward, in forced administration, due to uncontrolled behavior, agitation and poor eating (since she was sure the food is poisoned). To control her behavior, she was treated with sedative and antipsychotic medication. Simultaneously, extrapyramidal signs appeared. Due to the atypical presentation of psychosis (i.e., late onset and bizarre psychosis, extrapyramidal signs), an MRI and EEG was made, both demonstrated a picture typical for CJD, alongside with the discovery of Tau proteins in LP.

3.2. Mood changes

R.D. is a 65-year-old male, German origin, previously highly functioning, married and a father of six and worked until recently.

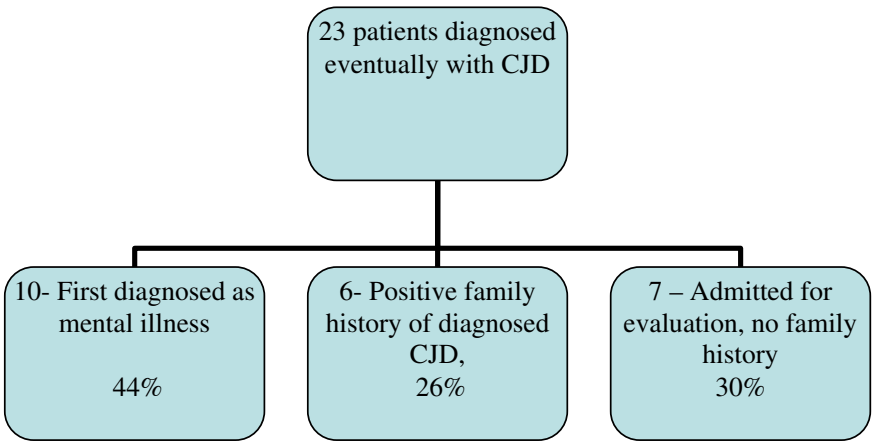

Fig. 1. Distribution of the patients diagnosed with CJD.