CASE REPORT

Sporadic Creutzfeldt-Jakob disease (sCJD) with asymmetric findings

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SUMMARY

We report a case of a patient with probable Creutzfeldt-Jakob disease (CJD) who had psychiatric manifestation in the form of withdrawn depressive behaviour at the onset, followed by rapidly progressive ataxia, parkinsonism, mutism and cognitive decline with generalised asynchronous multifocal myoclonic jerks. His EEG exhibited focal (lateralised) periodic triphasic sharp waves on the background of generalised delta slowing, which later on became more generalised. MRI of the brain showed hyperintensity in basal ganglia with cortical ribbon sign in bilateral frontal region. Clinical course showed progressive deterioration to an akinetic-abulic stage. He died 2 months after the onset of symptoms.

BACKGROUND

Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare and fatal degenerative disease resulting in rapidly progressive cognitive decline. Clinical diagnosis of sCJD can be made by using the WHO criteria, University of California San Francisco (UCSF) diagnostic criteria or MRI-CJD Consortium (MCC) diagnostic criteria.¹⁻³ Lateralised clinical, EEG and MRI findings are not uncommon in sCJD.⁴ Nevertheless, the diagnosis of sCJD with prominent focal manifestations in EEG and/or MRI may be missed, no matter which criteria is used. We report a case of a patient with probable CJD who had psychiatric manifestation in the form of withdrawn depressive behaviour at the onset, followed by rapidly progressive ataxia, parkinsonism, mutism and cognitive decline with generalised asynchronous multifocal myoclonic jerks. His initial EEG exhibited focal (lateralised) periodic triphasic sharp waves which later became generalised.

CASE PRESENTATION

A 58-year-old man was brought to the OPD with a history of withdrawn behaviour 10 days after he was scolded and humiliated in front of a large gathering, at a marriage ceremony of one of his close relatives. During those 10 days, the family noticed progressive imbalance while walking and sudden low amplitude jerky movements of the limbs. There was no history of fall. His sleep was normal and there was no history of hallucinations or delusions. There was no history of psychiatric disorders. There was no history of surgery or blood transfusions. He was not on any drugs. The family had attributed his symptoms to the particular incident of being humiliated at the function and felt that it

was stress related. He was admitted and evaluated. During the initial 2 days after admission, he was responsive though very slow and had reduced spontaneous speech. He felt no associated vertigo, diplopia, dysarthria and dysphagia. On examination, there was slowness in communication, impaired vigilance, reduced spontaneous speech and impaired memory. There was apraxia. He had gaze-evoked nystagmus, slow saccades and broken pursuit horizontally. He had mask-like facies, significantly asymmetric cogwheel rigidity, release reflexes and cerebellar signs, predominantly on his left side. There was no limb weakness. He had generalised asynchronous multifocal myoclonic jerks. He had rapid worsening, and clinical course speedily precipitated into an akinetic-abulic stage over 1 week and he could not sit without support and became incontinent of urine. Moreover, the multifocal asynchronous myoclonic jerks became very frequent to several in a minute. He was considered to have a rapidly progressive cognitive decline with parkinsonism and cerebellar involvement.

INVESTIGATIONS

His routine investigations such as haemogram, liver and renal function tests and serum electrolytes were normal. Random blood sugar, thyroid function tests and antithyroid antibodies were normal. Basic paraneoplastic workups such as ultrasonography (USG) of the abdomen, X-ray of the chest, prostatic-specific antigen and stool routine examination were normal.

His EEG showed generalised ϕ/δ slowing with predominantly right-sided triphasic sharp wave complexes that were periodically repeating at 1/s, not synchronous with myoclonic jerks (figure 1). Fluid attenuated inversion recovery (FLAIR) MRI sequence showed hyperintensity in the caudate nucleus and gyriform hyperintensity along the medial frontal gyrus and anterior cingulate gyrus (figure 2). Subsequent EEG performed after a week showed progression to diffuse δ slowing along with generalised sharp wave complexes repeating at 1/s (figure 3). His EEG, showing triphasic periodic sharp waves at 1/s, consolidated the diagnosis of probable CJD as per the WHO criteria (1998), UCSF 2007 criteria and even the MCC criteria, which accommodated his MRI findings as well.¹⁻³ A further diagnostic workup in the form of cerebrospinal fluid (CSF) 14-3-3 protein and brain biopsy was kept in plan, but could not materialise due to logistical constraints.

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Figure 1 EEG on admission showing lateralised periodic triphasic sharp waves (right hemisphere).

DIFFERENTIAL DIAGNOSIS

- ▶ Viral encephalitis
- ▶ Paraneoplastic disorder
- ▶ Depression
- ▶ Peripheral vertigo
- ▶ Alzheimer's disease
- ▶ Stroke
- ▶ Dementia, non-specified
- ▶ Central nervous system vasculitis
- ▶ Peripheral neuropathy
- ▶ Hashimoto encephalopathy⁵

Figure 2 EEG after 1 week showing generalised periodic sharp wave complexes.

Figure 3 MRI of the brain axial fluid-attenuated inversion recovery (FLAIR) sequence showing hyperintensity of the right caudate nucleus, medial frontal and anterior cingulate gyrus.

TREATMENT

Clonazepam was given for controlling myoclonic jerks, but there was only minimal response. He was subsequently discharged, as the relatives wished, after explaining the prognosis of the disease.

OUTCOME AND FOLLOW-UP

The patient died 2 months after the disease onset.

DISCUSSION

This patient had sCJD showing asymmetric features clinically and in EEG. In addition, the patient had psychiatric manifestations as prominent symptoms at the onset of the illness. We present this case to stress the fact that significant asymmetry of features (clinical and EEG) may be seen in case of sCJD.

The diagnosis of sCJD is made on the basis of the WHO criteria (1988), UCSF diagnostic criteria (2007) and MCC diagnostic criteria (2009).¹⁻³ If we strictly adhere to the WHO criteria, one may fail to recognise sCJD particularly in the early stages because focal findings may predominate and the classic red flag for CJD—bihemispheric periodic sharp wave complexes (PSWCs)—may not be present in the EEG. In our case, the EEG initially showed unilateral discharges in the form of periodic lateralised epileptiform discharges (PLEDs). However, after 1 week, EEG evolved into typical PSWCs. UCSF criteria added cortical and subcortical MRI hyperintensities to the WHO criteria and expanded the definition of positive EEG to include periodic epileptiform discharges other than PSWCs, including PLEDs. MCC criteria, which is the latest of all, retains the MRI criteria; however, it defines the positive EEG as typical PSWCs.³ In theory, if we apply these two criteria in place of WHO criteria, the diagnostic yield will improve. However, prominent asymmetric manifestations can still confuse the clinicians and result in misdiagnosis.

EEG is an important diagnostic tool in dementia, particularly when morphological lesions are not immediately apparent in MRI and in cases of rapidly progressive disease. Several case series have studied the conversion and evolution of EEG findings in sCJD with the clinical course. Findings such as runs of

frontal intermittent rhythmic delta activity (FIRDA), PSWCs, α coma and disappearance of PSWC have all been reported.⁶ Characteristic and typical EEG findings in CJD are bisynchronous periodic sharp waves.⁷ However, while interpreting the EEG in a patient with suspected sCJD, one should be aware that PLEDs can be seen and are not against the diagnosis of sCJD, as in our case. Typical 1/s PSWC becomes conspicuous during the course of the disease and a sensitivity of 67% and specificity of 86% are obtained if periodicity is diligently looked for and emphasised.⁷

Studies have shown that PSWC occurs within 12 weeks of the onset of the illness in 88% of patients with CJD who had comparable clinical and neuropathological findings, and its absence should be considered as a strong evidence against CJD diagnosis, unless in rare subtypes of those with long duration.⁸ Development of PSWCs in EEG in a case of CJD may be the beginning of a rapid downhill course.⁹ Periodic complexes are important in the diagnosis of sCJD, since biopsy and 14-3-3 CSF protein assay are fraught with logistical constraints and some patients may not have any MRI abnormalities.¹⁰

Lateralisation in CJD in the form of clinical symptoms, EEG and MRI findings has been described previously. Cambier *et al*⁴ described eight cases of CJD seen in Mayo clinic with focal EEG changes, which correlated with the clinical and MRI findings. Yamanouchi *et al*¹¹ described a case where the focal EEG changes persisted until death and the postmortem pathology revealed changes confined to one hemisphere. Lowden *et al*¹² had described a case of epilepsy partialis continua in a biopsy-proven case of CJD. This patient had focal spike and wave discharges originating from the right centrottemporal region, later progressing to develop generalised PSWCs. Lateralised periodic discharges so far have been described commonly in stroke and in conditions such as brain infections, tumours, haematomas and several other entities including anoxic encephalopathy, subarachnoid haemorrhage, craniocerebral trauma, migraine, multiple sclerosis and aminophylline intoxication.¹³ However, in the light of appropriate clinical scenario, a possibility of sporadic CJD should always be taken into account. Several molecular subtypes of sporadic CJD have been described and the clinical utility of EEG varies with the subtypes, usually positive in MM1 and MV1 subtypes.³

Although psychiatric manifestations predominate during the early stages of variant CJD, it was considered as rare and atypical in a classic sCJD.^{14 15} However, psychiatric presentation of sCJD was later described by different authors.¹⁶⁻¹⁹ In a retrospective analysis of 126 cases of definite or probable sCJD, 92% of them had psychiatric manifestations during their illness. Of

Learning points

- ▶ Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare and fatal degenerative disease resulting in rapidly progressive cognitive decline.
- ▶ Characteristic and typical EEG finding in CJD is bisynchronous periodic sharp waves.
- ▶ However, while interpreting the EEG in a patient with suspected sCJD, one should be aware that periodic lateralised epileptiform discharges can be seen and are not against the diagnosis of sCJD.
- ▶ Patients with sCJD can present with psychiatric symptoms such as depression.

these patients, 24% had depression as the presenting symptom similar to our patient.¹⁶ To summarise, presence of focal or lateralised discharges in EEG and psychiatric manifestations such as depression at presentation should not be considered against the diagnosis of sCJD.

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