Autoimmune Antibodies Positivity in Probable Sporadic Creutzfeldt–Jakob Disease: A Mini-Review of Literature

Dear Editor,

Sporadic Creutzfeldt–Jakob disease (sCJD) is a rapidly progressive neurodegenerative disease caused by the deposition of a prion protein (PrPSc). It is characterized by rapidly progressive dementia (RPD) in association with behavioral disturbances, ataxia, and myoclonus. Autoimmune encephalitis is a close differential diagnosis for sCJD.[1] There are a few case series that have reported the presence of autoimmune antibodies in sCJD, which causes a diagnostic conundrum in the management of

the patient. Hereby, we report a 58-year-old lady who presented with RPD, insomnia, myoclonus, and cerebellar ataxia of 3 months duration. Brain magnetic resonance imaging (MRI) and electroencephalogram (EEG) were suggestive of CJD, but serum autoimmune antibodies were positive for anti-gamma-butyric acid-B (GABA-B) antibodies, which necessitated the initiation of immunotherapy. However, the patient succumbed to the illness within 3 months of admission.

A 58-year-old lady presented with the history of progressive memory disturbance of 3 months duration. To start with, she started forgetting recent conversations, misplaced objects, and faced difficulty finding the objects. Subsequently, she was making mistakes in cooking in the form of missing the ingredients while cooking and missing the steps in cooking. She became withdrawn, lost interest in the daily household activities, personal hygiene, dressing, reduced her speech output, and had difficulty in comprehension. There was no disinhibition. She had reduced sleep in the form of increased sleep latency, frequent awakening, and early morning awakenings. She was self-ambulant at the time of the presentation. Within 2 months after discharge, she developed imbalance while walking with no diurnal variation and jerky movements of the limbs, which were stimulus sensitive. Three months after discharge, she became bed-bound with encephalopathy and myoclonic jerks. There was no family history. The systemic examination was unremarkable. At the time of her first admission, she was conscious, not oriented to time or place but to person, had poor attention span, comprehension difficulty, reduced verbal fluency, poor verbal and visual memory, and was

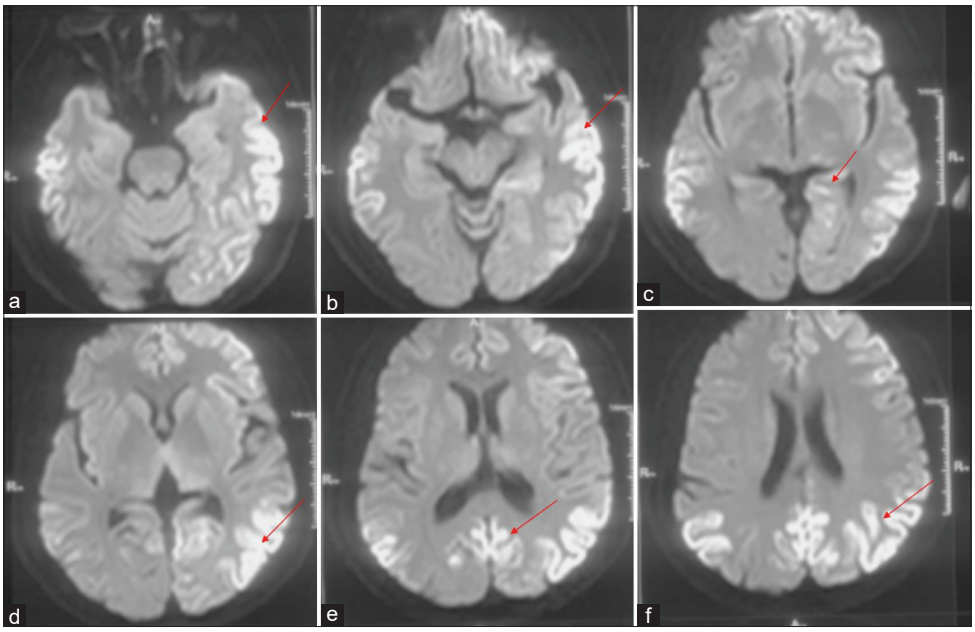

Figure 1: Diffusion weighted images showing diffusion restriction in (a, b) temporal cortex; (c) left hippocampus; (d-f) left temporo-occipital, left occipital, and left parieto-occipital, respectively (red arrows)

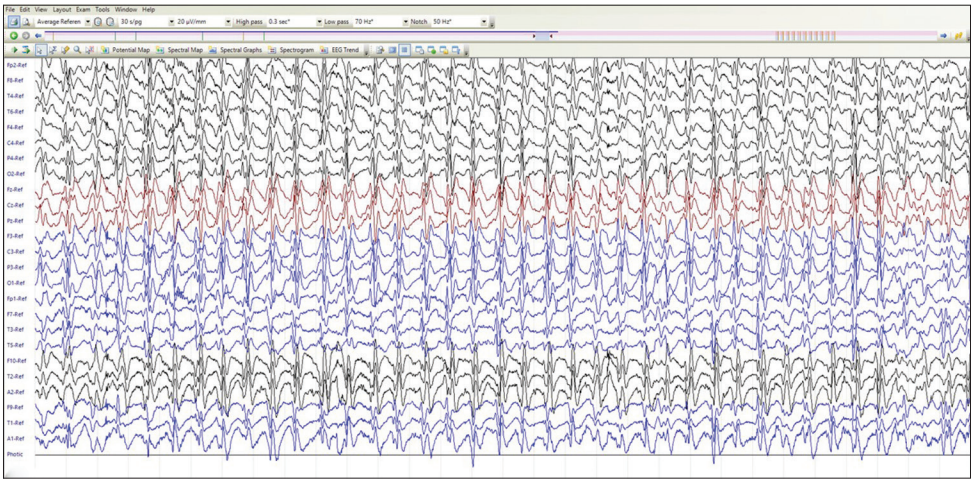

Figure 2: EEG showing generalized triphasic waves with no anterior-posterior lag

unable to identify familiar faces, objects, pantomime, or imitate actions. Motor examination showed normal tone, power, and reflexes. The sensory examination was normal. There were no frontal release signs. At her second admission, she was stuporous with multifocal myoclonic jerks. Complete hemograms, renal, hepatic, and thyroid function tests were normal. Serum sodium was slightly low (132 mmol/L). Brain MRI showed bilateral frontal and parieto-occipital gyral restriction (cortical ribboning) on diffusion-weighted imaging [Figure 1]. EEG showed generalized triphasic waves with no anterior-posterior lag (1-2 Hz) and no response to lorazepam [Figure 2]. Serum anti-thyroperoxidase antibodies were negative. Serum and cerebrospinal fluid (CSF) autoimmune antibody profiles showed positive anti-GABA-B antibodies. She was treated with 5 days of pulse methylprednisolone and three cycles of large-volume plasmapheresis with no improvement. She succumbed to illness within 3 months of her first admission. A diagnosis of probable sporadic CJD was made.

CJD is a rapidly progressive, fatal neurodegenerative prion disease. The clinical manifestations range from RPD, psychiatric symptoms, pyramidal, and extra-pyramidal involvement, ataxia, visual disturbances, sleep disturbances, stroke-like presentations, and finally, ending up in an akinetic, rigid state followed by death. Sporadic CJD is the most common form, accounting for about 85% of the cases.[2] Autoimmune encephalitis is a close mimic of CJD with similar symptoms. In this case, the positivity of GABA-B in the serum added to the diagnostic and therapeutic conundrum. A review of the literature has shown that patients diagnosed with immune-mediated encephalitis turned out to have CJD and vice versa.

Autoimmune antibodies are known to occur in CJD, probably due to the rapid destruction of the central nervous system, which exposes the neuronal epitopes to the immune system with the subsequent production of specific neuronal antibodies. Jammoul *et al*.,[3] (2014) reported a pathologically and genetically confirmed case of CJD with elevated serum VGKC complex antibody titers. Rossi *et al*., (2015)[4] evaluated referred and retrieved serum samples of patients with suspected CJD, which included 139 definite CJD cases. They found that less than 5% were positive for autoimmune antibodies, which included CASPR2, NMDAR, GlyR, and LGI1 antibodies. Fujita *et al*., (2015)[5] found that in the serum and CSF of CJD patients, titers of antibodies against peptides of the GluN2B subunit of NMDAR were significantly elevated. Hence, low titers of antibodies can occur in sporadic CJD and should be interpreted with caution. However, Grau-Rivera *et al*., (2014)[6] did not find autoimmune antibody positivity in 49 patients with definite CJD. Salazar (2018)[7] reported positivity of anti-Zic4 antibodies in an elderly patient with probable CJD. Our patient presented with a rapid clinical course, and during the initial visit, a differential autoimmune encephalitis was considered. It is difficult to differentiate, especially in the early stages, as in our case. Brain MRI showed cortical ribboning, as reported in CJD but also reported in other non-prion causes of RPD. The patient was given a trial of steroids and plasma exchange as serum and CSF GABA-B were positive. However, the patient became stuporous with multifocal myoclonus and succumbed to the illness.

Serum and CSF GABA-B positivity in CJD has not been previously reported, and we describe it to discuss this diagnostic and therapeutic conundrum. CJD is a fatal disease with no curative treatment, whereas autoimmune encephalitis is a potentially treatable and reversible condition. It is possible that antibodies can be due to secondary phenomena occurring because of PrPSc damaging neurons, leading to the release of neuronal antigens for which antibodies are formed, a false-positive result, or a potentially unknown mechanism that has not been discovered yet and potentially has implications in the future.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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