Received: 5 January 2019 | Accepted: 24 February 2019

DOI: 10.1002/agm2.12057

CASE REPORT

Aging Medicine Open Access WILEY

A case of rapidly progressive dementia: A diagnosis not to be missed

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KEYWORDS: Creutzfeldt-Jakob, diffusion restriction, periodic sharp wave complexes, prion

1 | INTRODUCTION

Rapidly progressive dementias have limited etiologies. One of the differentials is prion disease. Prion diseases are neurodegenerative diseases caused by misfolded infectious proteins.[1] Sporadic Creutzfeldt-Jakob disease (sCJD) accounts for 90% of sporadic prion diseases.[2] Though rare, such cases may present once in a while and it may be difficult for the geriatrician or physician in general practice to diagnose correctly. However, certain classic diagnostic elements must be remembered so that such cases are not missed.

2 | CASE REPORT

A 63-year-old woman presented with decreased memory of recent events, behavioral abnormalities in the form of aggressive and abusive behavior, and visual hallucinations since 1.5 months previously. The patient had had an episode of fever lasting 7 days, around 2 weeks prior to the onset of her symptoms, which had been diagnosed as malaria and managed by a local practitioner. Magnetic resonance imaging (MRI) of the brain done at a hospital in her locality at the onset of her psychiatric symptoms had been reported as normal, and a cerebrospinal fluid analysis was unremarkable. She had gradually become immobile and mute and had developed myoclonic jerks in bilateral upper limbs, which persisted for 5-10 min at a time. At presentation in this state, she was afebrile with stable vitals. Her Glasgow Coma Score was 9 (Eye 4, Verbal 2, Motor 3). Rigidity and muscle atrophy were absent. Bilateral plantar reflexes were flexor. On MRI of the brain, diffusion restriction was observed in bilateral caudate nuclei and bilateral frontoparietal cortices (Figure 1A). Electroencephalography (EEG) revealed periodic sharp wave complexes of 1-Hz frequency over all scalp regions (Figure 1B). Consent for cerebrospinal fluid 14-3-3 protein estimation was denied by the legal guardians of the patient. This was because: the test was not locally available; it would need the sample to be sent to the single central reference lab in the country, inciting significant delay; and because the dismal prognosis of sCJD and the unavailability of treatment options, even in case of a confirmed diagnosis, had been explained to them. A diagnosis of probable sCJD was made, and the patient was started on valproate for myoclonic jerks and discharged for home-based palliative care after adequate counseling of family members. It was not possible to track the response to valproate as the patient did not return for follow-up.

3 | DISCUSSION

Sporadic CJD results from either a somatic mutation in the prion protein (PrP) gene or a random structural change in the PrP causing formation of PrP^{Sc} (abnormal or scrapie type prion protein).[1] Onset usually occurs in the seventh decade of life, and the median time to death is 5 months, with 90% of patients dead by 1 year.[3] In the absence of neuropathological specimens, the Centers for Disease Control and Prevention criteria allow for the diagnosis of probable sCJD if rapidly

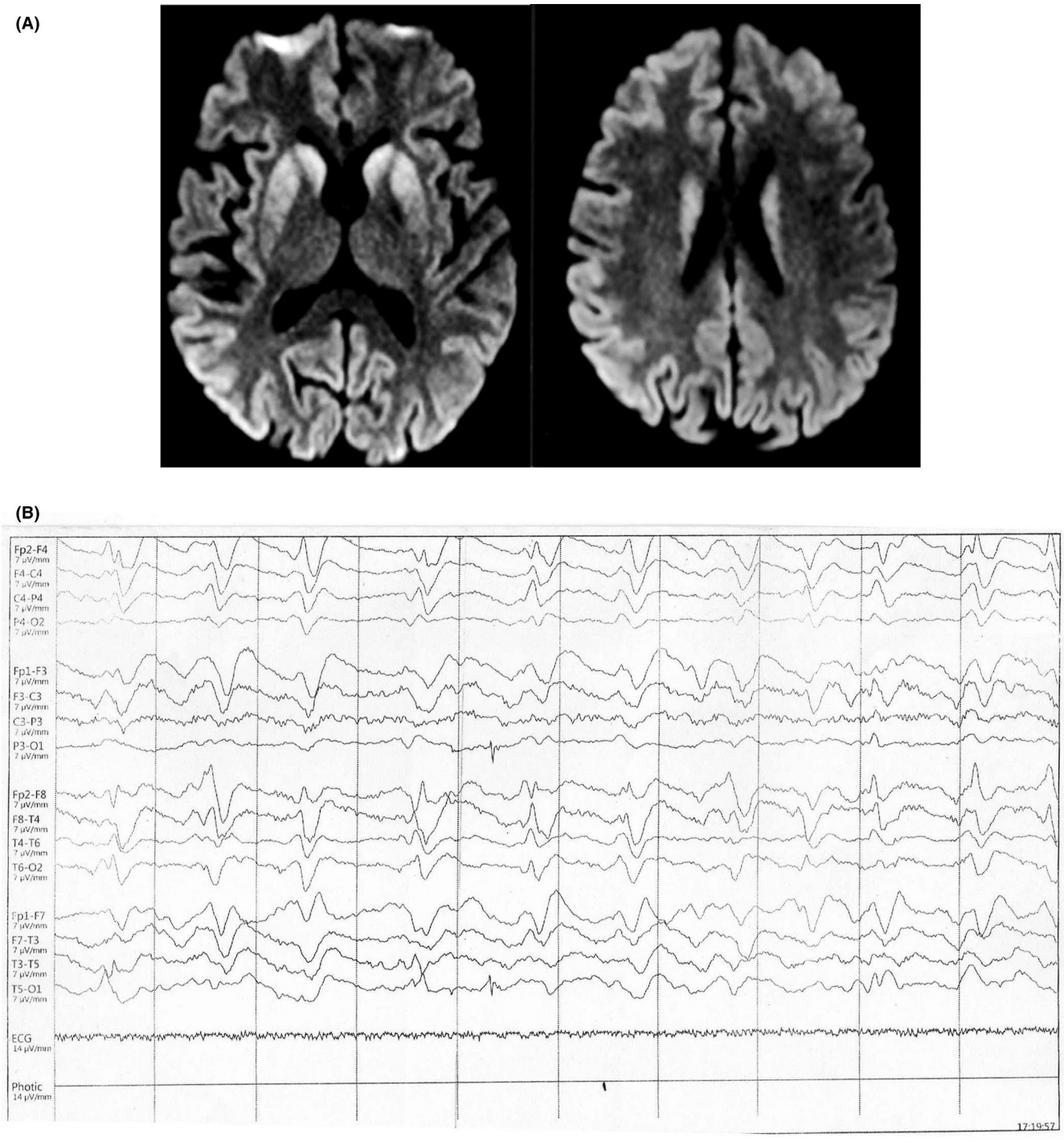

FIGURE 1 (A) Magnetic resonance imaging of the brain showing diffusion restriction in bilateral caudate nucleus and putamen, cortical surface of bilateral parietal and occipital lobes (diffusion-weighted images). (B) Periodic sharp wave complexes of 1-Hz frequency. There is no significant voltage asymmetry between right and left hemisphere

progressive cognitive decline is associated with at least two out of four clinical criteria, namely myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, and akinetic mutism. In addition, there should be any one out of: a typical EEG, a positive 14-3-3 CSF assay, or a typical MRI of the brain. Further, routine investigations should not indicate an alternative diagnosis.[4] In the current case, rapid-onset dementia was accompanied by myoclonus and akinetic-mutism with typical EEG and MRI features allowing us to make a diagnosis of probable sCJD. MRI of the CJD brain shows a characteristic diffusion restriction pattern involving the basal ganglia and at least two cortical regions (temporal, parietal, occipital), which correlates with spongiform changes seen at autopsy.[5] Periodic sharp wave complexes are found in the EEG recordings of approximately two-thirds of patients with sCJD.[6] The mainstay of treatment is symptomatic and supportive. Although prion diseases are rare causes of dementia, quite a few cases may turn up at specialized neurologic clinics in academic medical centers. However, fewer

numbers present at geriatric services and even if they do, the condition may be easily missed if the concerned geriatrician has not had prior exposure to this diagnosis. This is more common in developing countries, where infectious diagnoses are simply overwhelming in numbers. Even in the present case, the presence of a febrile episode around 2 weeks before the onset of symptoms may have erroneously indicated a post-infectious sequela but was most likely an unrelated event. At presentation, we had considered one of the differentials to be tubercular meningoencephalitis, an exceedingly common entity in India and which has diverse manifestations in the elderly. The absence of fever and generalized-onset seizures and the absence of suggestive MRI or cerebrospinal fluid findings made this diagnosis unlikely. Another strong possibility in such cases is autoimmune encephalitides of both paraneoplastic and non-paraneoplastic etiologies, which may also have diverse manifestations. However, the presence of true diffusion restriction on MRI and the gross involvement of the cerebral cortex, which is uncommonly affected in autoimmune encephalitis, precluded this diagnosis. The relative paucity of findings on most MRI sequences except diffusion-weighted images makes diagnosing sCJD more difficult for the unexposed specialist. In the current case, the previous MRI on re-analysis showed evidence of diffusion restriction, which had, however, been reported as normal at the local hospital, simply because no one had considered a diagnosis of sCJD.

Written informed consent was obtained from the legal guardian of the patient.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

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How to cite this article: Das P, Gupta S, Kumar I, Gambhir IS, Chakrabarti SS. A case of rapidly progressive dementia: A diagnosis not to be missed. *Aging Med*. 2019;2:94–96. https://doi.org/10.1002/agm2.12057