

Letter to the Editor

Symptomatic nonconvulsive status epilepticus erroneously suggestive of sporadic Creutzfeldt–Jakob disease



1. Introduction

Nonconvulsive status epilepticus (NCSE) may have heterogeneous presentations and differential diagnosis may be particularly difficult because clinical signs coupled with periodic EEG pattern are most often subtle or non-specific. Moreover, few cases of NCSE have been previously described as the presenting symptom of sporadic Creutzfeldt–Jakob disease (sCJD) [1,4,5,7]. We describe a patient with a NCSE strongly, but erroneously, suggestive of a probable sCJD.

2. Case report

A 66-year-old right handed man was referred to our clinic because of the onset, three months before, of progressive cognitive decline, gait ataxia with falls and sporadic visual hallucinations. His medical history was notable for hypertension and a right temporal–occipital ischemic stroke occurred one year before without neurological sequelae. At the admission, he displayed a waxing and waning mental status, ocular motor apraxia, left beating nystagmus and left-sided hemiparesis. A brain computed tomography (CT) scan documented right temporal–occipital hypodensity due to the previous stroke, without new lesions. During the neurological examination the patient exhibited a tonic-clonic generalized seizure followed by confusion and psychosis. Video-EEG monitoring (continuously performed for 12 hour periods each day) showed an asymmetry of background activity with pseudo-periodic high voltage discharges of spikes and bi-triphasic sharp waves on the right posterior regions, recurring every 1–2 s and lasting 300–500 ms, that were not interrupted by external stimulations (Fig. 1A) and that were persisting during sleep. EEG pattern was simultaneously accompanied by left forced eye and head deviation. Infusion of intravenous diazepam 20 mg did not modify either the EEG pattern or clinical context (Fig. 1B). Then, intravenous valproate was administered at doses of 800 mg in bolus followed by 1200 mg/24 h infusion, with gradual decrease of epileptic discharge frequency up to their disappearance within two days (Fig. 1C). Motor deficit, as well as oculomotor apraxia started improving, whereas recurrent nocturnal episodes of psychomotor agitation requiring antipsychotic medications persisted. Blood tests were unremarkable. At admission day 1 MRI showed restricted diffusion in right temporal–parietal–occipital cortex and ipsilateral pulvinar on diffusion-weighted images (DWI) and subtle T2 prolongation only in the right pulvinar on T2-fluid attenuated inversion recovery (FLAIR) (Fig. 1E–F–G). The CSF analysis performed on day 2 from admission revealed high levels of tau protein (1018 pg/mL) and a positive 14-3-3 protein measured by western blot. Additionally, methionine-methionine (MM) at codon 129 or the prion protein gene was detected.

Clinical presentation, EEG pattern, MRI abnormalities and CSF findings were suggestive of probable sCJD according to several CJD diagnostic criteria [8], rather than a NCSE associated with an old stroke.

The patient was discharged at day 10 on oral valproate (1200 mg/die) treatment with gradual improvement of the motor deficit and behavioral changes, although visual misperceptions and cognitive impairment (Mini Mental State Examination, MMSE 18/30) persisted. At six months of follow-up, the patient appeared oriented without neurological signs or cognitive impairment (MMSE 28/30) and diagnostic tests were performed once again. EEG recording showed a symmetric background activity without epileptiform discharges (Fig. 1D). Brain MRI did not reveal the previously detected abnormalities (Fig. 1H–I) and CSF detection of 14-3-3 and tau proteins was negative. Therefore, the definitive diagnosis was symptomatic NCSE, induced by previous right temporal–occipital ischemic stroke.

3. Discussion

Our case represents the first report of symptomatic NCSE resembling sCJD and highlights a high risk of misdiagnosis due to several factors.

3.1. Clinical presentation

Firstly, our patient exhibited three months of subacute cognitive decline, stroke-like hemiparesis, a convulsive seizure, and ocular and psychiatric disturbances which mimicked sCJD onset.

3.2. EEG findings

In general, EEG is helpful in making a specific diagnosis when taken in context with the clinical history, even though the underlying etiologies may be various. It is noteworthy that the EEG hallmark of sCJD consists of periodic sharp-wave complexes (PSWC) that may occur lateralized, mainly in the early stages and in patients with MM homozygosity [4,5,12]. In our patient, the first EEG monitoring showed PSWCs on the right posterior regions accompanied by forced head and eye deviation and that were not attenuated by external stimuli, suggesting a NCSE. On the other hand, benzodiazepine treatment failed to modify ictal EEG pattern as it usually occurs in non-epileptic encephalopathies including CJD. The latter hypothesis was also corroborated by the prompt electrical improvement by AEDS without subsequent clinical changes [4,5]. At the beginning, the epileptiform EEG pattern was consistent with NCSE and we hypothesized that it may be an onset form of sCJD, as previously reported in literature [4,5]. Further investigations were less conclusive, presenting considerable overlapping features.

3.3. MRI findings

It has long been suggested that acute DWI changes may play a prominent role in diagnosing sCJD, even in the early phase of the disease

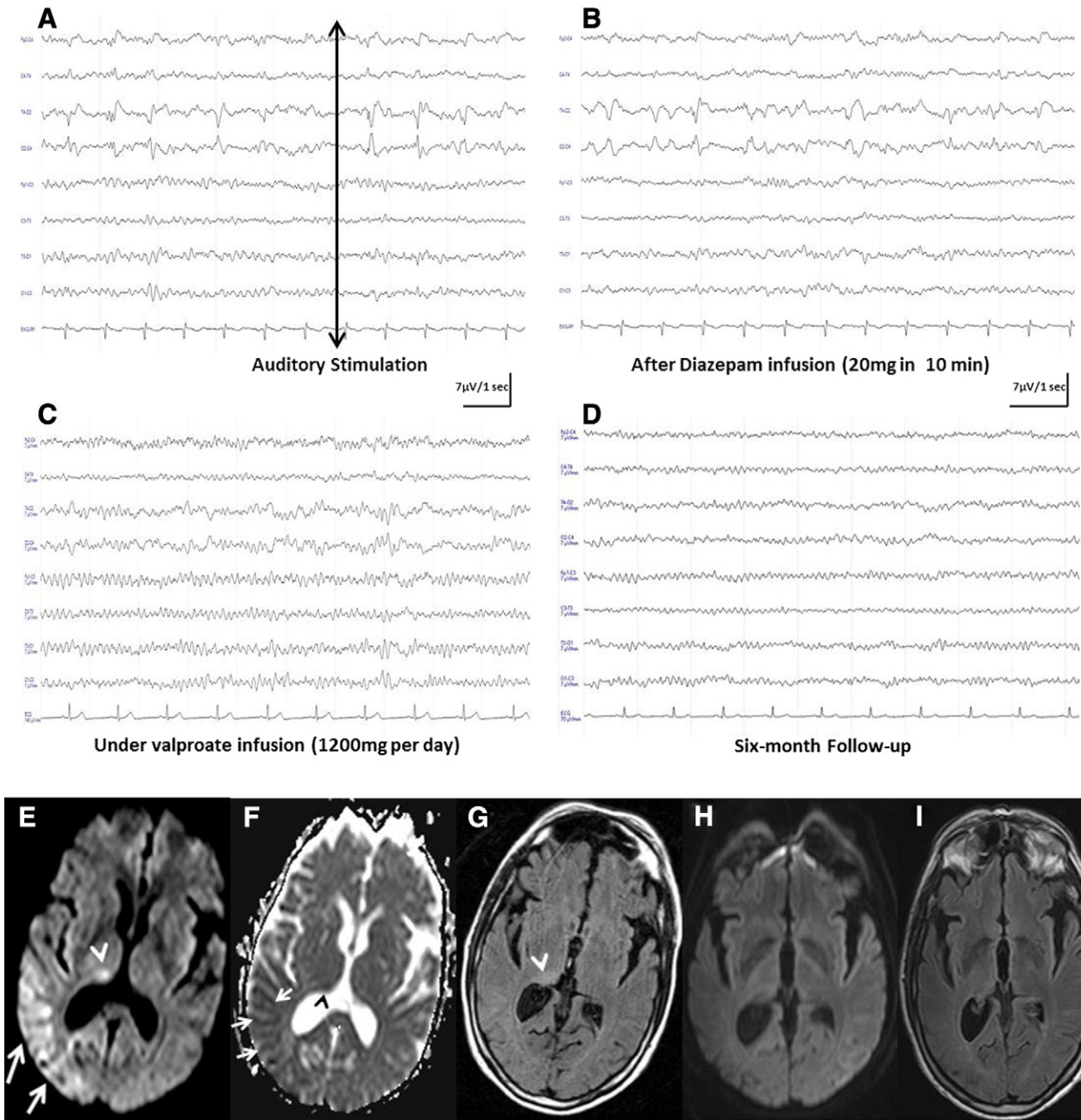


Fig. 1. EEG extracts in a bipolar longitudinal montage. Asymmetry of background activity with pseudo-periodic high voltage discharges of spikes and bi-triphasic sharp waves on the right posterior regions, recurring every 1–2 s and lasting 300–500 ms, not interrupted by external stimulations (A). Acute infusion of intravenous diazepam 20 mg did not modify the EEG pattern (B). Intravenous valproate was administered at doses of 800 mg in bolus followed by 1200 mg/24 h infusion, with gradual decrease of epileptic discharges frequency (C). EEG performed six months later showed symmetric background activity without epileptiform discharges (D). MRI scan: At admission day 1 diffusion weighted (DW) study demonstrated bright signal on isotropic images (E) and dark signal on ADC map (F) indicating restricted diffusion throughout the right temporal–parietal–occipital cortex (arrows) and ipsilateral pulvinar (white and black arrowheads respectively). Axial fluid-attenuated inversion recovery (FLAIR) image showed subtle T2 prolongation only in the right pulvinar (white arrowhead) (G). Six months later, no signal abnormalities were noted (H, I).

and before the typical EEG periodic pattern appearance [11]. The involvement of cortical and pulvinar regions has been described in both sCJD and symptomatic SE [9]. These MRI abnormalities induced by periictal vasogenic and cytotoxic edema may completely normalize within weeks in SE [3] and they may disappear later in sCJD [9,11]. Therefore, in our case the reversible radiological findings did not allow to clearly discriminate SE from sCJD. Such finding was compounded by clinical and EEG data leading us to suspect CJD.

3.4. CSF findings

Currently, the 14-3-3 protein is considered a useful marker for supporting the diagnosis of probable sCJD. Rarely, a first positive test may become negative with a second lumbar puncture in sCJD patients with long disease duration (>1 year), severe brain atrophy, or under anesthetic therapy [10], but none of these events occurred in our case. Hamlin et al. [6] have recently reported that tau protein

might be more suitable than 14-3-3 in diagnosing sCJD because of higher specificity. Both tau and 14-3-3 proteins tend to increase with disease progression in sCJD, but they may transiently increase in symptomatic SE due to any extensive neuronal damage, as probably occurred in our case [6]. In fact, several studies hypothesized that the occurrence of 14-3-3 isoforms within CSF may be induced by acute neurological insults and, notably, that their presence can also be a biomarker of acute seizure damage. Moreover, it has been recently demonstrated that 14-3-3 overexpression may confer protection against seizure-induced neuronal death in the mouse hippocampus [2].

4. Conclusions

In conclusion, our case supports previous evidence of overlapping features in NCSE and sCJD and shows that diagnosis can be tricky, even matching several diagnostic findings. In the light of this case report, we wonder whether a refinement of diagnostic criteria might be needed in order to avoid overdiagnosis of sCJD, also taking in consideration the usefulness of repeating MRI with FLAIR and DWI and CSF analysis.

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Conflict of interest

None of the authors have potential conflicts of interest to be disclosed.

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Maria Albanese

Fabio Placidi

Andrea Romigi

University of Rome “Tor Vergata”, Department of Systems Medicine,
Neurophysiopathology Unit, Epilepsy Center, Rome, Italy

Tommaso Schirinzi

University of Rome “Tor Vergata”, Department of Systems Medicine,
Neurology Unit, Rome, Italy

Claudio Liguori

Angela Marchi

University of Rome “Tor Vergata”, Department of Systems Medicine,
Neurophysiopathology Unit, Epilepsy Center, Rome, Italy

Francesco Garaci

Roberto Floris

University of Rome “Tor Vergata”, Department of Diagnostic Imaging,
Molecular Imaging, Interventional Radiology and Radiotherapy, Rome, Italy

University of Rome “Tor Vergata”, Department of Biomedicine and
Prevention, Rome, Italy

Nicola Biagio Mercuri

University of Rome “Tor Vergata”, Department of Systems Medicine,
Neurophysiopathology Unit, Epilepsy Center, Rome, Italy
Fondazione Santa Lucia IRCCS, Rome, Italy

Maria Grazia Marciani

University of Rome “Tor Vergata”, Department of Systems Medicine,
Neurology Unit, Rome, Italy

Francesca Izzi*

University of Rome “Tor Vergata”, Department of Systems Medicine,
Neurophysiopathology Unit, Epilepsy Center, Rome, Italy

Corresponding author at: University of Rome “Tor Vergata”, Department
of Systems Medicine, Neurophysiopathology Unit, Epilepsy Center, Viale
Oxford 81, 00133 Rome, Italy. Tel.: + 39 06 20902107.

E-mail address: fraizzi@tin.it.

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