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Focal status epilepticus in anti-Hu encephalitis

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Dear Editor,

Anti-Hu antibodies (or type 1 Anti-Neuronal Nuclear Autoantibodies, ANNA-1) are onconeural antibodies associated with paraneoplastic or autoimmune neurologic syndromes [1,2]. They present with several neurologic features such as limbic encephalitis (LE), peripheral neuropathy, cerebellar disorder and autonomic dysfunction. Seizures and status epilepticus, whether convulsive or not, have also been associated with anti-Hu antibodies [3–5]. Moreover, a small number of cases of persistent focal motor status epilepticus (FMSE), or epilepsia partialis continua (EPC) have been reported [6].

A 15-year old woman developed episodes of sudden ascending somatosensory feelings involving the left hand and shoulder, followed by hypertonic contractions of the homolateral arm and loss of contact, with subsequent convulsive seizures. Despite adequate anticonvulsivant therapy, similar episodes persisted in the following months. One year later, she experienced recurrent episodes of brief and arrhythmic contractions of the right thumb lasting for several seconds and occurring several times per week. At the age of 18, anti-Hu antibodies were detected in blood and CSF [2]. Repeated investigations for neoplasia gave negative results. She then started to complain contractions of abdominal and left lower limb muscles, also occurring during sleep, sometimes associated with asynchronous shoulder and head movements. At the age of 20, she continued to present irregular disabling myoclonic jerks of the right flank and left lower limb, together with infrequent tonic-clonic seizures. The EMG recordings detected multiple muscular contractions occurring with different spatial and temporal features. EEG showed sporadic interictal bilateral spikes or spike and waves, slightly predominant on the right frontal areas without any correlation with muscular contractions. Three EEG-EMG back-averaging analyses were performed over a period of five years, all showing pre-myoclonic EEG potentials that confirmed the cortical origin of myoclonic jerks. Brain MRI at the time of the right flank and left lower limb myoclonic jerks showed bilateral FLAIR hyperintense signals on the top of the precentral gyri (Fig. 1A, left). Because myoclonic jerks occurred also during ^{18}Fluorodesoxy-glucose infusion for PET Scan (^{18}FDG-PET), a strong metabolic increase was noted in both precentral gyri and in the striatum (Fig. 1A-B, right). In addition, the ^{18}FDG-PET whole body analysis showed strikingly increased metabolic activity within the jerking muscles (Fig. 1C). Immunosuppressive treatments (corticosteroids, IVIg, cyclophosphamide, rituximab, mycophenolate) gave only moderate effects on the myoclonia. This uncommon autoimmune epilepsy progressively evolved over more than 10 years and despite the permanent detection of anti-Hu antibodies in the blood and CSF, no malignancy has never been detected.

To date, FMSE associated to anti-Hu antibodies has been clearly reported in only 9 patients [6–11] (see Table 1). EPC is a variant of FMSE, characterized by repetitive muscle jerks, usually arrhythmic, persisting over prolonged periods of time, ranging from one hour to many years [12–14]. It presents as a chronic progressive disorder that can replace the initial intermittent epileptic semiology described by the patients. FMSE is frequently associated with a lesion in the sensorimotor area [6,8–10]. The EEG can detect abnormalities around the precentral gyrus, as well in temporal regions [7]. However, epileptic abnormalities on scalp EEG are not mandatory to confirm the diagnosis and some patients with FMSE do not show any abnormalities. Interestingly FMSE showing lateralized EEG abnormalities has been associated with better outcomes [12]. ^{18}FDG-PET is useful in the diagnosis of focal status epilepticus, when clinical semiology is equivocal or the EEG does not show clear epileptiform abnormalities [15,16]. Moreover, ^{18}FDG-PET can isolate a hypermetabolism associated to the ictal onset zone in EPC [16]. Actually there is no specific treatment of FMSE in paraneoplastic or autoimmune encephalitis. First line therapy combines the treatment of the underlying malignancy (if present) and immunomodulation therapies such as steroids and intravenous polyclonal immunoglobulin administration to taper the inflammatory process. Antiepileptic drugs are usually administered, but they usually fail to control the FMSE. Second line approaches usually include rituximab and cyclophosphamide and plasmapheresis [17,18]. In addition, neurosurgery may be proposed, as reported in one patient who underwent focal cortical resection [11].

Pathophysiological mechanisms related to anti-Hu encephalitis are

Abbreviations: LE, Limbic Encephalitis; FMSE, Focal Motor Status Epilepticus; EPC, Epilepsia Partialis Continua

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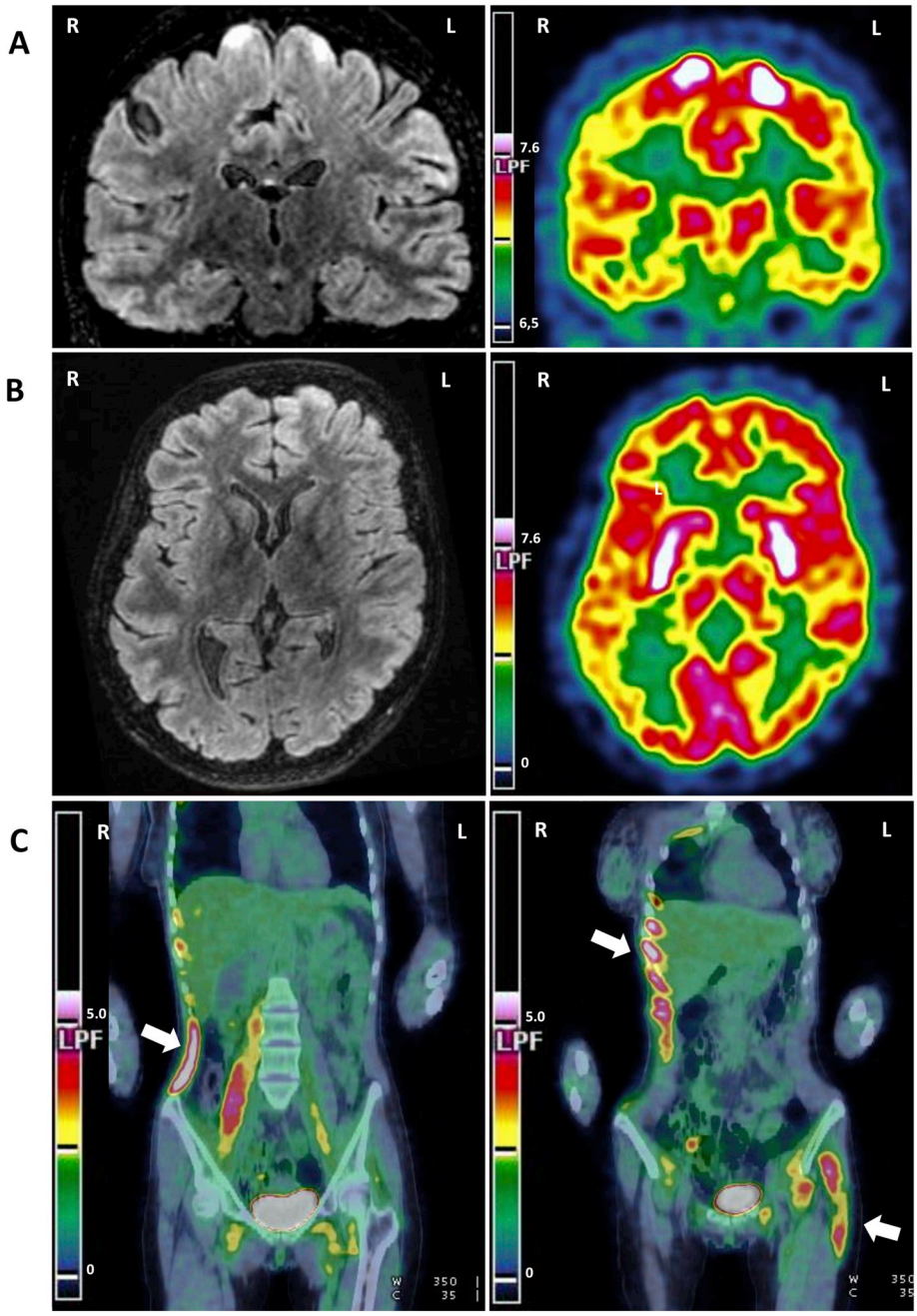

Fig. 1. Imaging of a migrating focal motor status epilepticus related to anti-HU encephalitis.
A. Coronal section of brain MRI and FDG-PET Scan performed during the focal motor status epilepticus. *Left:* FLAIR sequences showed bilateral hyperintense signals on the top of the precentral gyri. *Right*: a strong hypermetabolism (coded by white colour) was detected in the same regions on the ^{18}FDG-PET.
B. Axial section of brain MRI and ^{18}FDG-PET Scan performed during the focal motor status epilepticus. Left: normal FLAIR sequences. Right: Intense bilateral putaminal hypermetabolism (coded by white colour) was detected on the FDG-PET.
C. The whole body ^{18}FDG-PET also detected an increased metabolic activity in the muscles involved in the focal motor status epilepticus (arrows: right external abdominal oblique muscle, right psoas and right intercostal muscles together with left vastus lateralis and medialis). See also Video 2.

still unclear. It is accepted that the pathological processes affecting the brain are mediated, at least in part, by cytotoxic T-cell responses [19–21]. We suspect that multifocal infiltrates of inflammatory cells lead to the development of multiple foci of neuronal hyperexcitability and that myoclonic jerks may result from an atypical propagation of the neuronal activity along multiple networks. Such propagation may differ from that observed in typical motor seizures, resembling that observed in the "*a bascule*" tonic-dystonic seizures seen in anti-LGI1 antibodies encephalopathy [22]. Finally, an atypical presentation consisting of multifocal and migrating myoclonic jerks may represent a suggestive feature of an autoimmune process and should promptly guide the appropriate diagnostic procedures [23,24].

Disclosure

None of the authors has any conflict of interest to disclose. We

Table 1
Synopsis of the characteristics of reported patients with focal motor status epilepticus associated to anti-Hu antibodies encephalitis. PDs: periodic discharges.

	Reported patients	Clinical manifestation	EEG	MRI	PET	Neoplasm
Shavit et al.[6] (3 patients)	Pat. 1	Involuntary muscular twitching of the left leg	PDs in the right parietal area	T2-non-enhancing lesion in the right postcentral area	Not reported	Small cell lung cancer
	Pat.2	Focal clonic contractions of the right hand and face	PDs in the left parasagittal frontoparietal region	Not performed	Not reported	None
	Pat.3	Repetitive movements of the tongue. Left perioral twitching and rare clonies of the first two fingers of the left hand	PDs in the right frontoparietal area	Non-enhancing lesion in the right Rolandic area	Not reported	Gastric cancer
Porta-Etessam et al. [10] (1 patient)	Pat.1	Continuous involuntary clonic twitching of left face muscles	PDs in the right frontal lobe	One lesion involving the right frontal lobe Bilateral mesiotemporal hyperintensities	Not reported	Small cell lung cancer
Mut et al. [8] (1 patient)	Pat.1	Intermittent myoclonic right arm jerks	Not performed at time of EPC	Multiple lesions located in the left temporal, right frontal, left parietal areas	Not reported	Small cell lung cancer
Kinirons et al. [9] (1 patient)	Pat. 1	Continuous rhythmic myoclonic jerks of the tongue and palate	Rhythmical activity, in the right anterior temporal region	T2 hyperintensity in the mesial temporal structures predominantly on the right	Not reported	Small cell lung cancer
Nahab et al. [11] (1 patient)	Pat.1	Clonic contractions of the right face, arm, and leg	Epileptiform activity in the left fronto-central region	T2 hyperintensity in the left fronto-parietal region	Not reported	Small cell lung cancer
Rudzinski et al. [7] (2 patients, detailed information only for one)	Pat.1	Clonic contractions of the right face	Left frontotemporal rhythmic spike discharge	Precentral gyrus region lesion (in both patients)	Not reported	Small cell lung cancer (in both patients)

confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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