ORIGINAL ARTICLE

Epilepsia partialis continua after an anterior circulation ischaemic stroke

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Background and purpose: Although cerebrovascular disorders are the main cause of *epilepsia partialis continua* (EPC) in adulthood, the frequency of EPC after stroke is unknown. The aim was to prospectively ascertain its frequency 1 year after an ischaemic stroke.

Methods: This was a prospective study of consecutive acute anterior circulation ischaemic stroke patients, previously independent, with an admission National Institutes of Health Stroke Scale score ≥4, an acute ischaemic lesion on imaging and no previous epileptic seizures. During admission patients received standardized diagnostic and medical care and were submitted to a neurophysiological evaluation protocol. One year after stroke, patients were re-evaluated by an epilepsy expert neurologist and performed a video-electroencephalogram with electromyography co-registration whenever myoclonus was observed during neurological examination for jerk-locked back averaging analysis (JLBA). EPC was defined as continuously repeated fragments of epileptic seizures, with preserved consciousness, lasting at least 1 h, and representing locally restricted epileptic activity.

Results: In all, 151 acute anterior circulation stroke patients were consecutively included and prospectively evaluated, but 23 died in the first year. One year after stroke, from 127 patients alive, 117 (92.1%) underwent clinical and neurophysiological evaluation. In two (1.7%) patients, EPC diagnosis was made both by clinical and electroencephalographic criteria, namely JLBA. Both patients had a history of remote symptomatic seizures and one of them acute symptomatic seizures and non-convulsive status epilepticus criteria during the first 7 days after stroke.

Conclusions: Despite its low frequency, the high stroke incidence makes post-stroke EPC relevant. This study draws attention to this recognizable condition with therapeutic and eventually prognostic implications.

Introduction

Cerebrovascular disorders are the main cause of *epilepsia partialis continua* (EPC) [1,2] in adulthood. However, to our knowledge, the frequency of this type of focal status epilepticus [3] as a chronic post-stroke complication in large series has not been reported. Our hypothesis is that the subtle clinical signs in motor EPC make this disorder under-recognized.

In this study, the aim is to describe the frequency of this entity 1 year after an anterior circulation ischaemic stroke.

Methods

This was a prospective study of consecutive patients admitted to our stroke unit from October 2011 to

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October 2013 with an acute anterior circulation ischaemic stroke. The Ethics Committee 'Comissão de Ética para a Saúde' of the Hospital de Santa Maria – Centro Hospitalar Lisboa Norte approved the study. Signed informed consent was obtained from all patients or their next of kin.

Patients had to be previously independent (modified Rankin Scale score <1), have an National Institutes of Health Stroke Scale score ≥4 at hospital admission and an acute anterior circulation ischaemic lesion identified by brain imaging [computed tomography (CT) or magnetic resonance imaging]. Exclusion criteria were an acute posterior circulation ischaemic stroke and a previous history of epileptic seizures, traumatic head injury requiring hospital admission or brain surgery.

Included patients were submitted to standard cerebrovascular clinical and complementary evaluation during admission and after discharge. Seizure occurrence during the first year after stroke was prospectively quantified and seizures were classified as acute [4] or remote [5] symptomatic whenever they occurred within the first 7 days after stroke or after that time point in the absence of precipitating factors, respectively.

All patients underwent a neurophysiological evaluation protocol that included a 64-channel video-electroencephalogram (EEG) with a maximum duration of 60 min in the first 72 h after stroke, during admission (daily until day 7 and after that if neurological worsening), at discharge and 1 year after stroke.

A neurologist with expertise in epilepsy (CB) made a phone interview 6 months after stroke, accessing seizure occurrence by a free interview followed by a brief phone screening tool for identifying patients with epilepsy [6], and a scheduled appointment 12 months after the cerebrovascular event. On this occasion neurological examination was always performed and special attention was given to the observation of face and limbs at rest, and to the performance of myoclonus activation manoeuvres such as posture maintaining, passive mobilization and tactile stimulation. On the same day as this appointment, a video-EEG with a sampling frequency of 1000 Hz, at least 64 channels placed according to the 10/10 international system and 60 min maximum duration was performed. Whenever myoclonus was observed during the neurological examination, a synchronized electromyography (EMG) record of the involuntary movement was added to the examination. The EEG record included eyelid opening and closure, hyperventilation, photic stimulation and manoeuvres to elicit myoclonus, as previously observed in the neurological medical evaluation. Experienced technicians under medical supervision performed the EEG. The procedure allowed subsequent offline 'jerk-lock back averaging'. This analysis was performed using the BESA software, version 6.0 (BESA GMbH, Gräfelfing, Germany) with the aim of looking for an electroencephalographic transient temporally related to the involuntary movement. The identification of a wave with a coherent focal localization and a short latency to a myoclonus burst, lasting less than 100 ms, was considered an argument for a cortical correlate of the registered myoclonus [7].

The primary outcome of this study was the presence of EPC defined as a condition of continuously repeated fragments of epileptic seizures (motor or sensory), with preserved consciousness, lasting at least 1 h, and representing locally restricted epileptic activity [8]. The presence of a cortical correlate in jerk-lock back averaging of a suspect clinical motor phenomenon was considered as evidence of motor cortex hyperexcitability, supporting the diagnosis of EPC.

Results

In all, 151 patients (112 men and 39 women) with an acute anterior circulation ischaemic stroke were included, with a mean age of 67.4 (SD 11.9) years.

In 146 patients (96.7%) the acute imaging lesion was limited to middle cerebral artery (MCA) territory and in three (2.0%) to anterior cerebral artery (ACA) territory. Furthermore, in two patients both ACA and MCA territories were involved. In a brain CT scan performed at least 24 h after stroke, the median Alberta Stroke Programme Early CT Score (ASPECTS) [9] was 6 (interquartile range 4) and the median ASPECTS considering only the seven cortical territories of this scale was 4 (interquartile range 4). ASPECTS vascular territory in patients with an infarct limited to MCA territory in brain imaging study is disclosed in Table S1.

In the first year after stroke 23 patients had died (seven during admission and 16 after discharge) and one patient was lost to follow-up after the 6-month telephone interview. At 12 months after stroke, 127 patients were alive and 117 (92.1%) agreed to come to the scheduled clinical appointment and underwent an EEG.

At the 1-year appointment, two patients (1.7%), both with previous acute and/or remote sensorimotor symptomatic seizures (Table 1), presented with continuous and subtle involuntary movements of the upper limb contralateral to the ischaemic lesion, not spontaneously reported by the patient nor their family. Several fingers showed irregular, small amplitude, non-synchronized subtle and mainly jerky movements, suggesting described central minipolymyoclonus [10]. The involuntary movement semiology is shown in Videos S1 and S2. A cortical correlate of the aforementioned involuntary movements was found by the jerk-lock back averaging

Table 1 Clinical, imaging and neurophysiological characteristics of patients with post-stroke *epilepsia partialis continua*

	Patient 1	Patient 2
Clinical features		
Age (years)	71	77
NIHSS at admission	16	7
NIHSS after intravenous alteplase	14	7
NIHSS at discharge	12	8
Stroke aetiology after investigation	Undetermined	Undetermined
Acute symptomatic seizures[a] and their type	No	Yes Focal seizures (sensory) and non-convulsive status epilepticus criteria [14]
Remote symptomatic seizures[b] and their type	Yes Focal seizures (motor) of the left upper limb	Yes Focal seizures (motor) of the left limbs during sleep
Time of the first seizure	Between 6 and 12 months	Third day after stroke
EPC semiology (12 months after stroke)	Irregular, small amplitude, non-synchronized subtle mainly jerky movements of several fingers, accentuated by posture (Video S1)	Irregular, small amplitude, non-synchronized subtle jerky movements of several fingers, accentuated by posture (Video S2)
Anti-epileptic drugs	Levetiracetam started by the time of the EPC diagnosis	Levetiracetam started during admission, dose increased after EPC diagnosis
Modified Rankin Scale score at 12 months	3	3
Brain CT scan[c] features		
Vascular territory	Right middle cerebral artery	Right middle cerebral artery
ASPECTS (total score)	3	5
ASPECTS (infarct location[d])	I, L, C, IC, M2, M3, M6	I, IC, M2, M3, M6
Any type of haemorrhage transformation	Yes	Yes
Spared cortex islands within the infarct	Yes	No
Neurophysiological features		
Raw EEG analysis (performed 12 months after stroke)	Right fronto-temporal focal and rhythmic slow wave activity No interictal epileptiform activity	Right fronto-temporal focal slow wave Activity. No interictal epileptiform activity
Jerk-locked back averaging	A negative right central electroencephalographic transient preceding muscle activation (Fig. 1a)	A negative right central electroencephalographic transient preceding muscle activation (Fig. 1b)

ASPECTS, Alberta Stroke Programme Early CT Score (quantifying infarct size and location in middle cerebral artery territory); CT, computed tomography; EEG, electroencephalogram; EPC, *epilepsia partialis continua*; NIHSS, National Institutes of Health Stroke Scale score (quantifying stroke clinical severity). [a]Seizures occurring in the first 7 days after stroke; [b]seizures occurring after the first 7 days after stroke, in the absence of precipitating factors; [c]brain CT scan performed 24 h after stroke; [d]infarct location I, insular ribbon; L, lentiform nucleus; C, caudate; IC, internal capsule; M1, anterior middle cerebral artery (MCA) cortex; M2, MCA cortex lateral to the insular ribbon; M3, posterior MCA cortex; M4, M5, M6, anterior, lateral and posterior MCA territories immediately superior to M1, M2 and M3, rostral to basal ganglia.

technique (Fig. 1), adding neurophysiological criteria of EPC to clinical observation. In these patients, no epileptiform activity was detected in the raw EEG analysis. Clinical, imaging and neurophysiological characteristics as well as the treatment of patients with EPC are described in Table 1.

In our series, sensory symptoms as a manifestation of EPC were not recorded.

Discussion

In this study, the frequency of EPC as a remote complication of anterior circulation ischaemic stroke is very low. However, because stroke is a frequent neurological disorder, health professionals caring for patients with cerebrovascular disorders and aware of this disorder will find EPC in a significant number of patients.

Epilepsia partialis continua can be classified as a focal motor status epilepticus type [3], although some authors extend the meaning of EPC to cover other types of focal seizures which are continuous without spreading to a larger seizure or with only occasional spread [8]. Its physiopathology is not completely understood but the hyperexcitability of the sensorimotor cortex, the presence of cortical generators and

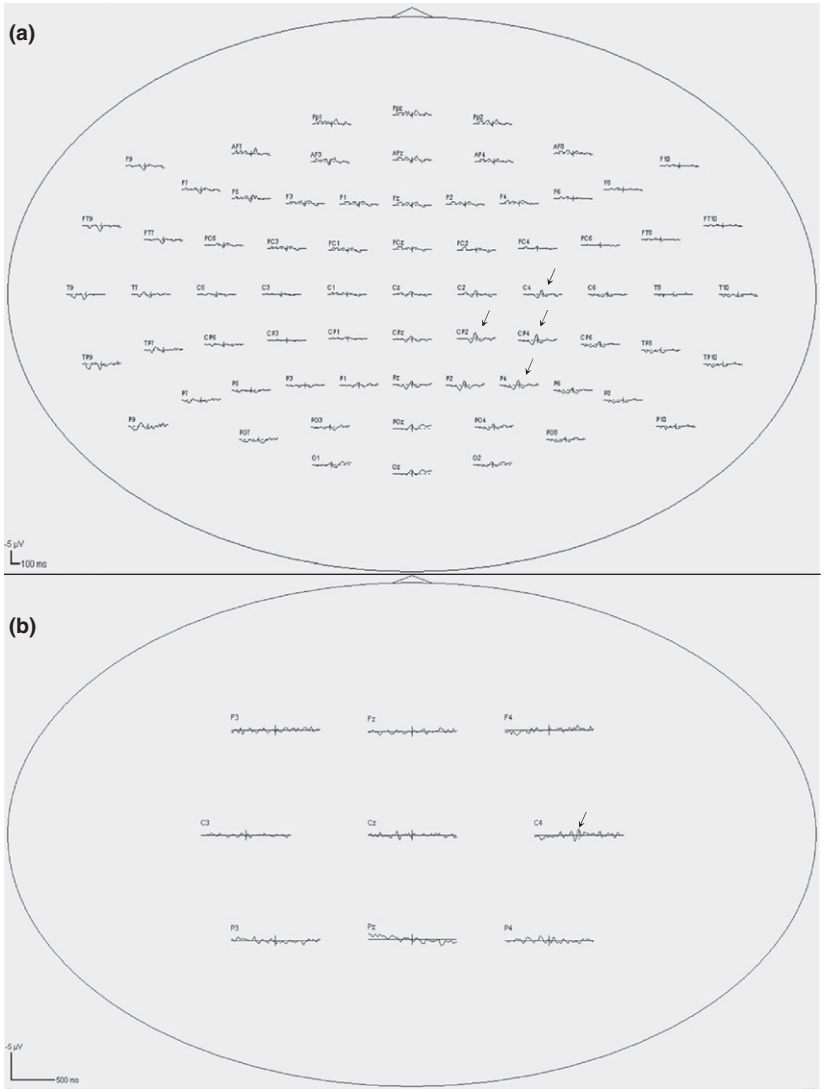

Figure 1 Jerk-locked back averaging analysis (JLBA). (a) Patient 1: JLBA analysis of 49 activations of the left flexor digitorum superficialis. There is a negative electroencephalographic transient starting 50 ms before the onset of the EMG activation (arrows). Top view of the average montage [EEG recorded with sensitivity 5 µV/mm, high frequency filter (HFF) 70 Hz, low frequency filter (LFF) 0.53 Hz, notch filter (50 Hz) on]. (b) Patient 2: JLBA of 259 activation of the left abductor pollicis brevis. There is a small amplitude negative electroencephalographic transient on the right central leads that starts 45 s before the EMG activation (arrow). Top view of the average montage (EEG recorded with sensitivity 5 µV/mm, HFF 70 Hz, LFF off, notch filter off). Montage was reduced to nine channels due to frequent artefacts in the remaining.

cortical-subcortical loops can contribute to the persistence of a focal cortical epileptiform activity [11]. The biological changes associated with post-stroke gliosis and meningocerebral cicatrix formation may result in hyperexcitability and neuronal synchrony [12] facilitating EPC.

The diagnosis of EPC frequently implies a high level of clinical suspicion and requires a careful clinical evaluation including myoclonus activation manoeuvres. In this prospective study, the subtle involuntary movements of the fingers not reported by the patient and only detected at clinical inspection, increasing with activation manoeuvres, resemble minipolymyoclonus [10]. Minipolymyoclonus of central origin was first described by Wilkins *et al.* in 1985 [10] in 11 heterogeneous patients with different types of epilepsy syndromes and neurodegenerative disorders. To our best knowledge, this paper is the first to describe this phenomenology in a prospective cohort of stroke patients.

Clinical suspicion of EPC must be corroborated by imaging and neurophysiology studies [7],

including jerk-lock back averaging analysis, as in our patients. This neurophysiological technique is of utmost importance because raw data visual analysis does not necessarily show continuous or persistent epileptiform or periodic abnormalities, such as in other types of focal or non-convulsive status epilepticus [13,14]. However, it must be reinforced that back averaging analysis only confirms the cortical origin of the involuntary movement. The clinical integration of these data is essential to the EPC diagnosis, since cortical myoclonus and minipolymyoclonus can be found in other pathologies [7,10]. The two patients of our study also had sporadic remote symptomatic non-provoked focal motor seizures supporting the diagnosis of this form of status epilepticus. In fact, the clinical phenomenology of EPC can be seen as continuously repeated fragments of motor seizures [8]. Furthermore, one of our patients had a diagnosis of non-convulsive focal status epilepticus without impairment of consciousness in the first week after stroke.

It should also be emphasized that, in stroke patients, involuntary movements can be caused by different mechanisms and that post-stroke focal myoclonus can additionally be a hyperkinetic movement disorder, where basal ganglia are most often involved. Although lesions in different parts of the brain can cause the same movement disorder, post-stroke myoclonus is usually associated with lesions in the midbrain, pons or thalamus and is frequently an acute stroke complication [15,16]. This was not the case for our patients. Furthermore, an involuntary movement cortical correlate was established in this work by back averaging analysis.

Regarding the treatment of EPC, studies that included patients with ischaemic stroke as the aetiology show the use of different anti-epileptic drugs and variable clinical response, frequently requiring polytherapy or even being refractory [1,2]. As in our study, the study by Mameniskiene *et al*. [8] showed that the control of EPC did not always correlate with control of other types of seizures in the same patient.

The consequences of post-stroke EPC are unknown although post-stroke epileptic phenomena (seizures and status epilepticus) [17–21] have been associated with a worse infarct outcome.

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Disclosure of conflicts of interest

Dr Bentes received the 2012 Research Grant in Cerebrovascular Diseases (Scientific Promoter: Sociedade Portuguesa do AVC/Sponsor: Tecnifar). Dr Ferro reports personal fees from Boehringer Ingelheim outside the submitted work. The remaining authors have no conflict of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. ASPECTS vascular territory in patients with an infarct limited to middle cerebral artery territory in brain imaging study.
Video S1. Irregular, small amplitude, non-synchronized subtle mainly jerky movements of several fingers of patient 1, accentuated by posture, are observed.
Video S2. Irregular, small amplitude, non-synchronized subtle jerky movements of several fingers of patient 2 are observed.

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