Seizure 50 (2017) 14–17

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Short communication

LGI1-antibody encephalitis is characterised by frequent, multifocal clinical and subclinical seizures

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ARTICLE INFO

Article history:
Received 23 April 2017
Received in revised form 15 May 2017
Accepted 24 May 2017

Keywords:
Autoimmune encephalitis
Leucine-rich glioma inactivated-1
Autoantibody
Neuroimmunology
Epilepsy

ABSTRACT

Purpose: To describe clinical and electrographic characteristics of seizures LGI1-antibody encephalitis, and their correlations with two-year outcomes.
Methods: Video-electroencephalography recordings were performed on a cohort of 16 consecutive patients with LGI1-antibodies from two UK neuroscience-centers over five-years.
Results: From 14 of 16 patients (13 males; age-range 53–92 years), 86 faciobrachial dystonic seizures were recorded at a median frequency of 0.4 per hour (range 0.1–9.8), and ictal EEG changes accompanied 5/86 events. In addition, 11/16 patients showed 53 other seizures – subclinical (n = 18), motor (n = 16), or sensory (n = 19) – at a median of 0.1 per hour (range 0.1–2) associated with temporal and frontal discharges. The sensory events were most commonly thermal sensations or body-shuddering, and the motor events were frequently automatisms or vocalisations. Furthermore, multifocal interictal epileptiform discharges, from temporal, frontal and parietal regions, and interictal slow-wave activity were observed in 25% and 69% of patients, respectively. Higher observed seizure frequency correlated with poorer functional recovery at two-years (p = 0.001).
Conclusions: Multiple frequent seizure semiologies, in addition to numerous subclinical seizures and interictal epileptiform discharges, are hallmarks of LGI1-antibody encephalitis. High overall seizure frequency may predict more limited long-term recovery. These observations should encourage closer monitoring and proactive treatment of seizure activity in these patients.

1. Introduction

LGI1-antibodies are closely associated with a limbic encephalitis (LE) which is characterised by confusion, disorientation and seizures, frequently with medial temporal lobe inflammation on imaging [1]. The seizures include typical medial temporal lobe events [2–4], and more distinctive semiologies including bradycardia, piloerection, and faciobrachial dystonic seizures (FBDS) [2,4–7]. These multiple seizure descriptions appear in several separate reports, largely based on retrospective histories. As patients often show some amnesia for the acute illness, and these reports lack the gold-standard of video-EEG monitoring [2,5,8], our aim was to systematically describe and quantify the electroclinical characteristics of seizures in patients with LGI1-antibodies, with a focus on seizure localisation, semiology and frequency, from consecutive patients attending video-EEGs.

2. Materials and methods

Sixteen consecutive adults with LGI1-antibody encephalitis and clinco-electrographic events during video-EEG recordings were seen at the author's two institutions between 2007 and 2012. Ethical approval for patient consent and data collection was available (references 07/Q1604/28, 16/YH/0013 and OUH10563). Forty-one EEGs from these 16 patients were reviewed by two

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http://dx.doi.org/10.1016/j.seizure.2017.05.017

Table 1
Clinical and electrographic characteristics of patients with LGI1-antibodies. LGI1-antibody level (end-point dilution shown; * = additional CASPR2-antibody positivity), A = arm, F = face, L = leg involvement during FBDS; [a] = lateralisation (R right; L left; BL bilateral); [b] = distribution (CT centrotemporal; Temp temporal; FT Frontotemporal; FC Frontocentral; FCP Fronto-Centro-Parietal); [c] = two patients had sensory aura preceding some motor events; [p] = patients who underwent prolonged recordings.

			FBDS			Motor/ subclinical seizures		Sensory seizures		Frequency (motor & sensory seizures)
Age (years)	Sex	LGI1-antibody level	Number per hour	Arm, face and/or leg involved	Ictal EEG changes	Semiology[a]	Ictal EEG[a,b]	Semiology	Ictal EEG[a,b]	Number per hour
71	M	540	Not captured		N	Clonic L arm and neck (3/4), automatisms (1/4)	L CT (n = 4)	–	–	1.4
67	M	14580	5.4	AF,AFL and L	N	–	–	Fear, tingling cold sensation, and flushing (n = 1)	Nil	0.6
61[p]	M	4860	4.2	A	N	–	–	–	–	
78[p]	M	4860	0.4	AF	N	Posturing,lip smacking, blinking and tachycardia (3/3)	R Temp (n = 3)			0.1
92[p]	M	14580	0.1	AFL	Y	–	–	–	–	–
63	M	1620	Not captured		N	–	–	Warm surge (n = 1)	Nil	2
69[p]	M	14580	0.2	AF	N	–	–	–	–	–
56[c,p]	M	14580	0.1	AF	N	L shoulder twitching, throat clearing, lip smacking, L hand posturing (1/7)	L FT (n = 1); FC (R 2/3, L 1/3), R Temp (n = 3)	Tingling (n = 2)	BL FC (1/2)	0.1
68	M	1620	2.4	AF and F	N	–	–	–	–	–
76[p]	M	1620	0.2	AFL, and F	N			Pain R face (n = 1)	Nil	0.1
64	F	4860	4.2	AFL, AF and L	Y	Arousal (1/6), no clinical change in 5/6	R FT (n = 6)	–	–	1.5
63	F	4860*	9.8	AFL	Y	Oral automatisms (1/1)	R Temp (n = 1)	–	–	0.1
69[c,p]	M	4860*	0.2	AFL, AF and LL	N	Nocturnal arousals (3/6), no clinical change (2/6); L hand twitching (n = 1/6)	L FT (n = 5)	Cold sensation (n = 9); lip quivering (n = 3);)	L Temp (1/9) and L FCP (1/9)	0.7
66[p]	M	4860*	0.4	AFL	N	–	–	–	–	0.1
64	F	14580	5.4	AF	N	Vocalisations, unresponsive, automatisms, post ictal confusion (8/8); L Head version (n = 3/8)	L Temp (n = 6) and R FT (n = 2)	Body shuddering and goosebumps (n = 2)	Nil	0.1
53	M	4860	0.1	AF	N	–	–	Body shuddering (n = 3)	Nil	0.1

consultant clinical neurophysiologists (TW and RK), and findings were systematically recorded in a database formatted as Table 1.

3. Results

3.1. Clinical and EEG characteristics

As shown in Table 1, 13/16 (81%) patients were male, and median age was 67 years (53–92). At times of EEG recordings, 15/16 (94%) patients had cognitive impairment, and were receiving AEDs (n = 16) and immunotherapies (n = 14). Eight of 16 patients underwent prolonged video telemetry (24–120 h); eight had EEGs of 20–30 min duration with video recordings.

3.2. Clinical and EEG features of FBDS

From 14 of 16 patients, 86 FBDS were recorded (median 6 per patient, range 1–28, Table 1). The face and arm were both involved in 70 attacks, of which 12 also involved the leg. A further four events involved the face alone, six the arm alone, and six events exclusively involved the leg. Twenty-two of 86 FBDS showed associated ictal features including dysphasia, fear, oral automatisms, vocalisations or loss of awareness. FBDS occurred during wakefulness (n = 48), from sleep (n = 32), and from drowsiness (n = 6), and their frequency varied from 0.1–9.8 per hour (median = 0.4).

EEG showed prominent muscle artefact (lasting 0.5 to 1.6 s) during 81/86 recorded FBDS. In the remaining five events (6%), three recorded from the same patient, preceding rhythmic delta wave activity was observed at onset over the left frontotemporal region (Supplementary Fig. 1). These were followed by muscle artefact and generalised EEG attenuation, and around seven seconds later, sharply contoured slow wave activity appeared and persisted for 30 s. In the other two events, preceding slow wave activity was seen in the left frontocentral electrodes before muscle artefact, and the FBDS were around five seconds in duration with prolonged post-ictal confusion (Video 1).

3.3. Motor, sensory and subclinical seizures other than FBDS

A variety of semiologies other than FBDS were also captured at overall frequencies similar to the FBDS (median = 0.1, range 0.1 to 2 per hour, Table 1). In total, 53 seizures other than FBDS were captured in 12 patients: 18/53 were subclinical, 16/53 had motor features and 19/53 showed sensory semiologies. Overall, accompanying electrographic changes were present in 37 of 53 events (70%).

The 18 subclinical seizures (example in Supplementary Fig. 2) showed ictal evolution in the frontotemporal (11/18, 61%), temporal (3/18, 16%) and frontocentral regions (4/18, 22%), within either the right (62%) or left (38%) hemispheres.

The motor semiologies (example in Video 2) showed features including automatisms (13/16, 81%), vocalisations (8/16, 50%), clonus (4/16, 25%), dystonic posturing (4/16, 25%), version (3/16, 18%) and eye blinking (3/16, 18%). All motor events were accompanied by ictal EEG changes seen in the temporal (62%), frontotemporal (18%), centrotemporal (18%) and frontocentral (18%) regions, within the left (62%) or right (38%) hemispheres.

The 19 sensory events were described as thermal alterations (n = 11, 58%, Video 3), body-shuddering (n = 5, 26%), tingling (n = 3,