

Case Report

Unusual seizure evolution: Focal-general-focal-general

Christopher Smelick^{a,*}, Jeffrey W. Britton^b, William O. Tatum^a, Anteneh M. Feyissa^a^a Department of Neurology, Mayo Clinic, 4500 San Pablo Rd, Jacksonville, FL 32224, USA^b Department of Neurology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

ARTICLE INFO

Article history:

Received 2 January 2018

Received in revised form 2 February 2018

Accepted 13 February 2018

Available online 14 March 2018

Keywords:

Focal-general-focal-general

Secondary focal

Focal evolution

Secondary focal evolution

Regeneralization

ABSTRACT

Seizure types have been described that do not conform to traditional classification schemes. We present another unusual type characterized by focal onset with secondary generalization, that is followed immediately by continued focal activity that generalizes again without an intervening break. Better understanding of these seizure types may allow improved targeted therapies and help shed light on the mechanistic underpinnings of epilepsy.

© 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Seizure types not conforming to traditional classification schemes have been described in the literature. These include generalized seizures with focal evolution and ping-pong seizures characterized by focal onset with switching lateralization [1–3]. We present another unusual type: focal onset with secondary generalization, but followed immediately by continued focal activity that generalizes for a second time before seizure cessation.

2. Case

A 57-year-old woman was admitted to epilepsy monitoring unit for focal epilepsy due to subarachnoid hemorrhage secondary to a ruptured/clipped right middle cerebral aneurysm two years prior. Coronal and axial MRI demonstrated sequelae of prior injury including temporal and perisylvian encephalomalacia. She had had two events without loss of awareness in the month preceding admission, one with bilateral limb shaking and another with left upper extremity burning sensation. She was then on lamotrigine 200 bid.

During admission, she had one seizure event. Clinically, approximately 60 s into the initial electrographic focal activity she reported a burning sensation in her left upper extremity and left lip. She was subsequently unable to squeeze with her left hand, but continued to be verbal and communicative until she developed leftward eye deviation and

clonic head movements. This evolved into tonic–clonic movements prominently involving her upper body lasting about 80 s. A few seconds after this abated she started to slowly respond. Two minutes later her eyes deviated to the left and she again exhibited generalized tonic–clonic activity lasting approximately 150 s.

Ictal EEG showed a right frontotemporal rhythmic delta at the seizure onset. This evolved in frequency and amplitude for a few seconds before spreading to right temporal and central regions, thereafter generalizing into a tonic–clonic discharge pattern. After approximately 2 min the generalized pattern was immediately replaced by a distinct right frontotemporal and central delta discharge. This pattern evolved in amplitude and frequency for about 2 min before again generalizing into a tonic–clonic discharge pattern (Fig. 1).

Given the unique seizure propagation features, we employed quantitative EEG (qEEG) trend analysis (Magic Marker Insight, Persyst Inc., Prescott, AZ) for further characterization. The rhythmicity spectrogram, asymmetry spectrogram, and the aEEG panels illustrate a right hemisphere onset focal seizure preceding generalization, followed immediately by right hemispheric seizure activity without any intervening break. The seizure then generalized for a second time before its cessation (Fig. 2).

3. Discussion

Focal events proceeding from generalized events have been described by Williamson et al. in six patients [1]. The secondary focal evolution is thought related to initial misdiagnosis as complex partial seizures in four of these patients. Improvement was noted with treatment for generalized seizures. Linane et al. also described generalized onset seizures with focal evolution in ten patients [2]. Six were

* Corresponding author.

E-mail addresses: Smelick.Christopher@mayo.edu (C. Smelick),britton.jeffrey@mayo.edu (J.W. Britton), Tatum.william@mayo.edu (W.O. Tatum),Feyissa.Anteneh@mayo.edu (A.M. Feyissa).

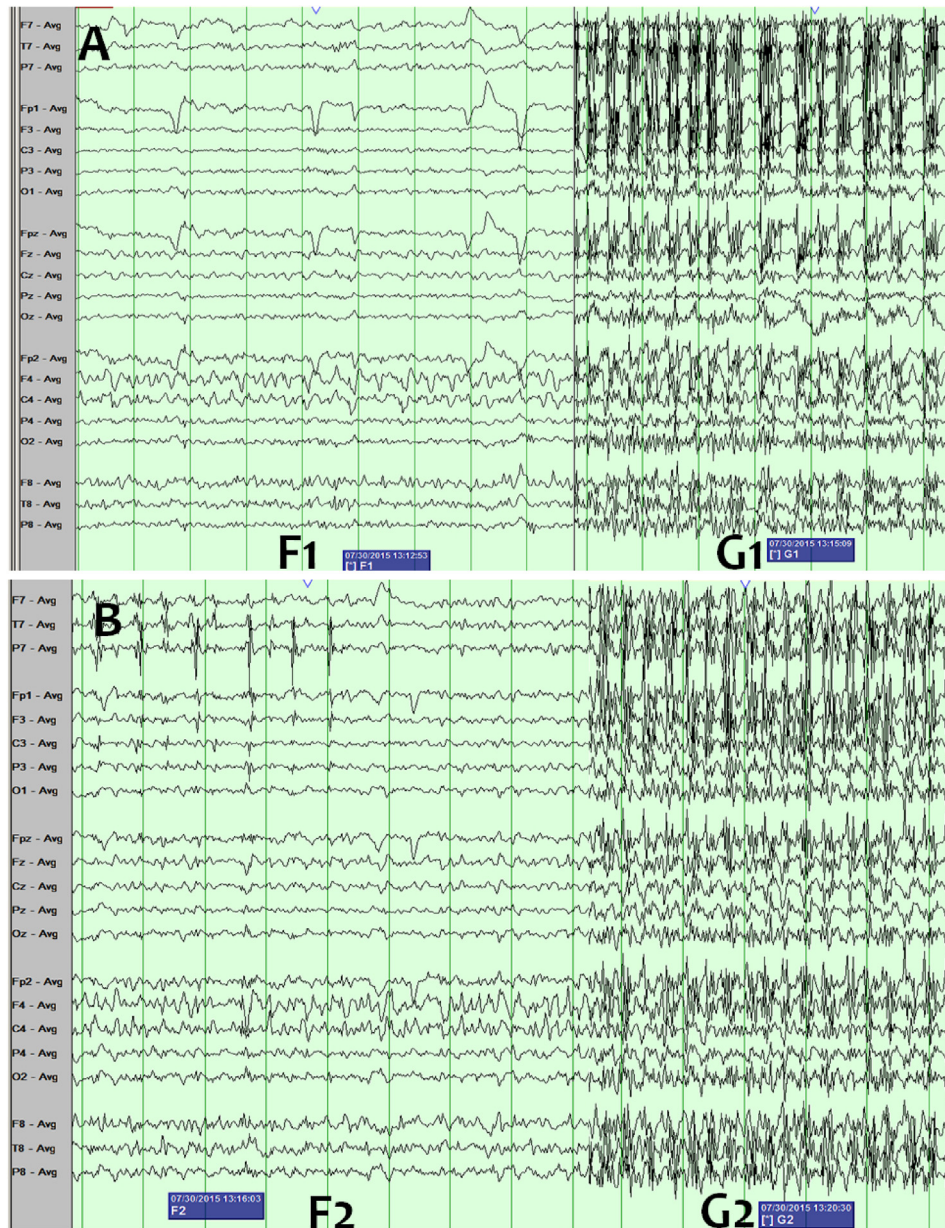


Fig. 1. A. EEG tracing showing a rhythmic right frontocentral discharge (arrow) at seizure onset (F1) with seizure generalization (G1) for the first time. B. Focal seizure with rhythmic right frontocentral discharge (F2) immediately reappearing before generalizing for the second time (G2). Blue boxes show exact time stamps for single seizure during the four phases.

eventually diagnosed with genetic/idiopathic etiology, and the other four as structural/metabolic/symptomatic—all improving with medicine changes targeting generalized onset. Another seizure type not fitting into traditional classification schemes is the ping-pong seizure, as described by Fisher et al. [3]. They report thirteen patients with shifting laterality at maximal seizure activity: rather than a focal seizure generalizing, a focal seizure switched to the contralateral side with cessation of seizure activity on the origin side. These authors converge on a few same teaching points: 1) unless an entire seizure episode is captured, partial electrographic recordings can lead clinicians to misdiagnose seizure type and/or origin; and 2) seizure types exist that do not conform to traditional seizure classification schemes, with neglect of this leading to misdiagnosis. Such misdiagnoses are associated with lack of seizure control, e.g. treating generalized seizures with focal-targeting drugs.

Herein, we describe an additional seizure type not conforming to classical classification schemes, characterized by: focal onset seizure evolving to bilateral convulsions, immediate return of focal seizure

activity, and again re-generalization before seizure cessation. It is not clear what exactly the focal activity immediately succeeding the first generalization represents. Possibilities include focal evolution of the general activity, or simply continuation of the original focal event despite attenuation of generalized activity. If the former type of evolution, conceivably the focal generator is more refractory to the underlying mechanisms of seizure termination that led to it being the generator in the first place. If the latter type of evolution with the generator acting like a pilot light, conceivably the continuation stems from asynchrony between the focal activity and subsequent general activity—i.e. synchrony that may be involved in seizure termination is present in the general component but not the “refractory” focal circuitry. In this patient synchrony differed between the initial generalization and secondary generalization phases, which might reflect the latter mechanism. Beyond the likely necessity of a focal generator/disturbance, it is unclear what is requisite to manifest this focal-general-activity. Further observations of the phenomenon with different structural lesions may provide insight into circuits that may be more salient, as well as what role synchrony may play.

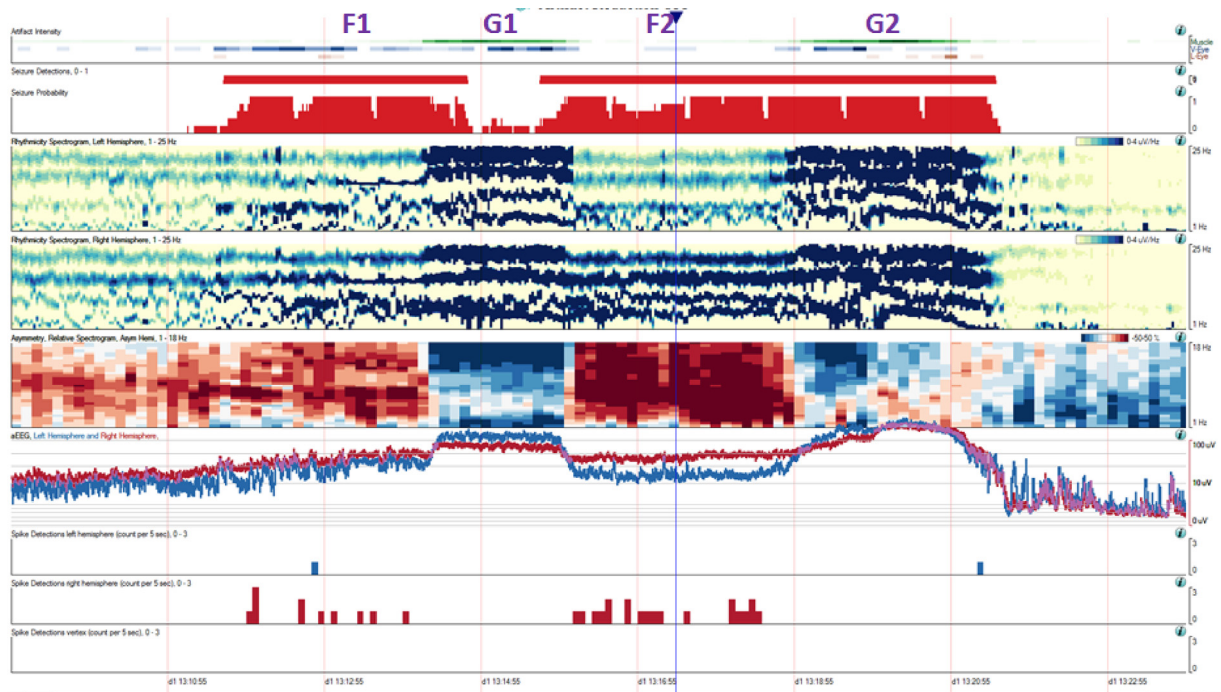


Fig. 2. Quantitative EEG showing a focal right hemispheric seizure (F1) that secondarily generalized (G1), reappeared immediately as a right hemispheric focal seizure (F2), and generalized for a second time (G2) before ceasing.

Synchronization may be a specific common component in seizure termination. This has been described as resynchronization, hypersynchronization, and thalamocortical oscillations in human partial seizure recordings [4]. Termination is characterized specifically by synchronous periodic bursting involving more diffuse cortical regions than at onset, as well as with progressive enhancement of burst activity and interburst interval. The associated longer post-burst depression may stop seizures by preventing further ictal network reactivation. Increased prevalence of EEG will allow capturing of more of these atypical seizures, with better characterization afforded by presurgical/surgical studies and improved technology (e.g. high-density electrodes, wider bandwidth, increased sampling rate, and improved analytic/qEEG algorithms). Such greater spatial & temporal characterization will more clearly depict ictal networks and phenomena such as hypersynchronization. This will

help inform the development of more targeted and efficacious therapies for these atypical seizure types.

References

- [1] Williamson R, Hanif S, Mathews GC, Lagrange AH, Abou-Khalil B. Generalized-onset seizures with secondary focal evolution. *Epilepsia* 2009 Jul;50(7):1827–32. <https://doi.org/10.1111/j.1528-1167.2009.02045.x>.
- [2] Linane A, Lagrange AH, Fu C, Abou-Khalil B. Generalized onset seizures with focal evolution (GOFE) - a unique seizure type in the setting of generalized epilepsy. *Epilepsy Behav* 2016 Jan;54:20–9. <https://doi.org/10.1016/j.yebeh.2015.10.005>.
- [3] Fisher RS, Blum DE, Shetter A, Ledin K, Archibald J. Ping-pong seizures. *J Epilepsy* 1995;8(1):29–32. IN1-IN4. [https://doi.org/10.1016/0896-6974\(94\)00005-K](https://doi.org/10.1016/0896-6974(94)00005-K).
- [4] Evangelista E, Bénar C, Bonini F, Carron R, Colombet B, Régis J, et al. Does the thalamocortical synchrony play a role in seizure termination? *Front Neurol* 2015 Sep 1;6:192. <https://doi.org/10.3389/fneur.2015.00192>.