Seizure 53 (2017) 51–54

Contents lists available at ScienceDirect

Seizure

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

A stereo EEG study in a patient with sleep-related hypermotor epilepsy due to DEPDC5 mutation

Lorenzo Ferri[a,b,1], Francesca Bisulli[a,b,*,1], Roberto Mai[c], Laura Licchetta[a,b], Chiara Leta[a,b], Lino Nobili[c], Barbara Mostacci[a], Tommaso Pippucci[d], Paolo Tinuper[a,b]

[a] IRCCS Bologna Institute of Neurological Sciences, Bologna, Italy
[b] Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[c] "Claudio Munari" Center for Epilepsy Surgery, Niguarda Hospital, Milano, Italy
[d] Medical Genetics Unit, Sant'Orsola-Malpighi University Hospital, Bologna, Italy

ARTICLE INFO

Article history:
Received 25 May 2017
Received in revised form 21 September 2017
Accepted 30 October 2017
Available online xxx

Keywords:
DEPDC5
SHE
Genetic epilepsy surgery
SEEG
Focal cortical dysplasia

ABSTRACT

Purpose: Dishevelled EGL-10 and pleckstrin domain-containing protein 5 (DEPDC5) mutations are found in a wide spectrum of focal epilepsies ranging from epilepsy caused by malformation of cortical development to non-lesional epilepsy, including sleep-related hypermotor epilepsy (SHE). A surgical approach has been anecdotally reported in patients with DEPDC5 mutations, but most of these cases had a lesional etiology.
Methods: We describe a stereo-EEG (SEEG) study in a patient with drug-resistant/non-lesional SHE. Patient was screened for known mutations associated with SHE.
Results: SEEG disclosed bilateral synchronous and independent activity prevailing on the right central-anterior cingulate cortex, without a clear spatially defined epileptogenic zone. Due to the lack of a clear epileptogenic zone, surgery was contraindicated. Years later a DEPDC5 mutation was identified.
Conclusion: We suggest that genetic analysis should be considered before performing SEEG study in a patient with drug resistant non-lesional SHE, in the presence of seizures in wakefulness and unclear anatomo-electroclinical correlation. If DEPDC5 mutations are identified, the presurgical evaluation should be tailored to look for MRI-negative focal cortical dysplasia and a wide epileptogenic network. The appropriate management and potential benefit of surgery for genetic non-lesional epilepsy have yet to be clarified.

1. Introduction

Focal epilepsy (FE) was long thought to originate from primitive/acquired lesions, whereas genetic factors were more likely to cause generalized epilepsy [1]. This dichotomous over-simplification has been challenged by growing evidence that FE can be due to genetic mutations. The first FE gene to be identified was *CHRNA4*, implicated in autosomal dominant nocturnal frontal lobe epilepsy [2], recently renamed sleep-related hypermotor epilepsy (ADSHE) [3]. Since 1995, many groups have reported mutations in other genes causing FE, such as nicotinic acetylcholine receptor mutations (*CHRNB2, CHRNA2*) and potassium channel (*KCNT1*) in ADSHE, and *LGI1* and *RELN* mutations in autosomal dominant epilepsy with auditory features (ADEAF). Recently, *DEPDC5* mutations were found to be the cause of several FEs, ranging from epilepsy caused by malformation of cortical development (MCD) to non-lesional inherited epilepsy. *DEPDC5* mutations have been reported as the main cause of familial focal epilepsy with variant foci (FFEVF) and in 13% of ADSHE families [4]. In particular in FFEVF families fronto-temporal epilepsies are the most frequent phenotype, but extra fronto-temporal/multifocal onset have also been reported [5]. Age of onset of *DEPDC5*-related epilepsy ranges from infancy to adulthood (mean age 9–14) [4–7]. In ADSHE families infrequent diurnal seizures have been reported, making the differential diagnosis with FFEVF arduous, especially in small pedigrees [6]. Interestingly, in small series of *DEPDC5*-ADSHE patients a higher prevalence of diurnal episode (60%) and higher rate of drug-resistance (78%) have been reported compared with classical cohorts of ADSHE patients [6]. Recently a high prevalence of DEPDC5 mutation in a large series of SUDEP cases has also been documented [8].A surgical approach may be the only effective

* Corresponding author at: IRCCS Istituto delle Scienze Neurologiche. Department of Biomedical and Neuromotor Sciences Bologna, University of Bologna, Via Altura 3, Bologna, 40139, Italy.
E-mail address: francesca.bisulli@unibo.it (F. Bisulli).
[1] These authors contributed equally.

https://doi.org/10.1016/j.seizure.2017.10.022
1059-1311/

treatment for MCD-associated drug-resistant FE, which usually requires invasive presurgical study including SEEG, a procedure with major complication rates of 1.2–2.6% [9]. Even if some anecdotal surgical cases with visible/non-visible lesions associated with *DEPDC5* mutations have been reported (Supplementary Table), the appropriate surgical management of genetic FE cases is still debated due to the lack of long-term follow-up data. Cases with a constitutional mutation, which likely affects all brain cells, raise concerns on the utility of resecting the focal epileptogenic zone (EZ).

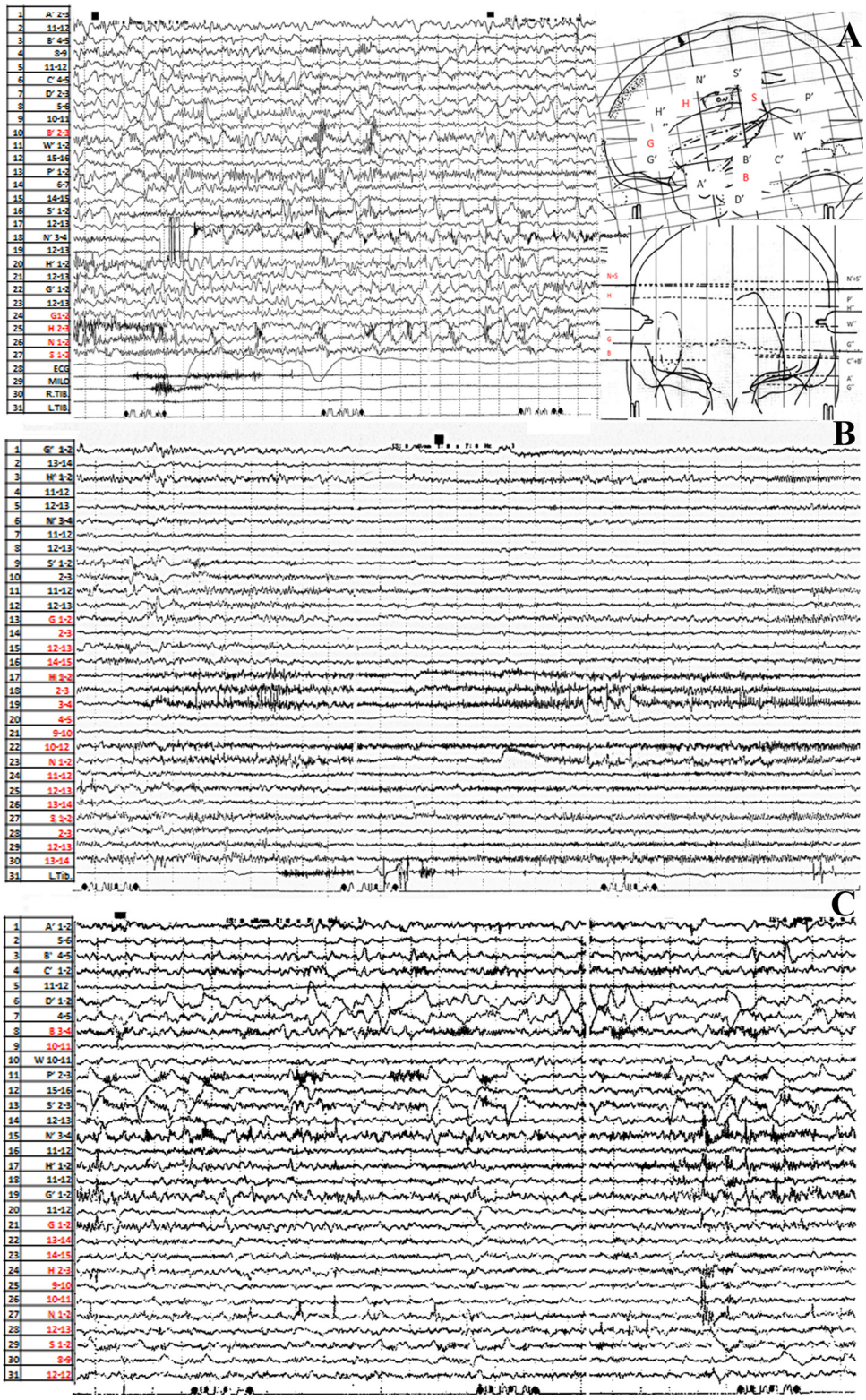

Fig. 1. (A) Fast polyspike activity over the anterior-mid cingulate gyrus bilaterally preceding a typical nocturnal hypermotor seizure. Note that interictal activity is also recorded in electrodes remotely from the ictal onset zone (B', B, P',S' and N'). Black letter indicates left side. (B) Polyspike activity over the right anterior-mid cingulate gyrus (H electrode). (C) Polyspike low wave activity involving the left mid-cingulate gyrus (H') with contralateral diffusion.