



Case report

Focal cortical dysplasia with prolonged ictal asystole, a case report

Ahmad wali^{a,b,*}, Fowzia Siddiqui^c^a Department of Neurophysiology, Aga Khan University Hospital (AKUH), Karachi, Pakistan^b Department of Neurology, Bolan Medical Complex Hospital, Quetta, Pakistan^c Department of Neurology, Aga Khan University Hospital (AKUH), Karachi, Pakistan

ARTICLE INFO

Article history:

Received 8 May 2019

Received in revised form 10 October 2020

Accepted 22 October 2020

Available online 3 December 2020

Keywords:

Focal cortical dysplasia FCD

Focal fast rhythmic epileptiform discharges

FREDs

Ictal asystole

Cardiac pacing

Cardioneuroablation

ABSTRACT

Introduction: Cortical dysplasia carries significant morbidities such as seizures and delayed milestones. Focal cortical dysplasia (FCD) causes refractory epilepsy with various seizure types depending on the location and extent of the dysplasia. FCD in the temporal region and the insular cortex may cause ictal bradycardia (IB) and ictal asystole (IA). Video EEG (VEEG) with simultaneous EKG recording can better diagnose these cardiac abnormalities in FCD. We describe a case of refractory epilepsy. The patient's clinical seizures were usually followed by syncope. VEEG revealed frequent seizures some of which were associated with prolonged ictal asystole.

Results: A 15 years old female was admitted to an epilepsy monitoring unit for VEEG. There were widespread fast abnormal discharges known as FREDs with a frequency of 16–20 Hz. She developed numerous habitual seizures and syncope. Some of these were associated with an EKG change in the form of asystole. The cardiac workup was normal. MRI revealed abnormalities in bilateral insular, temporal, and right parietal lobes.

Conclusion: This case highlights the significance of:

- Fast rhythmic epileptiform discharges (FREDs) in cortical dysplasia.
- Role of video-EEG monitoring.
- Prolonged asystole and the potential role of cardiac intervention in the form of cardiac pacing and cardioneuroablation in decreasing syncope.

© 2020 International Federation of Clinical Neurophysiology. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Focal cortical dysplasia (FCD) is well known for its presentation as refractory epilepsy with various seizures types. Some of these seizures are associated with syncope or falls. It usually presents with refractory complex partial seizures (Guerrini et al., 1992a, 1992b). In about 8–12% of juvenile patients and infants, these abnormalities in cortical development are associated with developmental delay, poor cognition, and intractable epilepsies (Li et al., 1995; Semah et al., 1998). The FCD, in adults, usually manifests as seizures. One of the important causes of death in epileptic patients is a sudden unexpected death in epilepsy (SUDEP) that may incorporate the incidence of postictal bradycardia and postictal asystole (Tassi et al., 2002). The diagnosis of these cardiac abnormalities in a patient with refractory epilepsy especially with syncope can only be confirmed via simultaneous EEG and EKG

recording (Novy et al., 2009). The confirmed diagnosis of FCD is done by histopathology however specific patterns in EEG are also important not only in diagnosis but in localization of the epileptic zone as well.

We report a child of FCD, identified by the specific EEG pattern known as focal rhythmic epileptiform discharges (FREDs) with a faster frequency of 16–20 Hz. Prolonged asystole of 23 s was observed in this case. To our knowledge, this is the longest asystole caused by cortical dysplasia.

2. Case presentation

A 15 years old school going, right-handed the girl was admitted to our epilepsy monitoring unit. She had a history of sudden episodes of absent-mindedness 3–4 times per day. Each episode lasted for several minutes. During a typical episode, the patient's head would turn towards the left side; she would talk irrelevantly and respond poorly ending in sudden syncope. Episodes were stereotypic with several times injuries secondary to falls. There was no change in her seizure semiology for the last several years.

* Corresponding author at: Department of neurology, Bolan medical complex hospital, Brewery road Quetta.

E-mail address: ahmadwaliakuh@gmail.com (A. wali).

In view of her frequent falls and syncope during seizures, her cardiac workup including EKG, echocardiography, Holter monitoring, etc was normal.

She had an abnormal postnatal history of severe neonatal hypoglycemia after a normal vaginal birth. Parents had noticed seizures since the age of five months. Her cognitive function test was normal but her school performance was poor due to refractory seizures. She was admitted to an epilepsy monitoring unit for seizure evaluation. Her medications included levetiracetam, lacosamide, clonazepam, and oxcarbazepine.

On examination, she was a cheerful young girl, cooperative and responding well to questions and commands. Her detailed neurological examination was unremarkable.

Her brain MRI scan revealed possible focal cortical thickening, agyria, and poor grey-white matter differentiation in bilateral insular, temporal, and parietal lobes (Fig. 1).

Her video EEG was performed with simultaneous EKG monitoring. During recording, there were intermittent abnormal focal fast discharges in the posterior aspect of the brain (mainly right temporo-occipital) both during awake and sleep state. These discharges were most likely FREDs (Fig. 2).

During the VEEG there were multiple habitual seizures. These were typical with two of them having asystole and fall. In one such

event, the EKG had baseline tachycardia that changed to bradycardia for 12 s and then followed by prolonged cardiac asystole lasting for 23 s. (Figs. 3, 4). During this period the patient was initially sitting on the bed, turned her head towards her left side, and started automatism of the right hand. This continued for several seconds until she fell down on the bed. There was complete asystole in EKG with complete body atonia. This was resumed by a normal cardiac rhythm. Simultaneous EEG demonstrated abnormal, rhythmic epileptiform discharges in the bilateral temporo-occipital regions, predominantly on the right side (Fig. 3).

3. Discussion

Abnormalities in cortical development in the form of FCD is associated with developmental delays, poor cognition, and intractable epilepsy in about 8–12% of the cases (Li et al., 1995; Semah et al., 1998). Such abnormalities are not only evident in MRI, but affected FCD patients also have certain EEG patterns. The phenomenon of abnormal discharges associated with cortical dysplasia is described with various forms and frequencies namely rhythmic epileptiform discharges (REDs), continuous epileptiform discharges (CEDs) (Gambardella et al., 1996) and focal fast rhythmic epileptiform discharges (FREDs) (Kuruvilla and Flink, 2002).

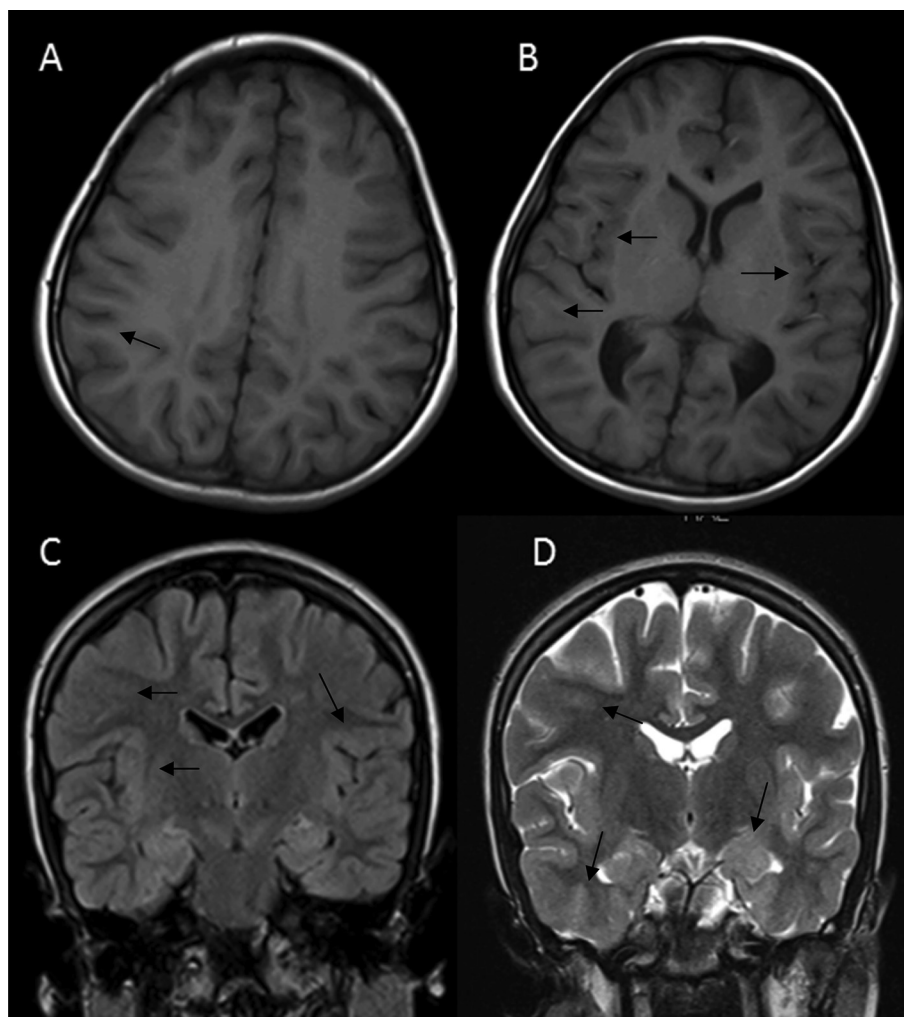


Fig. 1. MRI sequences of axial T1 (A & B), coronal FLAIR (C) and T2 (D) showing possible focal grey matter thickening with blurred grey and white matter differentiation involving various temporal and adjacent parieto-occipital lobes (arrow heads).

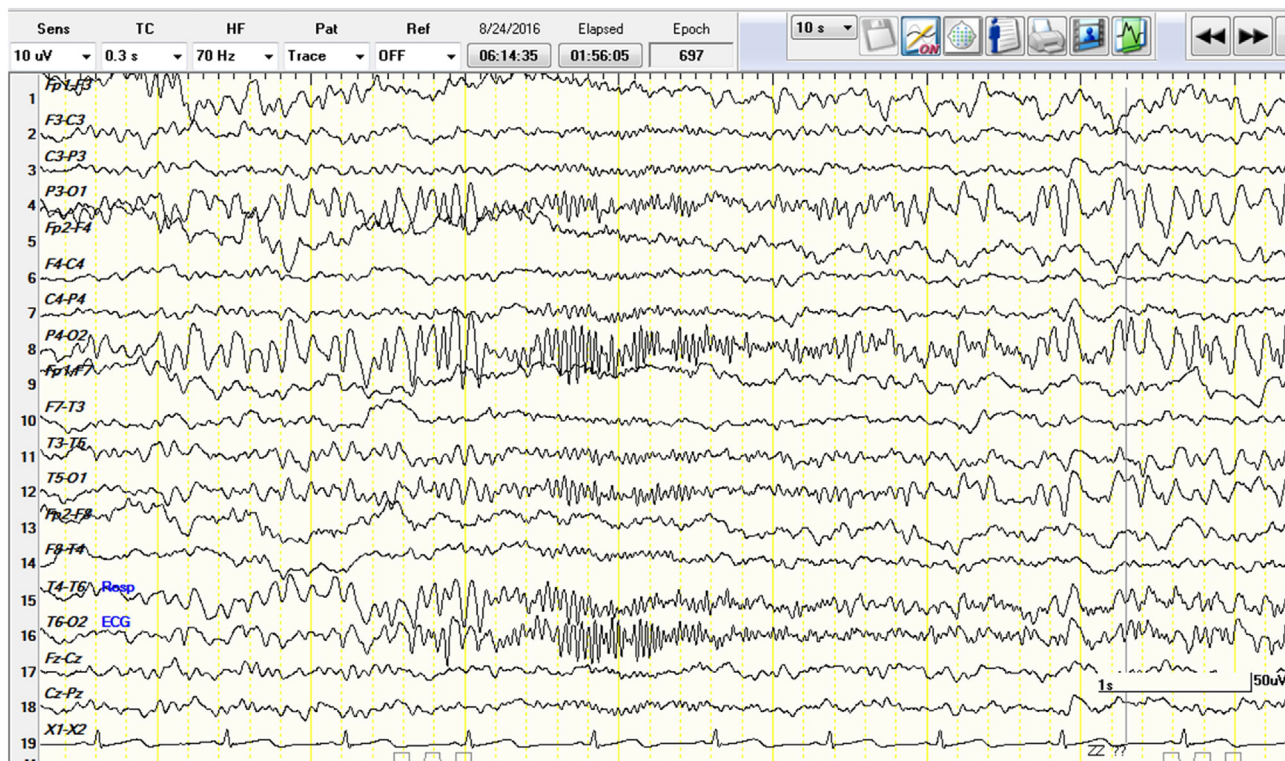


Fig. 2. A 10 s scalp EEG showing interictal, focal fast rhythmic epileptiform discharges (FREDs) (channel 8, 15 and 16) with amplitude (>100uV) and frequency of 16–20 Hz in the posterior quadrants of the brain (predominantly right temporo-occipital with spread to the left occipital region).

Our patient's discharges are most likely FREDs but with higher frequencies of 16–20 Hz and having a discrete localization (Fig. 2). The high amplitude fast rhythmic activity associated with sharp waves were considered highly specific for severe cortical dysplasia by Quirk et al. (Quirk et al., 1993).

FCD can involve any region of the brain, including the temporal, insular, orbitotemporal, or parietal lobes with peculiar EKG abnormalities including bradycardia and asystole. FCD with a prolonged IA is less defined (Seeck et al., 2003; van der Lende et al., 2016). For the diagnosis of these cardiac abnormalities in a patient with cortical dysplasia with syncope, simultaneous EEG, and EKG recording is essential (Novy et al., 2009). The initial localization depends upon the MRI however the exact ascertainment of the epileptic zone is only possible with VEEG, occasionally including invasive EEG as well (Tassi et al., 2002).

The abnormal cortex in our patient is most likely the initial triggering zone. During the habitual seizure of the patient, there was rhythmic activity in the bilateral temporo-occipital regions (right more than left) followed by ictal asystole (Figs. 3, 4). This was a prolonged IA lasting for 23 s. IA is a relatively benign condition as compared to the post ictal asystole (van der Lende et al., 2016). This is a self-limiting phenomenon that is not reported as one of the potential causes of death in SUDEP, yet we believe a prolonged IA needs to be investigated further. In our case, the reason for the complete body atonia with syncope is IA, which increases the morbidity of the patient. (Ghearing et al., 2007) (Figs. 3, 4). Moreover, both semiology and the abnormal EEG the pattern indicated this was purely seizure activity rather than a primary cardiac event.

When a specific region of the brain, most likely left insular cortex, is stimulated electrically, this produces bradycardia and asystole (Oppenheimer et al., 1992). Besides the role of the insular cortex, areas of the temporal and frontal cortices should also be

considered for symptom generation because the pathomechanism of IA is still unknown. Moreover, autonomic control of the heart rate may not be the same in all individuals (Reeves et al., 1996); it can be shifted to an atypical location in the brain by certain pathology (Leung et al., 2006). This is of interest because, despite identical semiology, only two seizures were associated with cardiac events. This could represent a different region of onset or spread to the adjacent posterior insular cortex that further propagates the initiation of bradycardia and asystole. In other words, focal epileptogenic lesions in one region mostly involve other distant structures, thus making an overall network of epileptogenic zones, especially in cases of FCD (Aubert et al., 2009).

In our patient's history, there are short intervals of disorientation, lack of awareness, or seizures that can best be explained by the frequent interictal FREDs; however, the true disruption to her functioning was the prolonged seizures with complete body atonia and syncope that the VEEG captured. The VEEG shows marked abnormal cardiac depressor responses during these prolonged seizures (Figs. 3, 4). This complete prolonged IA may necessitate further investigation regarding increased morbidity in this type of epilepsy with frequent syncope or body atonia. The role of placing a pacemaker for the ictal asystole is still controversial (Kepez and Erdogan, 2015), but Shihabuddin et al observed significant improvement and decrease in syncopal attacks mediated by ictal bradycardia and IA after insertion of cardiac pacemakers (Shihabuddin et al., 2014). Another relatively newer and successful option is cardioneuroablation that was first described by Pachon et al. in 2005. The procedure was performed successfully by Antolic and colleagues on a patient who did not suffer from IA again after the procedure (Antolic et al., 2018; Pachon et al., 2005). In the light of above facts, cardiac intervention seems to be optimistic. It may help patients who are refractory to AEDs and need long-lasting relief from their illness (Reeves et al., 1996; Strzelczyk et al., 2008).

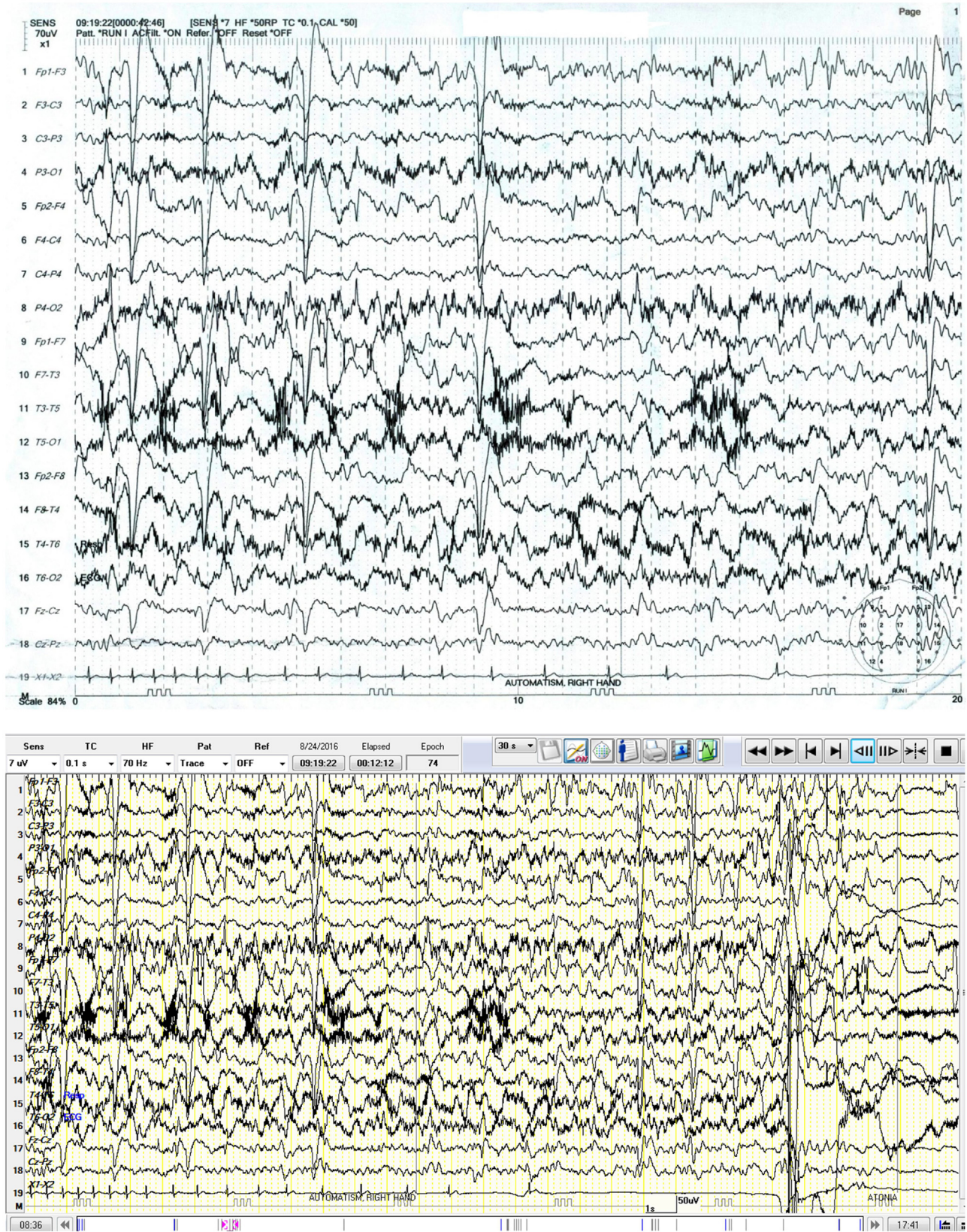


Fig. 3. Two consecutive traces EEG in a habitual seizure with syncope and fall. First with rhythmic seizure activity starting in bilateral (predominantly right) temporo-occipital region and second with bradycardia followed by complete asystole for 18 s. Note the minimal cerebral activity during asystole consistent with clinical syncope and fall with complete loss of body tone as well.

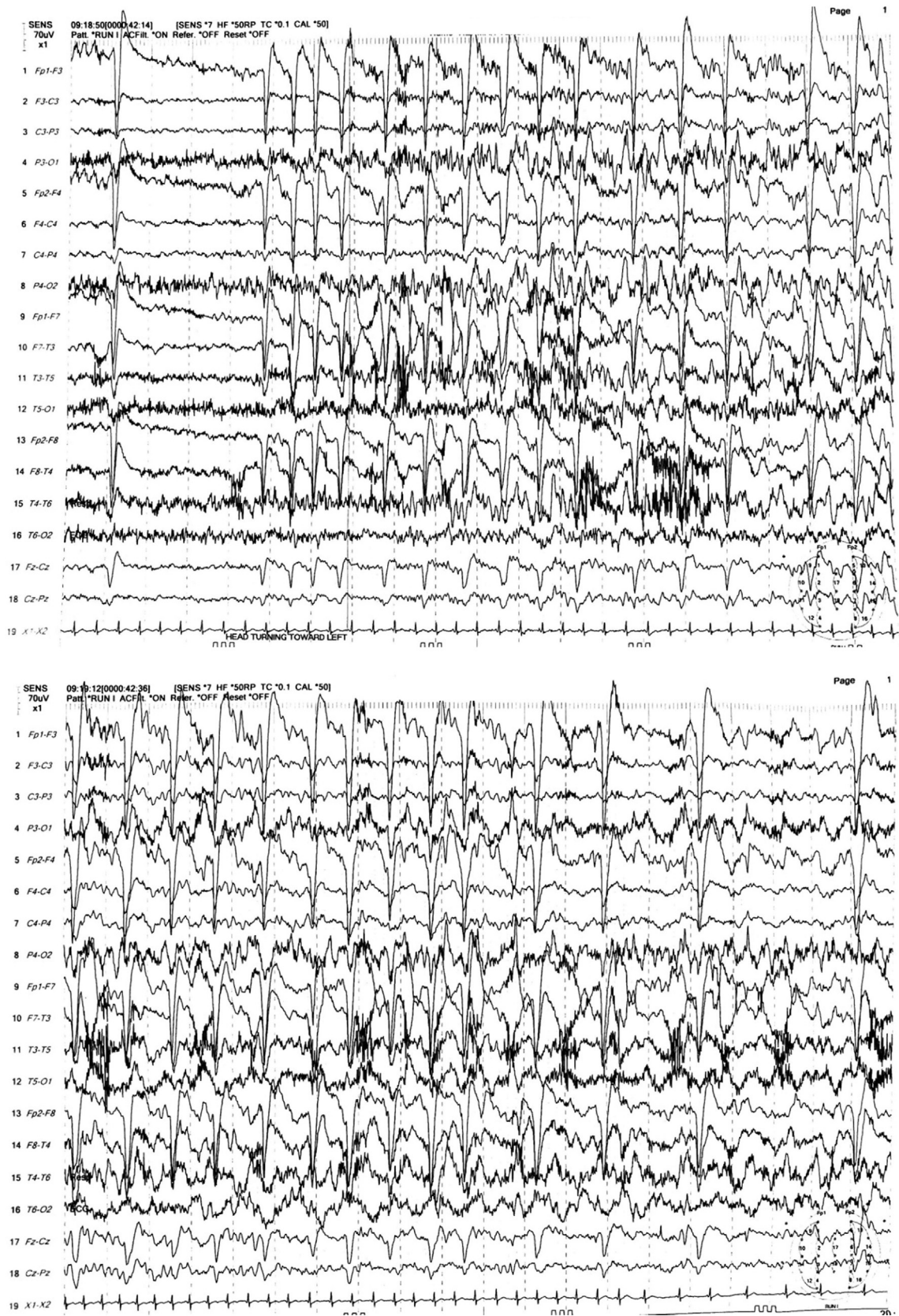


Fig. 4. Two consecutive EEG tracings few seconds before the seizures, showing rhythmic epileptiform discharges arising from bilateral temporo-occipital regions.

4. Conclusion

This case clearly highlights:

- Various clinical, EEG, and MRI presentations of cortical dysplasias.
- Fast rhythmic epileptiform discharges (FREDs) in cortical dysplasia.
- The superiority of VEEG in localization of the specific epileptic zone or a network secondary to the FCD.
- The potential role of pacemaker, cardioneuroablation, and other ways to lessen the morbidity in the form of falls and syncope.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We are very grateful to Miss. Zytoon Shivji RET and Mr. Ejaz Karim RET for the preparation of Video clips and EEG epochs relating to this case.

References

- Antolic, B., Gorisek, V.R., Granda, G., Lorber, B., Sinkovec, M., Zizek, D., 2018. Cardioneuroablation in ictal asystole—new treatment method. *HeartRhythm Case Rep.* 4 (11), 523–526. <https://doi.org/10.1016/j.hrcr.2018.07.018>.
- Aubert, S., Wendling, F., Regis, J., McGonigal, A., Figarella-Branger, D., Peragut, J.C., et al., 2009. Local and remote epileptogenicity in focal cortical dysplasias and neurodevelopmental tumours. *Brain* 132, 3072–3086. <https://doi.org/10.1093/brain/awp242>.
- Gambardella, A., Palmi, A., Andermann, F., Dubeau, F., Da Costa, J.C., Felipe Quesney, L., Andermann, E., Olivier, A., 1996. Usefulness of focal rhythmic discharges on scalp EEG of patients with focal cortical dysplasia and intractable epilepsy. *Electroencephalogr. Clin. Neurophysiol.* 98, 243–249. [https://doi.org/10.1016/0013-4694\(95\)00266-9](https://doi.org/10.1016/0013-4694(95)00266-9).
- Ghearing, G.R., Munger, T.M., Jaffe, A.S., Benarroch, E.E., Britton, J.W., 2007. Clinical cues for detecting ictal asystole. *Clin. Auton. Res.* 17, 221–226. <https://doi.org/10.1007/s10286-007-0429-9>.
- Guerrini, R., Dravet, C., Raybaud, C., Roger, J., Bureau, M., Battaglia, A., et al., 1992a. Neurological findings and seizure outcome in children with bilateral opercular macrogyric-like changes detected by MRI. *Dev. Med. Child. Neurol.* 34, 694–705. <https://doi.org/10.1111/j.1469-8749.1992.tb11505.x>.
- Guerrini, R., Dravet, C., Raybaud, C., Roger, J., Bureau, M., Battaglia, A., et al., 1992b. Epilepsy and focal gyral anomalies detected by MRI: electroclinico-morphological correlations and follow-up. *Dev. Med. Child. Neurol.* 34, 706–718. <https://doi.org/10.1111/j.1469-8749.1992.tb11506.x>.
- Kepez, A., Erdogan, O., 2015. Arrhythmic epilepsy and pacing need: a matter of controversy. *World J. Clin. Cases* 3, 872–875. <https://doi.org/10.12998/wjcc.v3.i10.872>.
- Kuruvilla, A., Flink, R., 2002. Focal fast rhythmic epileptiform discharges on scalp EEG in a patient with cortical dysplasia. *Seizure* 11, 330–334. <https://doi.org/10.1053/seiz.2001.0610>.
- Leung, H., Kwan, P., Elger, C.E., 2006. Finding the missing link between ictal bradyarrhythmia, ictal asystole, and sudden unexpected death in epilepsy. *Epilepsy Behav.* 9, 19–30. <https://doi.org/10.1016/j.yebeh.2006.05.009>.
- Li, L.M., Fish, D.R., Sisodiya, S.M., Shorvon, S.D., Alsanjari, N., Stevens, J.M., 1995. High resolution magnetic resonance imaging in adults with partial or secondary generalised epilepsy attending a tertiary referral unit. *J. Neurol. Neurosurg. Psychiatry* 59, 384–387. <https://doi.org/10.1136/jnnp.59.4.384>.
- Novy, J., Carruzzo, A., Pascale, P., Maeder-Ingvar, M., Genné, D., Pruvot, E., Despland, P.-A., Rossetti, A.O., 2009. Ictal bradycardia and asystole: an uncommon cause of syncope. *Int. J. Cardiol.* 133, e90–e93. <https://doi.org/10.1016/j.ijcard.2007.11.038>.
- Oppenheimer, S.M., Gelb, A., Girvin, J.P., Hachinski, V.C., 1992. Cardiovascular effects of human insular cortex stimulation. *Neurology* 42, 1727–1732. <https://doi.org/10.1212/wnl.42.9.1727>.
- Pachon, J.C., Pachon, E.I., Pachon, J.C., Lobo, T.J., Pachon, M.Z., Vargas, R.N., et al., 2005. “Cardioneuroablation”—new treatment for neurocardiogenic syncope, functional AV block and sinus dysfunction using catheter RF-ablation. *Europace* 7, 1–13. <https://doi.org/10.1016/j.eupc.2004.10.003>.
- Quirk, J., Kendall, B., Kingsley, D.P., Boyd, S., Pitt, M., 1993. EEG features of cortical dysplasia in children. *Neuropediatrics* 24, 193–199. <https://doi.org/10.1055/s-2008-1071538>.
- Reeves, A.L., Nollet, K.E., Klass, D.W., Sharbrough, F.W., So, E.L., 1996. The ictal bradycardia syndrome. *Epilepsia* 37, 983–987. <https://doi.org/10.1111/j.15281157.1996.tb00536.x>.
- Seeck, M., Zaim, S., Chaves-Vischer, V., Blanke, O., Maeder-Ingvar, M., Weissert, M., Roulet, E., 2003. Ictal bradycardia in a young child with focal cortical dysplasia in the right insular cortex. *Eur. J. Paediatr. Neurol.* 7, 177–181. [https://doi.org/10.1016/S1090-3798\(03\)00051-5](https://doi.org/10.1016/S1090-3798(03)00051-5).
- Semah, F., Picot, M.-C., Adam, C., Broglin, D., Arzimanoglou, A., Bazin, B., Cavalanti, D., Baulac, M., 1998. Is the underlying cause of epilepsy a major prognostic factor for recurrence? *Neurology* 51, 1256–1262. <https://doi.org/10.1212/WNL.51.5.1256>.
- Shihabuddin, B.S., Herlopian, A.S., Greenfield, L.J., 2014. Ictal asystole in epilepsy patients undergoing inpatient video-EEG monitoring. *Neurosciences (Riyadh)* 19, 317–321.
- Strzelczyk, A., Bauer, S., Knake, S., Oertel, W.H., Hamer, H.M., Rosenow, F., 2008. Ictal asystole in temporal lobe epilepsy before and after pacemaker implantation. *Epileptic Disord.* 10, 39–44. <https://doi.org/10.1684/epd.2008.0166>.
- Tassi, L., Colombo, N., Garbelli, R., Francione, S., Lo Russo, G., Mai, R., et al., 2002. Focal cortical dysplasia: neuropathological subtypes, EEG, neuroimaging and surgical outcome. *Brain* 125, 1719–1732. <https://doi.org/10.1093/brain/awf175>.
- van der Lende, M., Surges, R., Sander, J.W., Thijs, R.D., 2016. Cardiac arrhythmias during or after epileptic seizures. *J. Neurol. Neurosurg. Psychiatry* 87, 69–74. <https://doi.org/10.1136/jnnp-2015-310559>.