Annals of Noninvasive Electrocardiology

WILEY

CASE REPORT OPEN ACCESS

Manifested U-Waves Prior to Seizure Attacks in a Patient Who Had Remote Subarachnoid Hemorrhage: A Case Report

Nao Kaneko[1] | Masao Watanabe[2] | Shusuke Mori[3] | Isik Turker[4] | Ken Okamoto[5] | Takao Urabe[2] | Tomohiko Ai[6]

[1]Department of Laboratory Medicine, Juntendo University Urayasu Hospital, Chiba, Japan | [2]Department of Neurology, Juntendo University Urayasu Hospital, Chiba, Japan | [3]Department of Emergency Medicine, Tokyo Women's Medical University, Shinjuku, Japan | [4]Division of Cardiology, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA | [5]Department of Emergency and Critical Care Medicine, Juntendo University Urayasu Hospital, Chiba, Japan | [6]Department of Clinical Laboratory Medicine, Juntendo University Urayasu Hospital, Chiba, Japan

Correspondence: Takao Urabe (t_urabe@juntendo.ac.jp) | Tomohiko Ai (t-ai@juntendo.ac.jp)

Received: 28 May 2024 | **Revised:** 23 July 2024 | **Accepted:** 29 August 2024

Funding: Japan Society for the Promotion of Science, 18K08900.

Keywords: ECG | repolarization | seizure | U-wave

ABSTRACT

Sudden unexpected death in epilepsy (SUDEP) refers to unpredictable demise of a person following a seizure. Electroencephalograms can directly measure electrical activity in the brain; however, it cannot predict when seizures will occur. The use of electrocardiograms (ECGs) to monitor changes in brain electrical activity has gained attention, recently. In this case report, we retrospectively reviewed ECGs taken before and after seizure activity in a 75-year-old male who had a remote subarachnoid hemorrhage. Interestingly, U-waves appeared prior to his seizures and disappeared afterward, which suggests ECGs can be used to predict epilepsy in a certain population.

1 | Case Presentation

A 75-year-old male had suffered from a traumatic subarachnoid hemorrhage (SAH) due to fall at the age of 57 years. Following SAH, he had two presyncopal episodes at the age of 62 and 65 years and had been treated with valproic acid since the second presyncopal episode that was diagnosed as a partial seizure. In his 50s, he underwent elective percutaneous coronary intervention (PCI) of the right coronary artery for stable angina pectoris. There were no electrocardiographic changes including U-waves prior to or following the PCI.

He had a tonic–clonic seizure during a routine outpatient clinic visit at age 70 years. His head CT showed low-density lesions in the frontal lobes (Figure S1A). His ECG that was taken 1 month prior to this seizure activity showed "tee-pee sign" (Johri et al. 2009) in leads V_{2-5} (Figure 1 left panel). He was treated with diazepam and oral valproic acid was replaced with levetiracetam was started. His ECG immediately after the seizure episode still showed some tee-pee sign but it disappeared 5 months later.

Another tonic–clonic seizure occurred at age 71 years. He was treated with a diazepam injection (5 mg) followed by a levetiracetam drip (1000 mg/h). He stopped seizing within 5 min. His head CT scan showed low-density lesions in the frontal lobes like his previous CT (Figure S1B). He was admitted for observation, and an informed consent was obtained. Figure 2 shows chronological changes in the precordial ECG leads before and after the seizure. The ECG taken 10 days prior to the seizure episode (first panel) showed U-waves in leads V_{2-5}. The U-waves became more prominent immediately after the episode (second panel). Though the U-waves were still observed 5 months after the episode, the amplitudes became lower (third panel). The

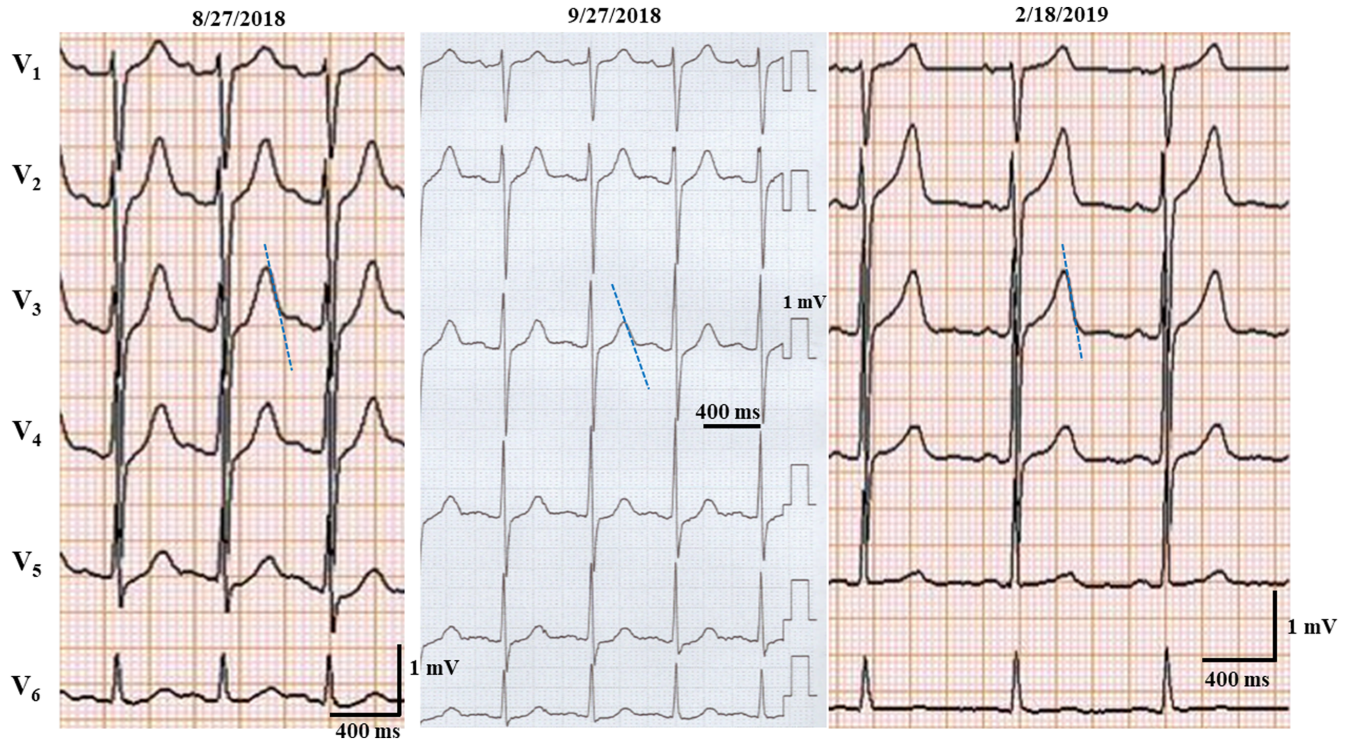

FIGURE 1 | Series of electrocardiograms (ECGs) taken before and after the first seizure attack. The patient had an attack on 9/27/2018. The blue dotted lines are tangent lines on the T-waves.

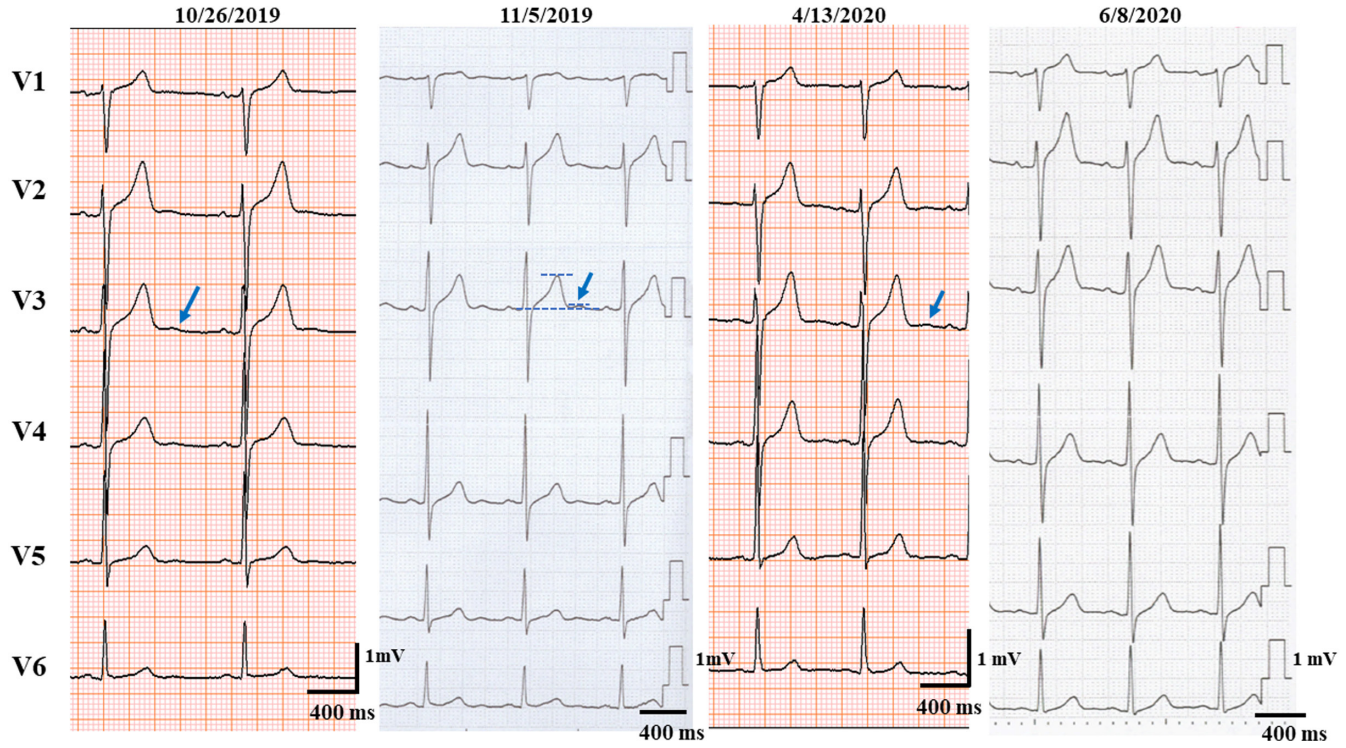

FIGURE 2 | Series of electrocardiograms (ECGs) taken before and after the second seizure attack. The patient had attack on 11/5/2019 (second left). The blue arrows indicate the U-waves; The blue dotted lines (11/5/2019) show the baseline and the peaks of T- and U-waves.

U-waves disappeared 6 months later (fourth panel). Table 1 summarizes the ECG parameters on each date. He did not have any seizure or syncopal episodes after this event. He did not have any abnormal blood chemistry values associated with U-waves at the time the ECGs were obtained (Table 2).

2 | Discussion

Patients with epilepsy syndromes often show abnormal ECG patterns such as ST-T changes including Brugada pattern and QT-prolongation (Hayashi et al. 2019). Our recent study

TABLE 1 | Electrocardiograms (ECGs) parameters.

Date	Seizure	HR (bpm)	QT (ms)	QT_c (Bazett)	QT_c (Framingham)	U/T ratio
8-27-2018	Before	127	320	466	401	NA
9-27-2018	Attack	100	320	413	382	NA
2-18-2019	After	73	380	419	407	0.07
10-26-2019	Before	55	440	421	426	0.10
11-5-2019	Attack	70	400	432	422	0.24
4-13-2020	After	73	400	441	427	0.4
6-8-2020	After	127	360	524	441	NA

Note: The ECG parameters were measured in V_3 (two examiners' agreement). The measurement methods were described elsewhere (Mori et al. 2021). QT_c intervals were corrected by Bazzet formula (QT/RR intervals^0.5) and Framingham formula ($QT_c = QT + 0.154\,(1 - RR)$). U/T ratio was calculated by dividing the U-wave amplitude by the T-wave amplitude; NA, U-wave amplitudes could not be measured due to "tee-pee-pattern" or U-waves did not appear.
Abbreviations: HR, heart rate (beat/min); QT, QT interval.

TABLE 2 | Blood test data.

	10-26-2019	5-11-2019 (attack)	4-13-2020	6-8-2020
Lactate (mg/dL)	NA	21.3	NA	22.9
BE (mEq/L)	NA	−0.6	NA	−4.3
pH (venous)	NA	7.343	NA	7.366
WBC ($\times 10^9$/L)	6.6	5.9	7.7	12.3
CK (g/dL)	274	181	315	648
Na (mEq/L)	141	144	141	140
K (mEq/L)	4.2	4	4.3	4.2
Cl (mEq/L)	104	104	104	106
Ca (mg/dL)	NA	8.6	NA	8

Note: NA represent data were not available.

demonstrated that post icteric QT intervals were significantly prolonged in patients who had remote brain abnormalities such as cerebral infarction, cerebral bleeding, and SAH compared to the patients without structural brain abnormalities (Mori et al. 2021). Although it is particularly important to predict seizure activity to prevent sudden unexpected death in epilepsy (SUDEP), we still do not know whether chronological changes in ECG parameters can be used to monitor patients with epilepsy. In our previous study, no patients showed cardiac arrhythmia during and after seizure episodes. One patient died suddenly 3 days after a seizure episode. His ECG only showed some notching in the beginning portion of the ST segment (Mori et al. 2021).

In our patient, U-waves appeared 10–30 days before the seizure episode. The U-waves then disappeared several months later. Though U-waves are mostly associated with electrolyte abnormalities such as hypokalemia (Johri et al. 2009), electrolytes were within normal range in our patient. It has been also reported that U-waves can be associated with stretch-induced delayed after depolarizations during rapid ventricular filling in the setting of increased adrenergic tone (Eyer 2015). This resembles the ECG changes observed in the acute phase of cerebral bleeding, subarachnoid hemorrhage (SAH) (Chatterjee 2011; Weintraub and McHenry Jr. 1974), and cerebral infarction (Komatsuzaki et al. 2021; Laundon and Littmann 2019). Specifically, De Swiet observed small U-waves in the precordial leads (V_{3-6}) of a 71-year-old female patient who suffered from SAH. Since the patient had deceased in acute phase, we do not know how the U-wave changed in her chronic phase (De Swiet 1969).

Although various methods have been tested to monitor neurocardiological signals (Ghaempour, Hassanli, and Abiri 2024), U-waves can be considered as a potential marker to predict seizure episodes in epileptic patients with structural brain diseases. We are planning to accumulate more data to investigate which parameter is useful in predicting epileptic attacks (e.g., U-wave/T-wave ratio).

3 | Limitation

Since this is a retrospective study, we did not monitor ECGs continuously. Thus, we do not know the exact duration when the patient showed U-wave. However, it is reasonable to speculate that he might have been more susceptible to having seizure attack while he was showing U-waves, although further prospective studies are warranted.

Author Contributions

Concept and funding: T.A.; Data analysis/interpretation: N.K.; Drafting article: N.K. and S.M.; Critical revision of article: I.T.; Approval of article: K.O., T.A., and T.U.; Data collection: N.K. and M.W.

Acknowledgments

The authors are grateful to the patient who participated in this study. This study was supported by Japan Society for the Promotion of Science (JSPS) 18K089000 (T.A.).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

Chatterjee, S. 2011. "ECG Changes in Subarachnoid Haemorrhage: A Synopsis." *Netherlands Heart Journal* 19, no. 1: 31–34. https://doi.org/10.1007/s12471-010-0049-1.

De Swiet, J. 1969. "Abnormal U Waves in the Electrocardiogram in Subarachnoid Haemorrhage." *British Heart Journal* 31, no. 4: 526–528. https://doi.org/10.1136/hrt.31.4.526.

Eyer, K. 2015. "Support for a Mechanico-Electrical Source of the "U" Wave." *Journal of Electrocardiology* 48, no. 1: 31–32. https://doi.org/10.1016/j.jelectrocard.2014.11.003.

Ghaempour, M., K. Hassanli, and E. Abiri. 2024. "An Approach to Detect and Predict Epileptic Seizures With High Accuracy Using Convolutional Neural Networks and Single-Lead-ECG Signal." *Biomedical Physics & Engineering Express* 10, no. 2: 25041. https://doi.org/10.1088/2057-1976/ad29a3.

Hayashi, K., R. Kohno, N. Akamatsu, D. G. Benditt, and H. Abe. 2019. "Abnormal Repolarization: A Common Electrocardiographic Finding in Patients With Epilepsy." *Journal of Cardiovascular Electrophysiology* 30, no. 1: 109–115. https://doi.org/10.1111/jce.13746.

Johri, A. M., A. Baranchuk, C. S. Simpson, H. Abdollah, and D. P. Redfearn. 2009. "ECG Manifestations of Multiple Electrolyte Imbalance: Peaked T Wave to P Wave ('Tee-Pee Sign')." *Annals of Noninvasive Electrocardiology* 14, no. 2: 211–214. https://doi.org/10.1111/j.1542-474X.2009.00283.x.

Komatsuzaki, M., T. Takasusuki, Y. Kimura, and S. Yamaguchi. 2021. "Assessment of the ECG T-Wave in Patients With Subarachnoid Hemorrhage." *Journal of Neurosurgical Anesthesiology* 33, no. 1: 58–64. https://doi.org/10.1097/ANA.0000000000000624.

Laundon, R. K., and L. Littmann. 2019. "Spiked Helmet Pattern ST Elevation in Subarachnoid Hemorrhage." *Journal of Electrocardiology* 52: 96–98. https://doi.org/10.1016/j.jelectrocard.2018.11.016.

Mori, S., A. Hori, I. Turker, et al. 2021. "Abnormal Cardiac Repolarization After Seizure Episodes in Structural Brain Diseases: Cardiac Manifestation of Electrical Remodeling in the Brain?" *Journal of the American Heart Association* 10, no. 9: e019778. https://doi.org/10.1161/JAHA.120.019778.

Weintraub, B. M., and L. C. McHenry Jr. 1974. "Cardiac Abnormalities in Subarachnoid Hemorrhage: A Resume." *Stroke* 5, no. 3: 384–392. https://doi.org/10.1161/01.str.5.3.384.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.