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Case presentation

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Brugada and Epilepsy: Recurrent Coincidence or Meant to Be?

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1. Abstract

Brugada syndrome, though rare, poses a significant risk of sudden cardiac death, particularly in young adults, and remains underdiagnosed globally. We present the case of a 22-year-old male initially presenting with a presumed seizure episode, later found to exhibit findings suggestive of type 1 Brugada pattern on his admission electrocardiogram [EKG]. Differential diagnosis between seizure and syncope was challenging, compounded by the difficulty in distinguishing convulsive syncope from seizure activity. While Brugada syndrome and epilepsy are not commonly associated, there is evidence suggesting a shared genetic basis, particularly in ion channel mutations. Our case underscores the importance of considering Brugada syndrome in patients presenting with seizure-like episodes and concerning EKG findings, prompting cardiology consultation and electrophysiological studies. The absence of a Brugada pattern post-ictally should not exclude diagnosis, especially in the context of appropriate clinical suspicion. Further research is warranted to elucidate the relationship between Brugada syndrome and epilepsy, and the potential implications for diagnosis and management.

2. Introduction

Brugada syndrome, though considered rare, poses a significant threat due to its propensity for sudden cardiac death, particularly in young adults. The syndrome exhibits variability in its clinical presentation, making it a diagnostic challenge. Incidence is often linked to familial patterns, with an onset typically between the ages of 20 and 40, and a predilection for males. Literature suggests that Brugada syndrome may be underdiagnosed, emphasizing the need for heightened awareness among clinicians. While its genetic basis is well-established, association of Brugada syndrome and/or EKG pattern with seizure disorder has not been well established. The brain and the heart work in harmony and are intimately linked, including common genes coding for ion channels highly expressed in both. Consequently, it is expected to have cardiac pathologies in the setting of neurological dysfunctions. This is specifically valid in electrical neurological disorder like epilepsy. Brugada and epilepsy are not known to be closely associated, but co-existence of those two phenomena have been reported. We present a 22-year-old male patient who presented to the emergency department with concern for seizure episode, found to have findings suggestive of type 1 Brugada on his admission EKG.

3. Case Presentation

We present a 22-year-old male with a past medical history of generalized anxiety disorder who presented to the ED accompanied by his girlfriend and Emergency Medical systems [EMS] due to a witnessed episode of unresponsiveness. The girlfriend reported a calm, non-triggering setting, where the couple were scrolling through his phone. There were no bright lights, strenuous activity or emotional distress. Suddenly the patient stopped responding to his girlfriend and lost consciousness. They were already in bed, so no fall was reported. The girlfriend reported lip cyanosis followed by bilateral upper extremity jerky movements, she couldn't denote whether lower extremity activity was also present. This whole episode lasted 2-3 minutes after which the patient regained consciousness. He was able to recognize the location, the time and his girlfriend with no paresis or weakness noted. Upon presentation to the Emergency department, his vitals were stable. His complete blood count, complete metabolic profile, troponins, lactic acid,

CPK levels, TSH were all normal. His CT head showed no acute intracranial abnormality. Medication review revealed he is on clonidine for insomnia, prescribed by his psychiatrist, and duloxetine for his generalized anxiety disorder. He denied any family history of seizures or early cardiac death or a previous similar episode. His orthostatic vitals were normal in the ED. The initial EKG noted ST elevation > 2 mm with a saddle ST shape in V1. No previous EKG was available. Due to concerns of Brugada EKG pattern and the possibility of an underlying syndrome, cardiology was consulted and recommended admitting the patient with telemetry monitoring. An echocardiogram was done and demonstrated normal systolic and diastolic function with no valvular abnormality. The next morning, a repeat EKG showed resolution of the concerning finding. He underwent electrophysiological studies that showed that the antegrade and retrograde AV Wenckebach, AV node ERP, atrial ERP were within normal limits. There was no inducible ventricular arrythmias upon stimulation of the right ventricular flow. Procainamide was infused and no brugada EKG changes noted, same protocol was repeated in 30 minutes with same results. Given the absence of induced arrythmias, loop recorder was implanted. In regard to concerns of underlying seizure, neurology were consulted and the brain MRI showed nonspecific T2 flair hypersignal in bilateral hippocampi, thought to be either artefactual or a sequela of a recent seizure. EEG was done and showed no epileptiform activity. The patient was not started on any AEDs and was recommended to follow up as outpatient with neurology.

4. Discussion

Brugada syndrome [BrS] is an autosomal dominant genetic channelopathy that poses a significant threat due to its propensity of sudden cardiac death, particularly in asymptomatic young adults. Different names are conferred to that syndrome in different languages, all revolving around nocturnal, sudden death. It is a rare entity reportedly affecting approximately 5 people of every 10 000 worldwide but known to be underdiagnosed globally. Variable genes have been identified as part of the syndrome's pathogenesis. Mutations in the SCN5A gene coding for the expression of voltage-gated sodium channels has been reported the most [1]. The classic EKG pattern is diagnostic, but the challenge resides in the variability of the clinical presentation thus prompting the need for a high index of suspicion among physicians. The ECG criteria adopted by the European Society of Cardiology used to identify the subjects with the "Brugada sign" are classified into 3 types [2] The Type 1 is the classic coved ST segment elevation >= 2 mm in more than 1 of the right precordial leads. Type 1 is diagnostic. Type 2 and 3 morphology have more subtle patterns and are not diagnostic but raise suspicion for BrS. Patients with type 2 or 3 need an inciting factor such as sodium blocker challenge, fever or medications that converts their EKG to type 1 to diagnose BrS. Summary of the subclassification is shown in (Table 1) with examples in (Figures: 1-4). [3] Clinically Brugada syndrome has been associated with 20% of cases of sudden cardiac death in individuals with no structural heart disease [4][5]

Our patient presented with presumed syncope, with noted tonic clonic activity in the upper extremities. The differentiation between a convulsive syncope and seizure was difficult to identify even when both the cardiology and neurology specialty teams were consulted. Syncope is defined as a sudden and transient loss of consciousness associated with loss pf postural tone and spontaneous recovery [6] Neurocardiogenic etiologies are the most identified, followed by primary arrythmias. [7] Convulsive syncope can be misleading, and history is sometimes incomplete or misleading. Tonic-clonic activity during a syncopal episode should not exclude an underlying cardiogenic etiology. Symptoms in convulsive syncope can range from myoclonic jerks, oral automatism, head turning and more rarely urinary incontinence. Sometimes, syncope itself through decreased cerebral perfusion can trigger a seizure in a patient who does not necessarily have epilepsy. In addition, syncope and seizure are not mutually exclusive.

Patients with Brugada syndrome may be asymptomatic but may accidentally be diagnosed on account of syncopal episodes. All presentations related to brugada are attributed to arrythmias which generally occur at rest or at nighttime. [8]A possible association between Brugada syndrome and epilepsy has been previously suggested in literature, through the identification of common mutations for ion channels implicated in both idiopathic epilepsy and Brugada. [9] The SCN5A gene linked to brugada, is also expressed in the limbic regions of rat brains suggesting a common underlying mechanism for both pathologies [10]. There has been also a report of a family with SCN5a gene mutation with its members diagnosed with both brugada syndrome and epilepsy [11]. Fauchier et al reported a patient with a longstanding history of epilepsy who was incidentally discovered to also have brugada later during his disease course [12] So, even in a patient who presents with a classic seizure, clinicians should always look for EKG patterns concerning for Brugada. This is particularly important in the setting of subsequent anti-epileptic drug prescription. Sodium channel blockers such as phenytoin have been reported to trigger a type 1 EKG brugada pattern. [13]. In addition to that, and to further shed the light on the interplay of those 2 mechanisms, one study observed post-ictal EKGs in 117 patients and noted that in abnormal post-ictal EKG, 8 patients demonstrated a Brugada ECG pattern of which two had type 1 morphology. When looking back at basal EKGs, only two had the brugada ekg pattern present and zero had brugada ekg pattern type 1. [18]

Our patient is 22 years old. Epilepsy is typically diagnosed in a younger population. The peri buccal cyanosis with tonic and clonic activity reported in history was slightly concerning for seizure. The MRI findings of bilateral hippocampi T2 flair hypersignal can sometimes be found following a seizure. In fact, bilateral hippocamp T2 flair hypersignal is nonspecific. This finding was reported

initially in children with febrile status epilepticus and was found to be associated with subsequent mesial temporal sclerosis. [14] A descriptive study in a southern tertiary care center in India suggested an association between unilateral hippocampal atrophy and focal complex seizure [15] but it is safe to say that this finding does not equate a diagnosis of epilepsy, nor should it influence the clinical reasoning as it could be a mere artefact. Our patient had no encephalitis symptoms, nor hippocampal atrophy to consider mesial temporal sclerosis.

Another consideration was medication induced brugada EKG pattern. He was on clonidine and duloxetine for over 3 years. Upon literature review, there was scarce data regarding effects of alfa 2 adrenergic agonists including clonidine and the association with Brugada. In theory, those agents may induce sympathetic suppression with vagal stimulation to the heart. For duloxetine and SNRIs, no data was found for an underlying association or previous reports. One report was found suggesting that tricyclic antidepressants might be the preferential treatment for depression and anxiety in patients with Bragada syndrome due to their anti-cholinergic effects, whereas SSRI risk to interefere with sodium channels and thus increase the risk of syncope or sudden cardiac death. [16] But in contrast, another report presented a brugada like EKG pattern induced by TCA. So in conclusion, there is not enough data to suggest any underlying mechanism for clonidine or duloxetine that would explain the EKG finding on presentation.

Table 1: EKG segments for different brugada morphology types

	Type 1	Type 2	Type 3
J- Wave Amplitude	≥ 2 mm	≥ 2 mm	≥ 2 mm
T Wave	Negative	Positive Or biphasic	Positive
ST-T Configuration	Coved-Type	Saddleback	Saddleback
ST-Segment	Gradually descending	Elevated ≥1 mm	Elevated <1mm

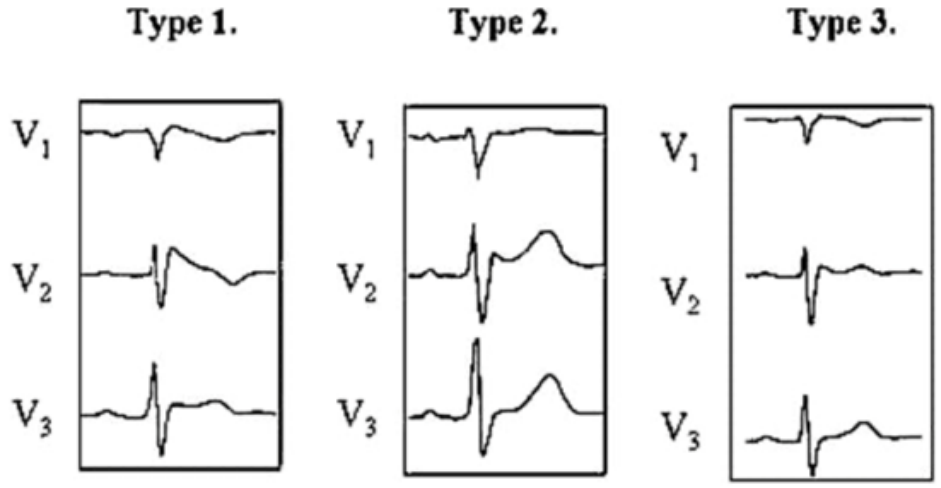

Figure 1: EKG patterns for different types of Brugada morphology

Type 1 morphology – classic with coved ST elevation >=2 mm in >=1 right precordial leads

Type 2 morphology with saddleback ST elevations ≥1 mm in 1 or more precordial leads. Type 3 morphology elevations; coved or saddleback, ≤ 1 mm with ST segment.

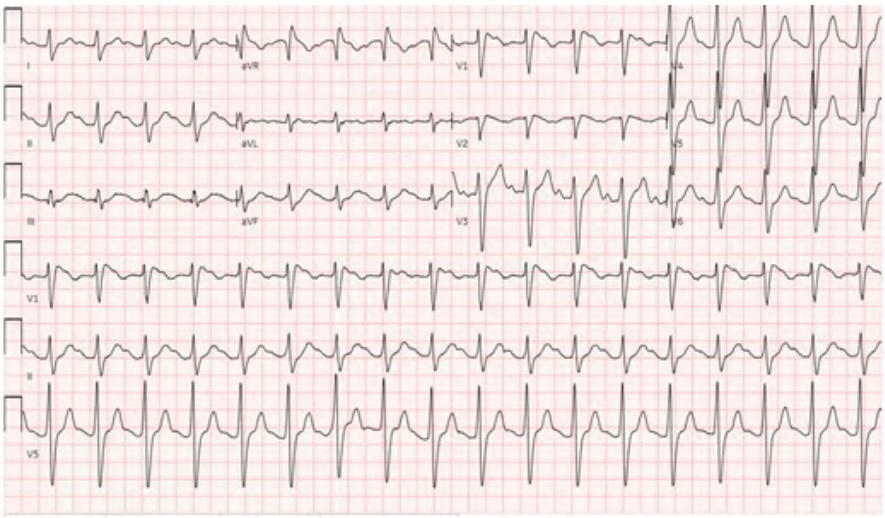

Figure 2: EKG on presentation

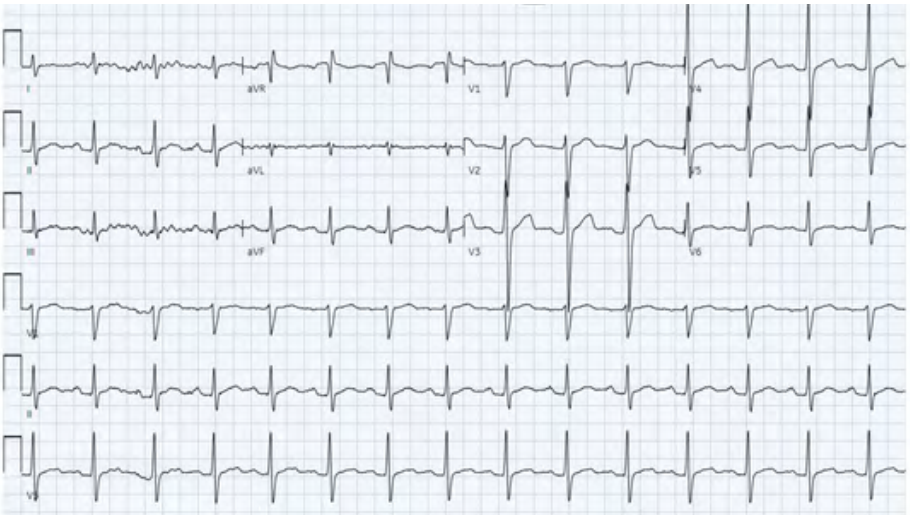

Figure 3: EKG in the next morning

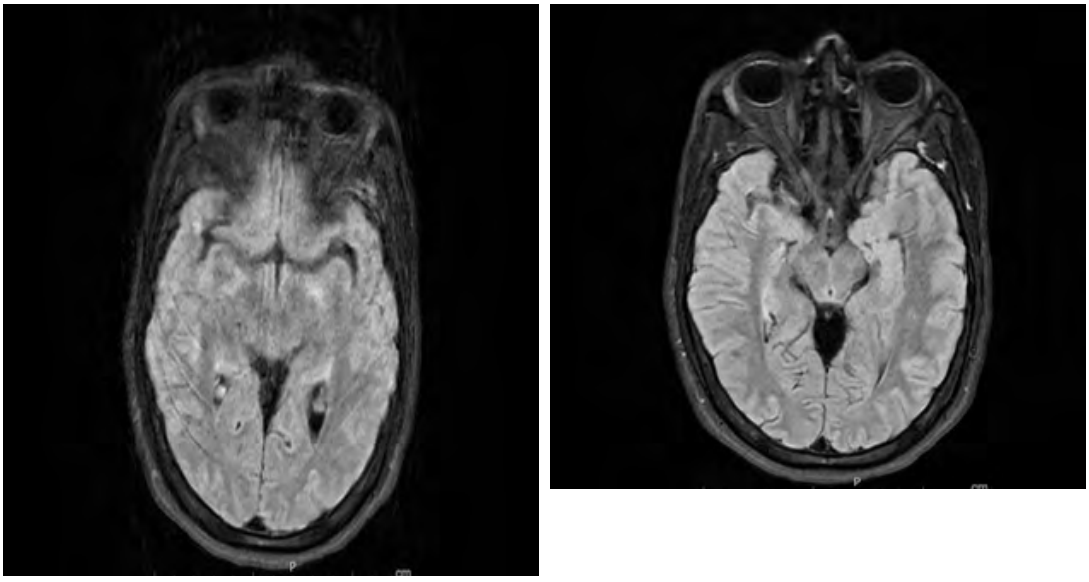

Figure 4: MRI with bilateral hippocampal signal on T2 flair

5. Conclusion

A type 1 brugada morphology on EKG is diagnostic of Brugada syndrome. Patients with type 2 or 3 prompt a high suspicion. There has been no established association between brugada syndrome and epilepsy or seizure, but available data does suggest a common underlying mechanism in certain population. Patients presenting with seizure episode with concerning EKG should incite a cardiology consult for eventual electrophysiological studies. The Brugada ekg pattern can be present only during the post ictal phase but its absence afterwards should not exclude the diagnosis, especially in the appropriate clinical setting or when the history is ambiguous.

6. Conflicts of Interest

The authors declare that they have no conflicts of interest.

7. Consent to Publication

Informed verbal consent was obtained from the patient for the publication of this case report. The patient was assured of complete anonymity, and efforts were made to exclude any identifying information. The patient's verbal agreement to participate and have the case details published was documented in the medical record.

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