Seizure related bradyarrhythmia: To Pace or not to Pace?

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Introduction

Transient loss of consciousness (TLOC) is a frequent presentation encountered by medical professionals in both primary and secondary care. Its definition lacks specificity simply implying loss of consciousness due to any cause, including seizures, syncope, psychogenic or traumatic. A thorough history, clinical examination and corroborative history often provide sufficient information to enable the skilled physician to reach a diagnosis or tailor investigations appropriately. However on occasion it can be difficult to clinically define the cause of TLOC. In particular the clinical distinction between cardiac syncope and epilepsy can present challenges. Syncope is defined as a loss of consciousness due to transient global cerebral hypoperfusion and may be associated with symptoms that resemble seizures. . In particular, fixed gaze, myoclonic jerks and atonia can resemble epilepsy making the correct diagnosis difficult.

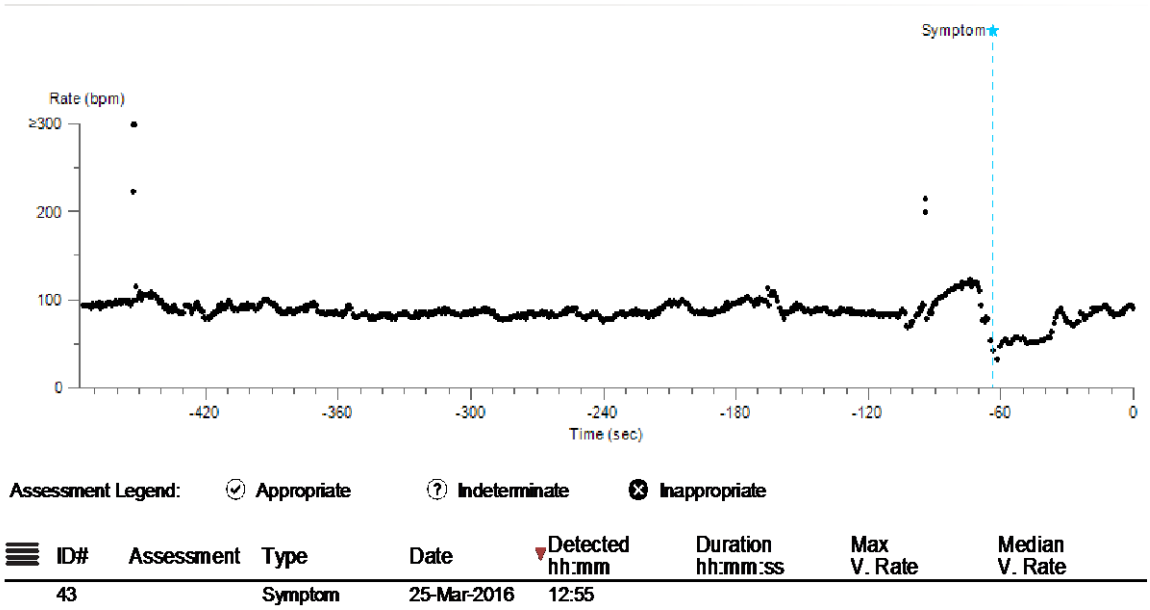
In this article we present a case of TLOC in a patient who had findings suggestive of temporal lobe epilepsy with ictal bradyarrhythmia. We describe the diagnostic challenges and uncertainties that surround this area.

Case

A 32 year old male was admitted to the cardiology department with multiple episodes of total loss of consciousness. The patient described previous episodes of TLOC fifteen years prior to this presentation however no formal diagnosis had been reached. He had remained symptom free until the most recent presentation. The patients recollection of events was ambiguous: he reported no clear precipitant and no premonitory or post event symptoms. Cardiovascular and neurological examinations were normal. Electrocardiogram was normal. A chronic cough was noted, however respiratory and gastrointestinal investigations revealed no evidence to suggest cough syncope as a potential cause. Carotid sinus massage, transthoracic echocardiogram and exercise stress

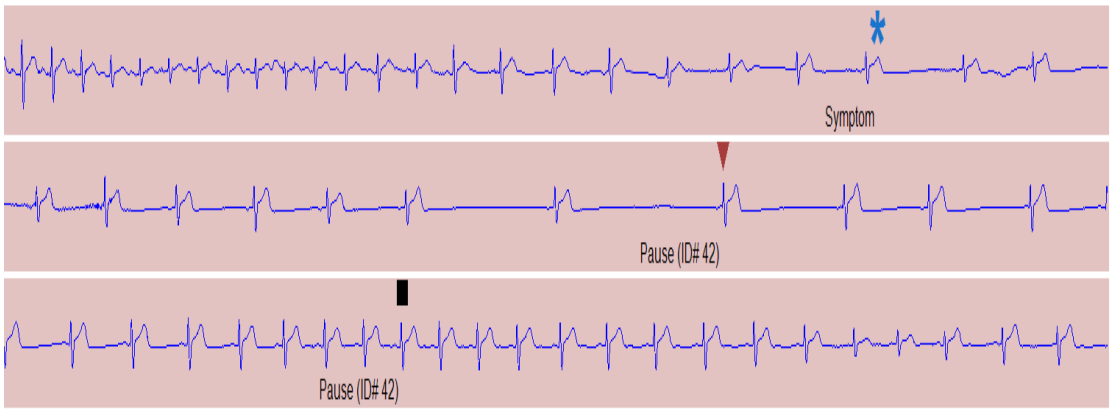
testing revealed no abnormalities. During his inpatient admission daytime telemetry revealed a 10 second pause coincident with loss of consciousness.. It was noted following this event that the patient experienced a prolonged period of mild confusion and lethargy and the suspicion of epileptic activity was raised. Magnetic resonance imaging of the brain revealed no abnormalities. Electroencephalography (EEG) revealed slow waves over the temporal regions with no obvious epileptiform activity. Subsequent review by the neurology department led to a provisional diagnosis of temporal lobe epilepsy. It was felt that his syncope arose due to reflex bradycardia following temporal lobe seizure activity. Sleep deprived EEG provided further evidence to support temporal lobe epilepsy with slow waveform activity noted over the temporal lobe. A temporal lobe volumetric MRI was performed with no abnormality noted. The patient was commenced on levetiracetam and discharged for on-going cardiology and neurology follow-up. He represented within one month of discharge with further episodes of TLOC and at this stage we elected to implant a loop recorder (ILR). In addition levetiracetam was up-titrated and the patient remained symptom free for a six week period. Subsequent readmission led to interrogation of his ILR which revealed evidence of a short burst of tachycardia immediately prior to his symptoms followed by a period of self terminating bradycardia (figures 1,2,3). This was felt to be in keeping with his diagnosis of temporal lobe epilepsy with reflex ictal bradyarrhythmia and due to the absence of prolonged asystole a further alteration in his antiepileptic medication was made following discussion with the neurology team.

Figure 1



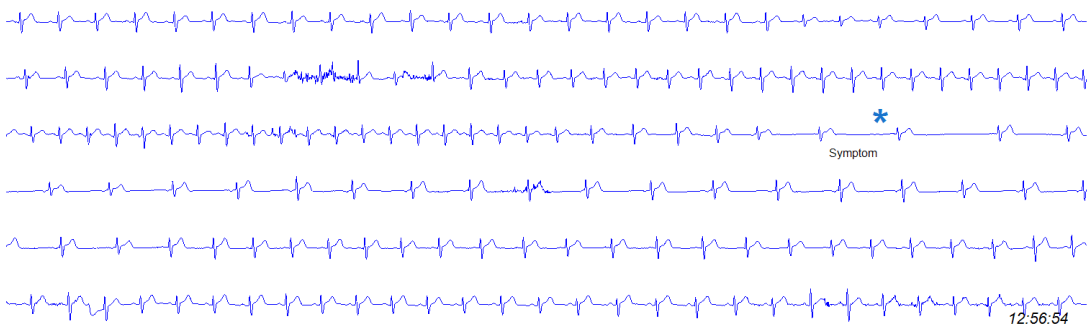
Loop recorder histogram revealing tachycardia immediately prior to symptoms followed by bradycardia

Figure 2



EGM at the time of reported symptoms

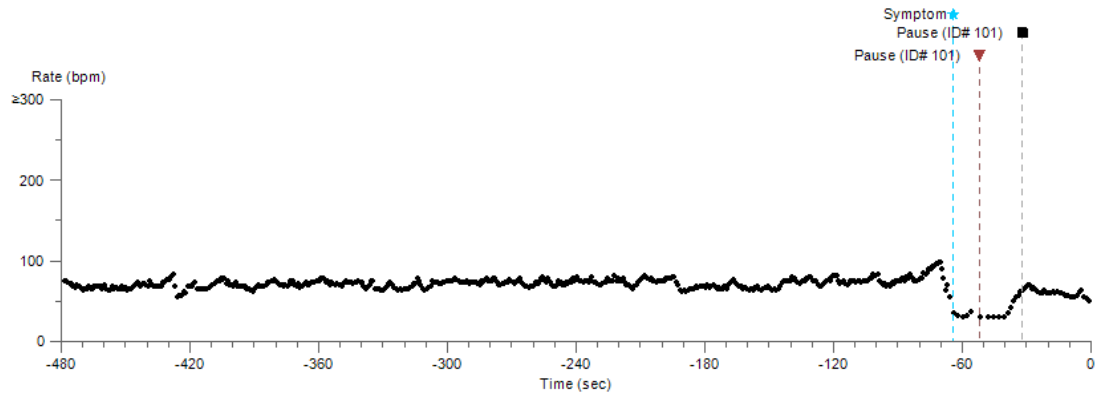
Figure 3



EGM demonstrating tachycardia preceding symptoms and bradycardic event

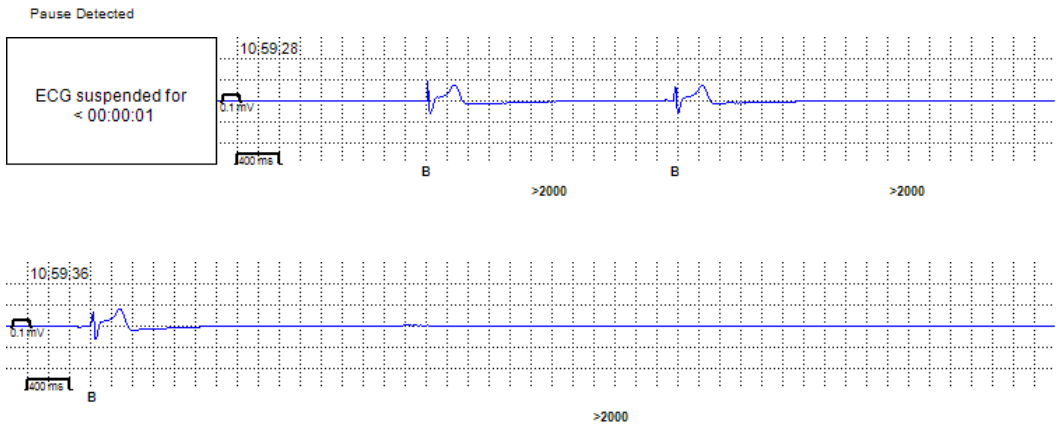
Despite up-titration of his AEDs the patient presented again with a further TLOC event episode. As shown in figures 4 and 5 interrogation of his ILR revealed a period of 10s asystole which had been preceded by a brief period of tachycardia. At this stage the decision was taken to implant a permanent pacing system.

Figure 4



ILR histogram showing transient tachycardia preceding symptoms and period of asystole

Figure 5



EGM demonstrating period of detected asystole

Following permanent pacing, follow up at 52 days revealed no further TLOC episodes. Pacemaker interrogation revealed 19% atrial pacing requirement in the post implant period with settings DDD 60 -120. To limit the potential of inappropriate pacing in this young individual the clinical decision at this time was to re-programme the device to DDI with a lower base rate.

Discussion

The association between epileptic seizures and cardiac arrhythmias has long been appreciated. Most commonly this represents tachyarrhythmias which have been identified in 90 - 100% of patients under-going simultaneous video gated electroencephalogram (VEEG)/ electrocardiogram monitoring.(1,2) The increased sympathetic and reduced parasympathetic activity that follows seizures, particularly those with frontal lobe origin, leads to a reflex tachycardia and in some cases has been associated with ischaemic ECG changes and supraventricular arrhythmias.(3) Cortical stimulation studies suggest that tachyarrhythmias are more likely to occur in those with right hemispheric seizure origin. This is further supported by VEEG with localization of seizure activity to the right hemisphere and inter/postictal tachycardia on ECG monitoring.(3,4) However there is inconsistency in data produced in literature which has led to the localization theory being challenged and consensus opinion is lacking.(1) Tachyarrhythmias have been proposed as a potential cause of sudden cardiac death in epilepsy (SUDEP) particularly in patients receiving antiepileptic medications that prolong the QT interval. However the evidence to support this is largely anecdotal arising from case reports and again there is a lack of consensus opinion in relation to this. In general it is felt that the increased heart rate following seizures is transient and of a benign nature.(5)

Ictal bradycardia/ asystole occurs less commonly in patients with epilepsy, with the prevalence estimated anywhere between 0.4 – 21% with bradycardia occurring more frequently than asystole.(1,5) This wide variance arises due to the diagnosis of ictal bradycardia requiring demonstration of bradycardia/asystole clearly induced by seizure activity recorded on EEG.(1) Secondary syncope can arise as a result of these bradycardic events and apnoea occurring as a result of seizures. It has been proposed that interictal/ postictal increases in vagal activity and intense release of neuroactive peptides, with profound autonomic effects, act as potential mechanisms for ictal bradycardia.(1,4) Additionally brainstem depression occurring during seizures

leads to reduced activation of pulmonary stretch receptors with subsequent hypoxia and increased carotid chemoreceptor sensitivity and bradycardia.(1,3) An alternative theory is that ictal bradycardia may arise from reflex vagal activation which is aimed at counter-regulating the tachycardia which frequently occurs with seizures. This is supported by documentation of tachyarrhythmias immediately prior to monitored ictal bradycardic events.(6) Temporal lobe epilepsy, in particular, is associated with a higher incidence of ictal bradycardia compared to other forms of epilepsy.(5) Cortical stimulation studies suggest that bradycardic activity is more common in those with left hemispheric seizure origin, particularly the left temporal lobe, and this is further supported by the finding of bradycardia during left insular stimulation in temporal lobectomy.(1,3,4,7) Additionally seizures recorded on VEEG with localization to the left temporal lobe have also demonstrated bradycardia/ asystole on ECG monitoring. However as previously mentioned the localization theory lacks robust data and no consensus opinion exists. Ictal bradycardia has also been proposed as a potential mechanism for SUDEP, however evidence to support this theory is lacking and is difficult to obtain due to the inherent difficulties of demonstrating this association. Nei et al (8) reported in 2004 that half of the patients they investigated with SUDEP demonstrated ECG changes in the immediate ictal/ postictal period. It was however noted that similar abnormalities occurred in a high number of patients who did not experience SUDEP and this finding has been supported by further studies which have failed to provide robust evidence to enable ECG abnormalities to be included in risk stratification criteria for SUDEP.(5,8) Regardless of the mechanism, ictal bradycardia is generally short lived with an average duration between 20-30 seconds and therefore generally well tolerated. Seizure induced syncope most frequently results from ictal asystole which has a typical duration of 13- 24 seconds.(6) As this occurs more frequently with non-generalized temporal lobe seizures the syncopal episode is typically preceded by classical signs of aura, staring, unresponsiveness and automatisms. As a result of cerebral hypoperfusion arising from asystole the ictal features are then replaced by atonic motor symptoms.(6) In the absence of firm evidence revealing a link to SUDEP ictal bradycardia/asystole is generally considered a benign event. Indeed

several authors propose that ictal bradycardia actually reduces seizure duration through cerebral hypoperfusion and anoxia. (6,9) It must be considered however that syncope occurring as a result of ictal bradyarrhythmias can result in significant falls and injuries.

Guidelines on the management of patients with ictal bradycardia/ asystole do not exist due to a lack of randomized trials in this area. As seizure activity is the precipitating event it seems reasonable to consider initiation and up-titration of anti-epileptic medication as a first line strategy. Indeed several small studies and anecdotal case reports have demonstrated that appropriate initiation and up-titration of antiepileptic medication has led to resolution of seizure related asystole and averted the need for pacing.(2,4,9) Our case demonstrated that this technique, whilst not abolishing syncopal events, lead to a reduction in their frequency. Whilst some authors suggest that permanent pacemakers are required in all patients with ictal syncope the decision to implant must be based on careful risk-benefit analysis. Often, as in our case, these are young patients who will require lifetime follow-up and multiple device changes with the inherent associated risks. We felt that a period of adequate AED treatment with prolonged cardiac monitoring using a loop recorder provided an effective strategy to determine whether escalation of treatment was required. On review of the literature similar strategies have been employed by many professionals with clinical outcomes ranging from successful control of syncope with AED's to requirement of pacing. In our patient the recurrence of syncope despite AED treatment led to the implantation of a dual chamber pacing system.

Conclusion

Whilst Ictal bradycardia/ asystole is an infrequent cause of TLOC it has important implications for the patient. Clinicians should consider this potential diagnosis when reviewing patients presenting with TLOC and tailor investigations accordingly. Whilst guidelines do not exist we believe that an appropriate treatment strategy is to aim to render patients symptom free by optimization of AED treatment. If this fails consideration should be given to the

implantation of a pacing system to reduce the risk of syncopal related injuries. Further studies in this area will be required to provide robust data to inform guidelines.

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