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Marked elevation of the atrial pacing threshold in a patient with sinus dysfunction on lamotrigine therapy

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Abstract

A 69-year-old female patient with bipolar disorder on lamotrigine therapy presented with recurrent presyncope due to severe sinus dysfunction. Lithium carbonate had been administered, but was withdrawn on admission. She underwent permanent pacemaker implantation; the atrial threshold markedly increased immediately after interruption of atrial pacing occurred despite a low threshold during successful pacing. Although the high threshold after interruption of atrial pacing decreased over 9 days, it increased again when lithium carbonate was additionally administered a few weeks later. One year later, this high threshold decreased after stopping lamotrigine treatment and continuing lithium therapy. Lamotrigine may affect the atrial pacing threshold for initial capture in patients with sinus dysfunction.

Keywords

lamotrigine; lithium; bipolar disorder; sinus dysfunction; pacing threshold

Abbreviations

AP: atrial pacing; VS: ventricular sensing; VP: ventricular pacing; AFL: atrial flutter; RAA: right atrial appendage

Introduction

Lamotrigine is an anti-epileptic medicine used for epilepsy and bipolar disorder, as it has an inhibitory effect on the voltage-gated sodium channel and voltage-gated calcium channel in neurons [1]. Many patients with sinus node dysfunction or atrioventricular block after treatment with anti-epileptic drugs such as carbamazepine have been reported [2,4], possibly because of the inhibitory effects of these agents on cardiac ion channels [1]. However, little is known about the effects of lamotrigine on sinus node function or the pacing threshold. Herein, we describe a patient with sinus dysfunction on lamotrigine therapy for bipolar disorder who showed a marked elevation of the atrial pacing threshold on an implanted pacemaker.

Case Presentation

A 69-year-old woman was referred to our hospital, and she presented with recurrent presyncope

due to long sinus pauses. She had bipolar disorder and was treated with lamotrigine (300 mg/d). Lithium carbonate had been administered previously, but it was withdrawn because of worsening bradycardia. On admission, her 12-lead electrocardiogram showed an atrial flutter (AFL) with a heart rate of 50 beats/min. Her echocardiogram showed almost a normal heart structure. In addition, results of all examinations, including blood tests, chest radiography, electrocardiography, and echocardiography, did not suggest amyloidosis or sarcoidosis in this patient. She underwent permanent pacemaker implantation. A ventricular lead was fixed to the right ventricular septum, and the pacing threshold was 0.5 V/0.5 ms. An atrial lead was placed on the right atrial appendage (RAA), and the AFL was terminated by burst pacing. However, her own atrial electrical activity did not emerge. Due to the high pacing threshold, the atrial lead was moved to another RAA site where the threshold was 0.8 V/0.5 ms during successful pacing. Yet, when the leads were connected to a pacemaker generator, a 3.5V/0.4ms stimulus failed to capture the atrium after the atrial pace was briefly suspended (Fig. 1A-B). At that time, 8.0V/0.4ms was required for atrial capture, but the threshold during successful pacing remained at 0.8 V/0.4 ms. The output setting for the atrial pace resumed to 3.5V/0.4ms at the end of the operation.

Postoperatively, the atrial threshold was measured after precisely stopping the atrial pace for 3 minutes (the initial capture threshold) and during successful pacing, as shown in Table 1. The high initial capture threshold decreased over 9 days. A few weeks later, lithium carbonate was administered while the patient was in the Department of Psychiatry. At the next checkup, the initial capture threshold increased to 8.0 V/0.4ms again while the threshold during successful pacing was maintained around 1.0 V/0.4 ms. In the pacemaker record, a paroxysmal AFL was observed. Notably, after the AFL was spontaneously terminated, the atrial capture was lost, and it took a few hours to recover the successful atrial capture.

One year later, the thresholds were 1.0 V/0.4 ms for the initial capture threshold and 0.75 V/0.4 ms during successful pacing after stopping lamotrigine treatment and continuing lithium therapy.

We confirmed that there was no problem with the position of the pacemaker lead by radiography during subsequent inspections.

Discussion

Adverse cardiac effects of lamotrigine have only been speculated [5], although carbamazepine, a similar anti-epileptic drug that inhibits the voltage-gated sodium channel [6], induces sinus dysfunction and atrioventricular block [4]. Considering the pharmacological effects of lamotrigine, this drug may have at least in part contributed to our patient's worsening impaired sinus function. The marked increase in the pacing threshold can be explained by a prolonged refractory period due to severe sinus dysfunction while a patient is on lamotrigine therapy. Once an initial pacing stimulus captures the atrium, the refractory period can be shortened; hence, the threshold can decrease during successful pacing. After adding lithium to the patient's drug regimen, the atrial threshold increased again. As lithium can induce sinus dysfunction [7], it should additively affect the high atrial threshold. The reason why the elevated threshold decreased over 9 days might be because the sustained cardiac effect of lithium was wearing off after withdrawing it. Lithium carbonate was prescribed at an ordinary dose for this patient, and its plasma level was not in a toxic range (peak level: 0.41 mmol/L) [8]. Although the plasma concentration

of lamotrigine was not measured, it should be within the ordinary levels, but not at a toxic level, as no adverse effects in the ventricular pacing threshold or mental state were observed. We think the reason why the ventricular pacing threshold was not affected is that the atrium may be more susceptible to the effect of lamotrigine at this dose than the ventricle in this patient who had impaired sinus function and atrial conduction before this drug was administered. Further analyses are required to understand the cardiac effects of lamotrigineinin combination with other anti-psychotropic drugs to avoid sudden unexpected arrhythmic events in patients with bipolar disorder or epilepsy.

Figure

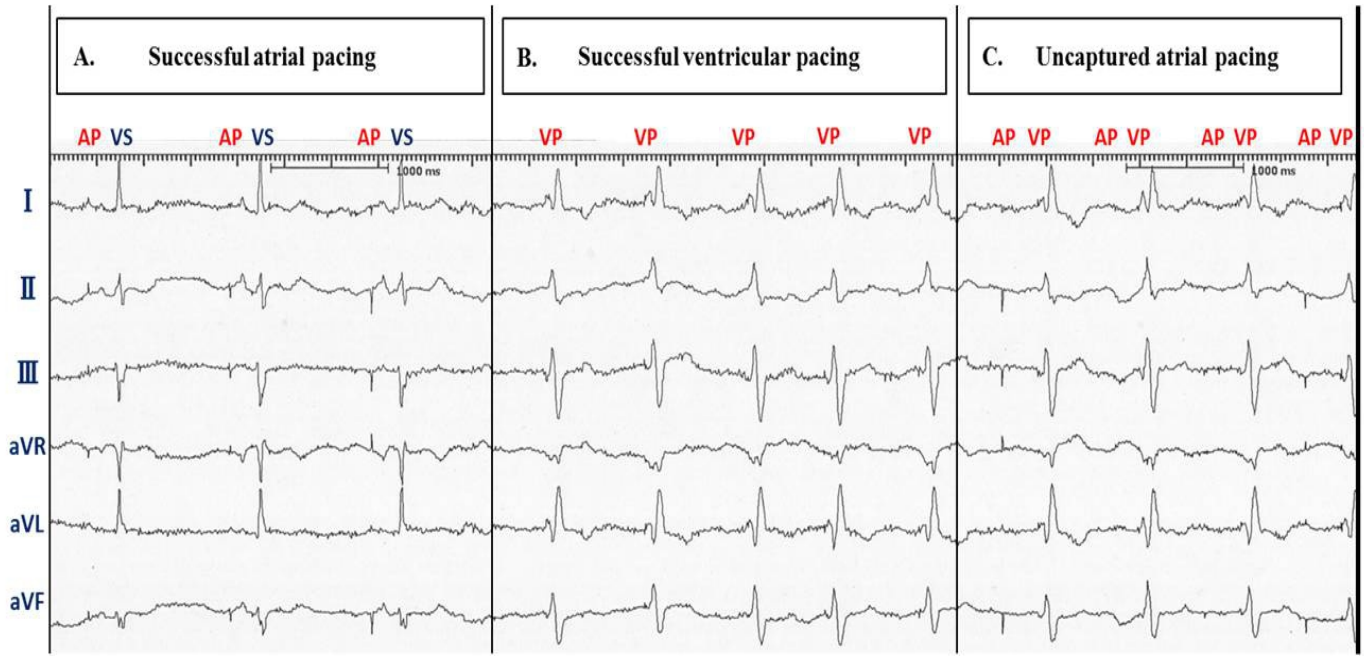

Figure 1: Electrocardiograms at the time of pacemaker implantation. A: Successful atrial pacing (AP) followed by ventricular sensing (VS). B: Successful ventricular pacing (VP) without atrial pacing. C: Uncaptured AP followed by VP.

Table

Table 1: Atrial pacing threshold after pacemaker implantation

Duration after the operation	Initial capture threshold (V/0.4ms)	Threshold during successful pacing (V/0.4ms)
1 hour	8.0	0.8
1 day	3.5	1.25
9 days	1.25	1.0
36 days	8.0	1.0
1 year	1.0	0.75

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