CASE REPORT

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Carbamazepine-Induced Symptomatic Bradycardia in a Middle-Aged Female

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ABSTRACT

Carbamazepine is an anticonvulsant drug commonly used to treat seizure disorders and trigeminal neuralgia. Although its hematological and hepatic side effects are well known, the rare cardiac side effects, mainly bradyarrhythmias, and atrioventricular blocks, are not discussed often in the literature. As per evidence, it has negative chronotropic and dromotropic effects on the cardiac conduction system. This case report discusses the life-threatening cardiac side effects of carbamazepine therapy and the significance of detailed cardiac evaluation before initiating this drug. We report a case of symptomatic bradycardia in a middle-aged female as the consequence of carbamazepine administration for seizure prophylaxis after meningioma resection.

Keywords: Carbamazepine, Adverse Effects of Carbamazepine, Carbamazepine-Induced Bradycardia, Cardiac Arrhythmia, Atrioventricular Block

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INTRODUCTION

Carbamazepine is an extensively used anticonvulsant for seizure disorders. It has also been used for treating peripheral neuropathy and trigeminal neuralgia. There are reports in the literature that bradyarrhythmia and atrioventricular blocks can develop as a potential cardiac side effect of carbamazepine, particularly in elderly females.[1] However, literature reporting the incidence of cardiac side effects of carbamazepine therapy in middle-aged females is rare. In this report, we present a case where a middle-aged female developed symptomatic bradycardia as a consequence of carbamazepine therapy.

CASE REPORT

A 48-year-old middle-aged female came to the emergency room with a one-month history of progressive dizziness with impairment in her day-to-day performance. She did not report any history of syncope, loss of consciousness, weakness, chest pain, breathlessness, and abnormal body movements. She had a history of surgical resection of petrous meningioma three years back. Since then, she has been on oral carbamazepine therapy in which the dosage was set to 600 mg/day in two divided doses.

The initial examination upon arrival showed a blood pressure of 140/80 mmHg and a pulse rate of 38 beats per minute, regular. On general examination, the patient was conscious, cooperative, and well-oriented to time, place, and person. No motor deficits were noted, with muscle strength 5/5 bilaterally. The sensation was intact bilaterally. Reflexes were 2+ bilaterally. Cranial nerves and cerebellar function were intact with no gait abnormalities. On auscultation, S1 and S2 were heard and were of normal intensity. No murmurs, gallops, or rubs were auscultated. Other system examinations were within normal limits. The patient was admitted and ECG was done which showed bradycardia with a heart rate of 38 beats per minute **(Figure 1).** Laboratory blood tests including serum electrolytes, thyroid function tests, liver function tests, complete blood count, and serum

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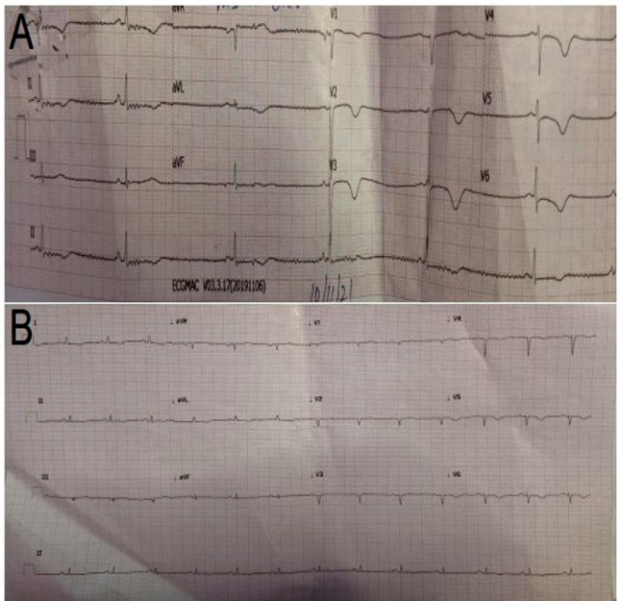

Figure 1. Electrocardiogram of the patient. A: Initial ECG showing bradycardia with a heart rate of 38 beats per minute. B: ECG of the patient on the day of discharge, showing a normal sinus rhythm and heart rate

troponin, were within the normal limits. Arterial blood gas (ABG) was taken and it was normal. 2D-Echo and chest X-rays were normal. Serum carbamazepine level during her presentation was 5 mcg/l.

The patient was admitted and administered a 0.5 mg intravenous atropine bolus dose. After a thorough neurology examination, the carbamazepine dose was lowered to half of the initial dose (i.e., 300 mg in 2 divided doses). Over the next 5 days during her course in the hospital, her heart rate returned to normal from 38 beats per minute to 75 beats per minute. She did not report dizziness or loss of consciousness during this period. Following improvement in her hemodynamic status, the patient was discharged with clear follow-up advice **(Figure 2).**

The patient was followed up monthly for six months post-discharge. There have been no episodes of dizziness or loss of consciousness since then. Her pulse rate was within 72-76 beats per minute during the follow-up visits, and her ECG showed a normal sinus rhythm. As per the advice of the neurologist, the patient continued 300 mg carbamazepine therapy post-discharge.

DISCUSSION

Carbamazepine is a commonly used medication for seizures, affective disorders, and trigeminal neuralgia. It works by blocking the voltage-gated sodium channels and voltage-gated potassium channels of the cardiovascular system, which can potentially lead to cardiac conduction problems.[2]

Summary of other published articles about carbamazepine-induced arrhythmias.

Study	Study Design	Age (years) (Mean ±SD)	Male/Female (n)	Carbamazepine Dosage (mg/day)	Duration (days)	Outcome
Asoglu et al. (2020)	Cross-sectional	29.4 ± 12.2	38/28	Not given	Not given	Female patients are prone to ventricular arrhythmia compared to control group (p=0.01).
Sathyaprabha et al (2018)	Cross-sectional	24.5 ± 8.1	22/14	Not given	360-960	No significant differences in heart rate and electrocardiogram interval rate were observed between the subject and control.
Celik et al. (2015)	Case report	56	1/0	400	450	2:1 atrioventricular block was observed on the electrocardiogram.Withdrawal of carbamazepine resulted in complete resolution of the arrhythmia.
Amin et al. (2010)	Case control	19.4	27/23	600	4401	11 out of 50 patients developed corrected QT interval prolongation.
Ide and Kamijo (2007)	Case report	66	0/1	200	365	Discontinuation of the carbamazepine led to a normal sinus rhythm.
Kaul et al (2000)	Case report	24	0/1	600	Not given	24-hour electrocardiogram monitoring showed sinus bradycardia .Withdrawal of carbamazepine resulted in pulse rate of 74 beats per minute.

Figure 2. Summary of other published articles showing the association between carbamazepine use and arrhythmia

Available studies showed varying results regarding the use of carbamazepine. It has been shown that carbamazepine use results in an atrioventricular block, bradycardia, and tachycardia. In the study done by Ide and Kamijo et al., a complete atrioventricular block occurred in a 66-year-old woman after receiving 200 mg carbamazepine for twelve months to treat temporal lobe epilepsy.[3] Similar studies done by Herzberg et al. depicted the development of a complete heart block in a 66-year-old female after increasing the dosage of carbamazepine for trigeminal neuralgia.[4] Takayanagi et al. reported sinus node dysfunction and atrioventricular block in 4 elderly female patients after starting carbamazepine therapy for trigeminal neuralgia.[5] Studies done by Beermann et al. and Boesen et al. reported occurrences of Adams-Stokes attacks in elderly female patients who were given carbamazepine therapy.[4,6] Because carbamazepine has the property of moderating the phase 4 depolarization of the pacemaker cells, it tends to suppress the rhythm aggravating bradycardia of a complete heart block.[7] Cardiac conduction problems are more commonly reported in old female patients,[8,9] however, there are also some cases noted in old male patients such as in the study done by Celik et al. wherein a 2:1 atrioventricular block was observed in a 56-year old man who was given carbamazepine 400 mg/day for 15 months for treating temporal lobe epilepsy.[10] Although the majority of the reported cases of carbamazepine-induced arrhythmia are observed in old female patients, a few incidents have been reported in middle-aged and young patients.[11] In our report, bradycardia was observed in a 48-year-old female who was on carbamazepine therapy post meningioma resection. Kaul et al. reported a case of sinus bradycardia in a 24-year-old woman as a consequence of a carbamazepine 600 mg/day for 8 months for treating seizure disorder.[12] In all these mentioned studies, termination of carbamazepine use resulted in the normalization of the arrhythmia to sinus rhythm. Although the exact working mechanism of this drug and its effect on the heart is not completely understood, it should be given much significance to avoid life-threatening cardiac complications as carbamazepine is widely used in the treatment of many neurologic and psychiatric conditions. These reports spotlight the significance of extensive cardiac evaluation and careful monitoring of ECG in patients before starting carbamazepine therapy. A summary of reports on carbamazepine-induced arrhythmia is presented in **Figure 2.**

CONCLUSIONS

Carbamazepine therapy can have serious cardiac side effects like atrioventricular blocks and bradyarrhythmia. At times, carbamazepine-induced bradycardia can be severe requiring vasopressors and on occasions even cardiac pacemakers. This case report highlights the significance of detailed cardiac evaluation before initiating carbamazepine therapy. Based on this case report and other literature which have reported carbamazepine-induced bradycardia, we recommend doing a routine cardiac evaluation for all patients before starting carbamazepine therapy. This drug should also be avoided in patients with pre-existing cardiac conduction abnormality and in those with electrolyte abnormalities which can potentially increase the risk. Although carbamazepine does not increase the risk of bradyarrhythmia in all patient groups, more scientific discovery is required in this relatively underexplored subject to avoid potentially life-threatening cardiac complications of carbamazepine therapy.

END NOTE

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