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Three Types of Atrioventricular Block Induced by Oxcarbazepine in a Young Adult

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ÖZET:

Genç bir erişkinde okskarbazepine bağlı üç tip atriyoventriküler blok

Yeni bir antiepileptik ilaç olan okskarbazepin'in yan etkileri ve özellikleri tam olarak bilinmemektedir. Karbamazepin ile yakından ilişkili olduğundan okskarbazepin'in de kalp ileti sisteminde kinidin-benzeri etkiler yapması olasıdır. Bu makalede bir yıldır okskarbazepin tedavisi gören bir genç kızda tedavi sırasında gelişen ve Türkiye'de ilk kez gözlenen bir atriyoventriküler blok olgusu sunulmuştur.

Anahtar sözcükler: Okskarbazepin, atriyovenriküler blok, epilepsi, kalp ileti sistemi

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ABSTRACT:

Three types of atrioventricular block induced by oxcarbazepine in a young adult

Oxcarbazepine is a new antiepileptic drug that has been introduced recently. The side effects and properties of the drug are unique and largely unknown. Because oxcarbazepine is structurally similar to carbamazepine, it might have quinidine-like effects on cardiac conduction. In this report, we discuss a rare case of a young girl, who was followed up for treatment of epilepsy for 1 year with oxcarbazepine and had atrioventricular block during therapy.

Key words: Oxcarbazepine, atrioventricular block, epilepsy, cardiac conduction

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INTRODUCTION

Oxcarbazepine is a relatively new drug with unique side effects and properties that are largely unknown (1). Because oxcarbazepine (OXC) is structurally similar to carbamazepine, it might have quinidine-like effects on cardiac conduction. In this report, we discuss the first case of a young girl, who was followed up for treatment of epilepsy for 1 year with oxcarbazepine and had an atrioventricular block during therapy.

CASE

With a complaint of frequent episodes of dizziness (2-3 times a month), a 17-year-old girl without a previous history of heart disease consulted the Department of Neurology of our hospital, where she had been treated for epilepsy with oral administration of OXC for one year. The daily dosage was 600 mg/day, given in two divided doses. Therapeutic drug monitoring (TDM) is likely to be useful in many clinical settings including assessment of adverse effects and clinical efficacy, especially for the newer antiepileptic drugs like OXC; however, the serum concentration of the drug could not be measured because of insufficient laboratory resources at the time of admission.

The patient was alert and cooperative. Her body temperature was 36.7^{0}C; blood pressure was 120/80 mm Hg; and heart rate was 65 beats/minute. Physical and neurologic findings and radiologic examinations, including a computed tomography of the brain, were unremarkable. The patient's laboratory findings and biochemical results were also normal. Then she was admitted to the department of cardiology for evaluation. Her ECG demonstrated normal sinus rhythm. An echocardiogram was

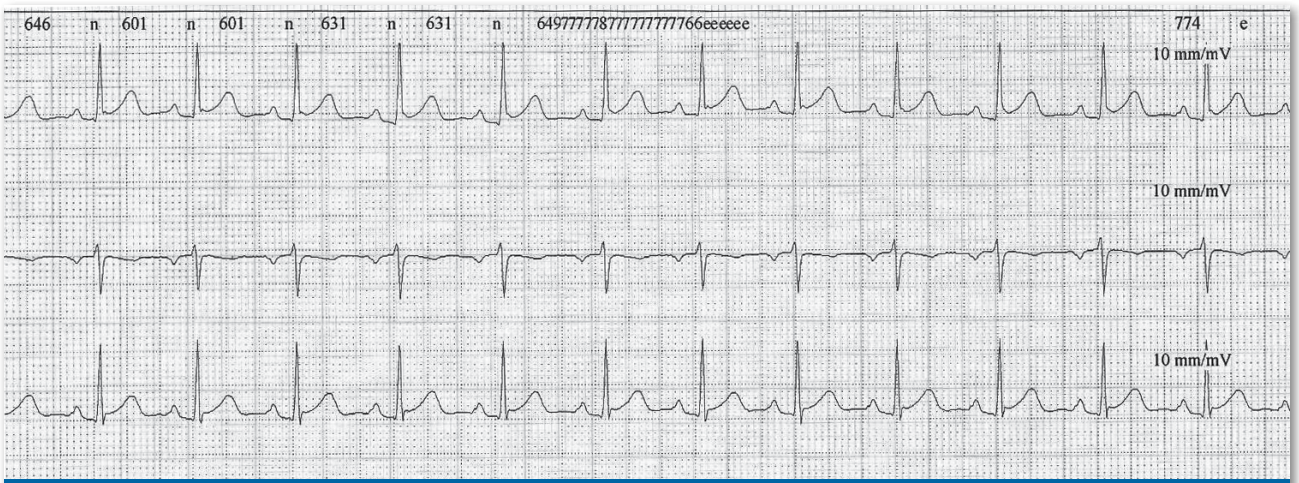

Figure 1: Normal sinus rhythm recorded by Holter monitoring

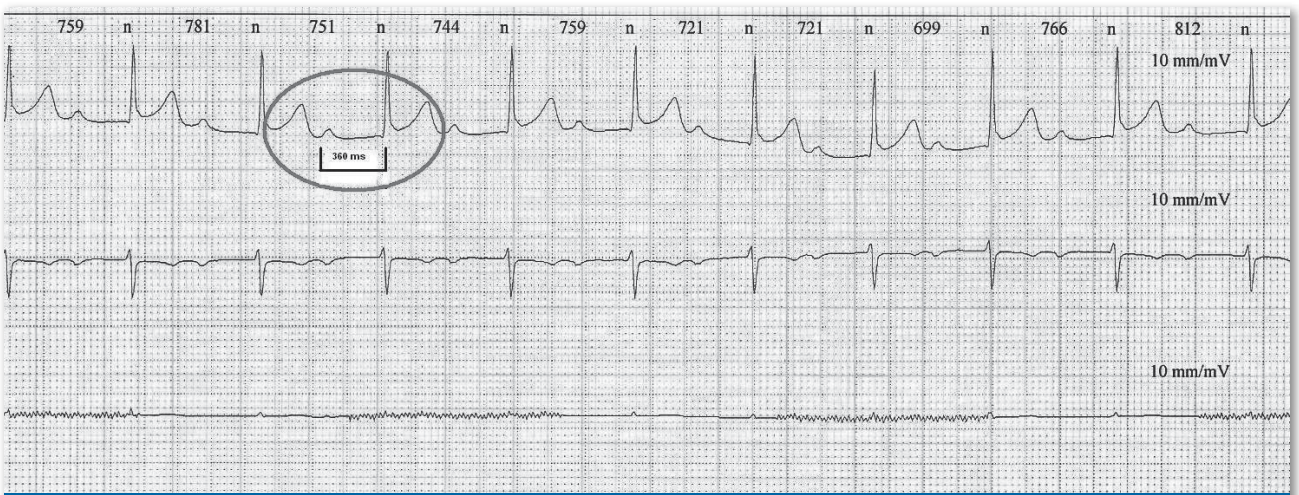

Figure 2: An episode of first degree AV block recorded by Holter monitoring

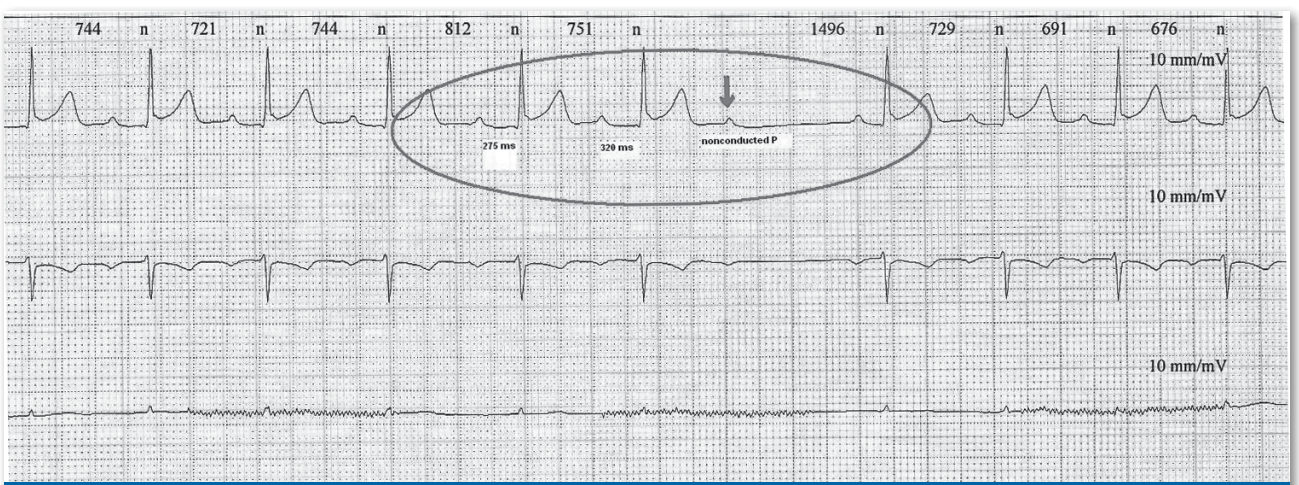

Figure 3: An episode of Mobitz type I (Wenckebach) AV block recorded by Holter monitoring

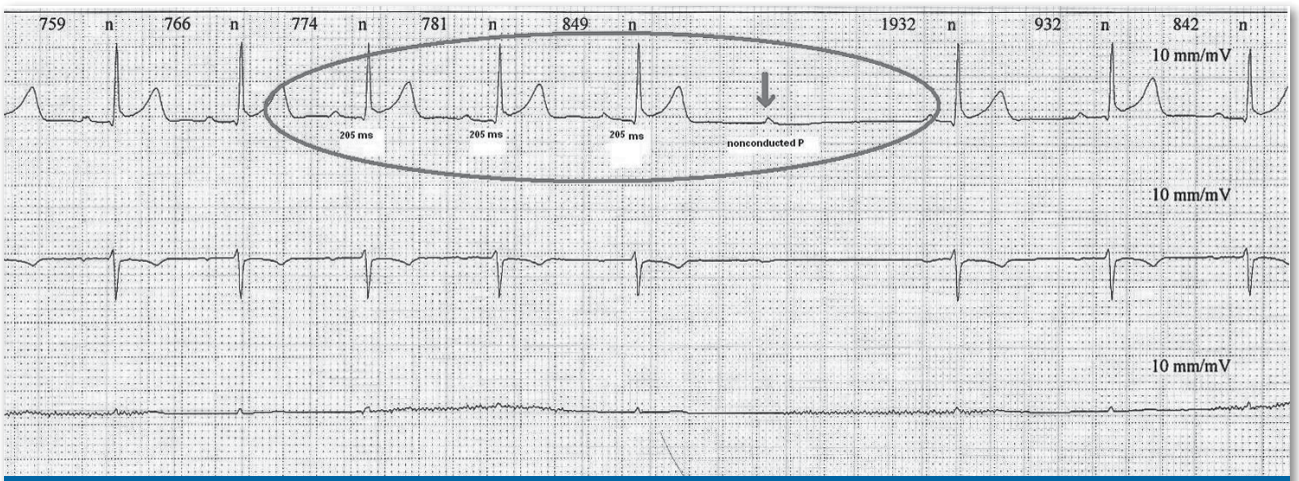

Figure 4: An episode of Mobitz type II AV block recorded by Holter monitoring

performed and no abnormal echo findings were reported. However, Holter monitoring documented normal sinus rhythm (Figure 1), sinus rhythm with first degree atrioventricular (AV) block for a few minutes with a PR duration of 360 ms (Figure 2), three instances of Mobitz type I (Wenckebach) AV block in 24 hours (Figure 3) and two occurrences of Mobitz type II AV block (Figure 4). She was hospitalized for continuous ECG monitoring and OXC was replaced with sodium valproate, as an alternative antiepileptic. Two days after the replacement, her ECG returned to normal sinus rhythm without signs of conduction disturbance.

DISCUSSION

Oxcarbazepine is a new second-generation antiepileptic drug with a chemical structure similar to carbamazepine (2). It was developed to improve the side effect profile of carbamazepine without reducing its antiepileptic potency. There are several reports about carbamazepine-induced arrhythmia and atrioventricular block in the literature(3-6). Furthermore, AV-block was listed as a very rare adverse effect (0.07 %) mentioned in the package insert leaflet for oxcarbazepine users. Therefore, this case is important to emphasize the fact that a very rare adverse effect could be a serious one and clinicians should be aware of the condition.

Although, Olesen et al. found that OXC was associated with increased risk of stroke, and cardiovascular death, here we report the very first case of first and second degree AV block occurring one year after the initiation of OXC therapy in a 17-year-old girl without a previous history of heart disease (7). Second degree type I block is the phenomenon described by Wenckebach as progressive PR interval prolongation preceding a nonconducted P wave and second degree type II block is the condition where the PR interval remains unchanged prior to a P wave that suddenly fails to conduct to ventricles. It has been reported that the risk of adverse cardiovascular outcomes and all-causes of death were increased in patients with epilepsy without previous cardiovascular disease history like our patient (8).

Antiepileptic drug-induced arrhythmia has some particular characteristics. For example, arrhythmia predominantly occurs in young adults after long periods of therapy as our 17-year-old patient. Therefore, the relationship between the arrhythmia and the use of the drug may be overlooked. Our patient's duration of OXC therapy can be considered as a long period in the treatment of epilepsy in a young adult. Arrhythmia can be associated with either therapeutic or modestly elevated serum concentrations of the drug. Therapeutic drug monitoring is very important to observe adverse effects and drug-drug interactions in OXC therapy (9-11).

It has been recently shown that OXC toxicity could be triggered by a drug-drug interaction. (12). Clarithromycin, a macrolide antibiotic, may lead to an increase in OXC concentration by inhibiting the active blood-brain barrier. Unfortunately, we couldn't quantify serum concentrations of OXC due to a lack of required laboratory equipment. Moreover, our patient did not report a history of medication except OXC. Concerning the patient in our case, it was so dramatic that the arrhythmia resolved rapidly following the withdrawal of OXC.

The incidence of adverse effects during OXC therapy seems to be age related (13,14). New drugs are poorly investigated in children and young adults. Also, pharmacokinetic parameters are different in children and young adults. For example, a decrease in plasma binding proteins may increase the concentration of free drug in plasma and can result in a greater drug effect and/or toxicity. Also, alterations in hepatic or renal functions may effect the serum concentration of OXC. The best criteria in our case would have been the assay of serum concentration of OXC.

OXC exerts its antiepileptic effect via blockade of voltage-sensitive sodium channels. In addition, increased potassium conductance and modulation of high-voltage activated calcium channels may contribute to antiepileptic effects. These channels are also expressed in myocardium and important in cardiac conductance. Excess plasma concentration of OXC may cause an additional effect on these channels in myocardium in addition to their effects in the brain.

The present case suggests that atrioventricular block may occur long after the initiation of OXC therapy in a young adult without heart disease. If dizziness or syncope occurs in a young adult taking any dose of OXC, the possibility of OXC-induced atrioventricular block should be considered and cardiac conduction must be evaluated. Therefore clinicians must be aware of the symptoms of side effects caused by these novel drugs. A proper questioning of symptoms will guide the clinician in assessing the side effects of drugs at every visit of the patient in clinical practise. Adverse clinical consequences can be minimized by careful monitoring of clinical response and serum drug concentrations, if available.

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