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Case Report

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QT PROLONGATION IN A PEDIATRIC PATIENT AFTER USING OXCARBAZEPINE FOR PARTIAL SEIZURE: A CASE REPORT

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ABSTRACT

Several reports of drug-induced prolonged QT interval have been published, but to the best of our knowledge, there has not been any report of oxcarbazepine inducing prolonged QT interval in a paediatric age group. Here We described one case of prolonged QT interval in 7 years old Saudi girl with partial seizure who treated by Oxcarbazepine (Trileptal). This is unusual case of prolonged QT interval in pediatrics age group due to usage of Oxcarbazepine. We conclude that prolonged QT interval should be included among the adverse drug reactions of Oxcarbazepine.

KEYWORDS: QT prolongation, oxcarbazepine, partial seizure.

INTRODUCTION

Oxcarbazepine is a newer antiepileptic agent that has been approved for the treatment of seizure in both adult and pediatric age groups[1]. Oxcarbazepine is marketed in the united states and many other countries as oxtellar XR and Trileptal. Its uses in the pediatric epileptic population include its use as monotherapy for partial seizures in children aged 4 years old and above[1, 2].

The QT interval represents a period of ventricular muscle depolarization followed by repolarization measured in milliseconds (ms) on an electrocardiogram (ECG)[3]. Ventricular depolarization is mediated by currents generated by the inward flow of sodium and calcium ions while depolarization is the result of the outward flow of potassium ions. Dysfunctional ion channels, either due to a genetic aberration or administration of a drug, prolongs the time of ventricular repolarization by increasing the intracellular concentration of positive ions[4]. Early after depolarization (EAD) occur with prolonged ventricular repolarization which in turn induce re-entry, torsade de pointes morphology and fatal ventricular arrhythmias[5]. A prolonged QT interval is defined as one exceeding 450 msec (0.450 s)[6]. Although, virtually unreported in the pediatric population, we present a case of oxcarbazepine-induced QT prolongation leading to bradycardia in a pediatric patient being treated for partial complex seizures.

CASE PRESENTATION

A 7 years old Saudi female, recently diagnosed to have complex temporal epilepsy based on the seizures semiology, and The EEG showing right temporal lobe spikes. MRI brain was negative as well as ECG and metabolic workup.

The patient was started on Oxcarbazepine (Trileptal) at dose of 10 mg/kg/day.the seizure improved, and there was no acute reaction due to medication. After one week of starting the treatment, the patient developed an attack of similar abnormal movements, and she was admitted for observation. During the admission there were no further seizures however, the patient was found to be bradycardic. Heart rate monitors showed a rate ranging between 55-65 (bpm). Pediatric cardiology was consulted, and ECG was done. The ECG showed a prolonged correct QT interval of 475 milliseconds (msec)(Figure 2). The corrected QT (QTc) length was calculated by using Bazett's formula[7, 8]. Trileptal was discontinued to discern whether it was the cause of the prolonged QT interval.

The ECG repeated 2 days after discontinuation and yielded a QTc length of 456 msec. Trileptal was discerned to the have been the causative agent and the patient was switched to another antiepileptic drug to control her seizures. The patient was then discharged on levetiracetam. An ECG was repeated one week after starting the therapy and yeiled a QTc of 440 msec (Figure 3).

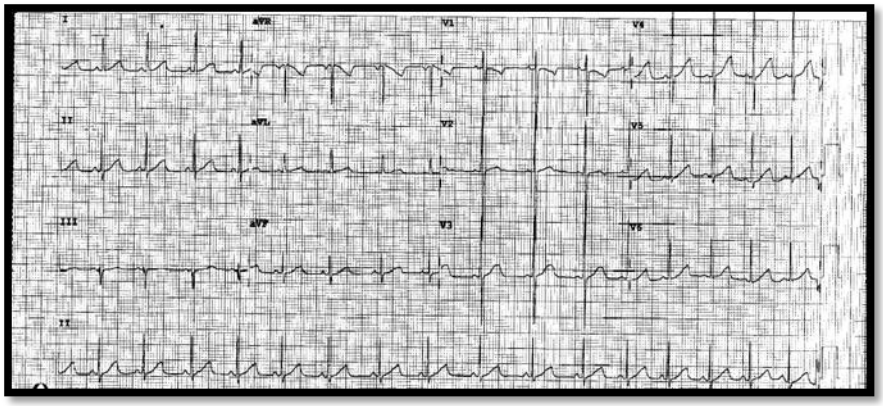

Fig.1 Baseline ECG, before starting the treatment, QTc (423 msec)

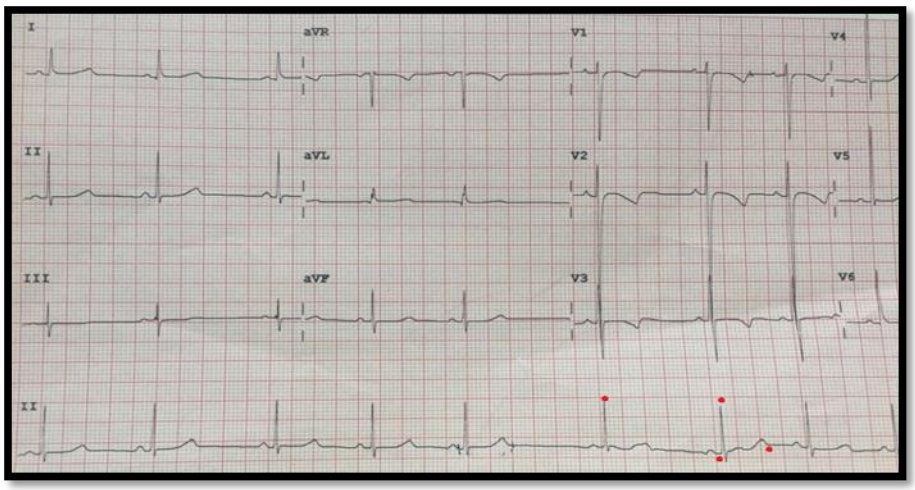

Fig. 2. ECG after 1 week of starting Trileptal shows QTc of (475msec)

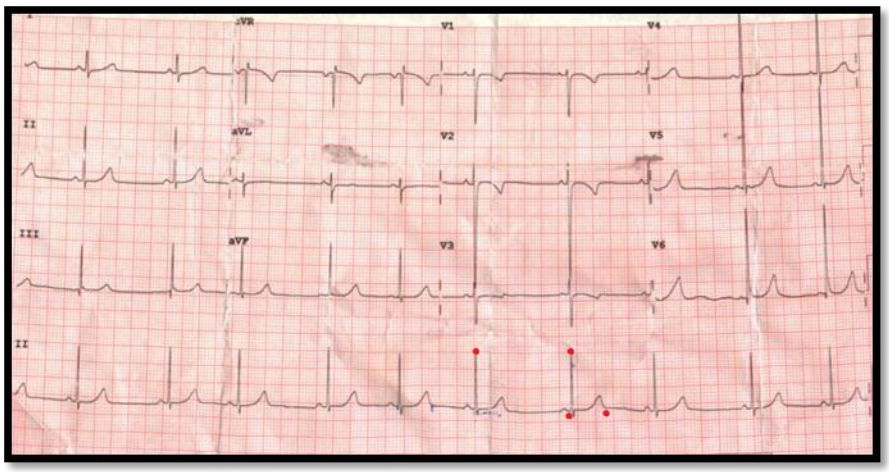

Fig. 3 ECG follow up after 1 week discontinuation of Trileptal and initiation of Levetiracetam therapy.Shows QTc of (435msec)

DISCUSSION

Oxcarbazepine (Trileptal) is a structural derivative of carbamazepine whereby a ketone group replaces its benzylcarboxamide group[9]. This chemical alteration in structure was found to reduce the impact of hepatic metabolism as well as reduce the incidence of known carbamezipine-associated aplastic anemias. Though it has a more favorable side effect profile, it is still possible to encounter major adverse reactions when it is used[1, 2]. Oxcarbazepine and its pharmacologically active metabolite, 10-monohydroxy derivative (MHD) display antiepileptic potency that is comparable to that of carbamazepine and phenytoin. Oxcarbazepine and MHD act to prevent partial seizure activity by blockade of voltage-dependent sodium channels in the brain, thus delaying neuronal recovery[9].

A prolonged QT interval is the single most important risk factor for the development of ventricular arrhythmias and sudden cardiac death. There are many causes of QT prolongation, which include congenital long QT syndrome and medications that affect the ion channels of the myocardium[4]. Genetic variations in the structure and function of ionic channels in the heart are recognized as possible factors that potentiate the ability of certain drugs to induce QT prolongation[10]. QT prolongation is one of the most common reasons for discontinuation and withdrawal of drugs from the market. The lethality of QT prolongation, although rare, is often considered more significant than the potential benefit that these drugs may confer for patients[11].

A review of the literature has revealed the scarcity of studies regarding the potential of QT prolongation due to antiepileptic medications in the pediatric population. A study conducted in Korean pediatric patients assessed the potential for QT prolongation when antiepileptic medications were administered to establish whether their use contributes to sudden unexpected cardiac death. The study reported that there was no significant difference in the QT lengths amongst different antiepileptic medication nor were there significant differences when these drugs were administered as monotherapy or as combinations. The study has a major limitation due to its small sample size (178 patients) and thus cannot be considered conclusive in ruling out the possibility of QT prolongation[7].

Between January 2000 (the introduction of Tripleptal to the market) and October 2012, a total of 176 Trileptal drug adverse event reaction were reported, of which 31 cases involved children[12]. Of the adverse drug reactions reported, there was a single case report of a Oxcarbazepine (Trileptal) QT prolongation resulting in a ventricular arrhythmia. The case reported the prolongation of QT interval in seemingly healthy 30 year old male taking Trileptal. Soon after administration of the drug, the patient developed a highly resistant ventricular arrhythmia that required multiple attempts of cardioversion. Further investigations revealed that the patient had Brugada syndrome[13]. Until now, no reports of QT prolongation in the pediatric population have been made.

CONCLUSION

Our case is of clinical importance in bringing this potential adverse drug reaction to the attention of neurologists prescribing Tripleptal as an antiepileptic as this is emerging as one of the commonly used medications for the treatment of pediatric partial seizures. We conclude that Tripleptal may cause QT interval prolongation at its starting dose and thus patients should be monitored for any change in usual seizure activity which may herald cardiac morbidity.

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