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Valproic Acid as a Cause of Transient Atrio-Ventricular Conduction Block Episodes

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Abstract

Herein we share, to our knowledge for the first time, a a case of valproic acid use complicated by symptomatic atrio-ventricular conduction block episodes on Holter monitoring. Symptomatic atrio-ventricular block episodes should be considered as an unusual side effect of valproic acid despite normal blood therapeutic level. Before consideration of pacemaker implantation in such cases, valproic acid usage should be investigated, and dose reduction should be attempted.

Case Report

A 19-year old female patient was referred to the Cardiology Department for implantation of pacemaker with the diagnosis of symptomatic recurrent transient atrio-ventricular conduction block. The patient had a history of epileptic seizures which was treated and controlled with valproic acid. Over the last two years, the patient experienced multiple episodes of near syncopes with most of them occurring in the six months before admission. During her evaluation of of presyncope, multiple transient atrio-ventricular block episodes lasting between 20-26 s were discovered on 24 hour Holter rythm monitoring performed in in an outside facility. Her Holter monitoring was repeated seven times and each test revealed revealed similar findings. Her history revealed that most episodes happened in resting position. The patient was referred to our clinic for further work up and recommendation of pacemaker implantation. At the admission, her physical examination was unremarkable. Her ECG and echocardiography were within normal limits. Exercise test revealed adequate chronotropic competence. The patient underwent 48 hour Holter monitoring. We discovered multiple episodes of atrio-ventricular conduction blocks lasting 28 s on Holter monitoring [Figure]. Before consideration of pacemaker implantation we decided to .to reduce the dose of valproic acid from 500 mg t.i.d to 500 mg b.i.d. After four weeks patient was called to hospital for control. Valproic acid serum level was 49.5 ug/mL. The patient was asypmtomatic except one attack of self limited seizure.

The 48 hour Holter monitoring revealed complete disappearence of previous atrio-ventricular block episodes. We decided that atrio-ventricular blocks was stemming from valproic acid at the doses of 500 mg t.i.d despite normal blood therapeutic level (71.7ug/mL). We considered changing the anti epileptic drug and pacemaker implantation was canceled.

Key Words

Vaproic acid, Atrio-ventricular block, Drug.

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Discussion

Our case indicates that the electrocardiographic atrio-ventricular conduction blocks as an unusual side effect of valproic acid should be kept in mind. In such a case, unless there is a compelling reason, the dose of valproic acid should be reduced or changed to another anti epileptic drug to avoid unnecessary pacemaker implantation.

It should be noted that drug induced bradyarrythmia should be differentiated from peri ictal or seizure related bradyarrhythmias [1]. Seizure-related bradyarrhythmias including sinus bradycardia, atrio-ventricular conduction blocks and asystole have been reported rarely in case series studies and sudden unexpected death in epilepsy accounts for 8–17% of the deaths in patients with epilepsy [2].

Although the most frequent cardiac arrhythmia seen during epileptic seizures is sinus tachycardia that occurs in most seizure episodes and is usually of no consequence, autonomic alterations during seizures potentially can result in cardiac dysfunction." Then begin next sentence as "Some postulated mechanisms for this phenomenon, which may also be associated with sudden cardiac death, are heart rate variability, ictal bradycardia, atrio-ventricular block, and asystole. that have been postulated to be some of the underlying mechanisms for sudden unexpected death including heart rate variability, ictal bradycardia, atrio-ventricular block and asystole. Peri ictal atrio-ventricular conduction block has been rarely reported [2].

The differentiation of epileptiform seizure-induced cardiac arrhythmias from drug associated atrio-ventricular conduction block is paramount. It is thought that seizure activity predominantly in the left temporal lobe potentially can activate parasympathetic function and results in bradyarrhythmias [3]. In order to differentiate drug induced bradyarrhythmias from seizure related bradyarrhythmias the most important point is simultaneous Holter monitoring and video electroencephalogram documentation of bradyarrhythmia during an ictal discharge which usually starts 10–30 s after the seizure initiation

and apparently after the seizure discharges become bilateral [3]. It should be known that the all undesirable cardiac effects of epilepsy can best be avoided by complete seizure control with administration of appropriate anticonvulsant drugs whereas drug induced bradyarrhythmias necessitate drug cessation or modification of given

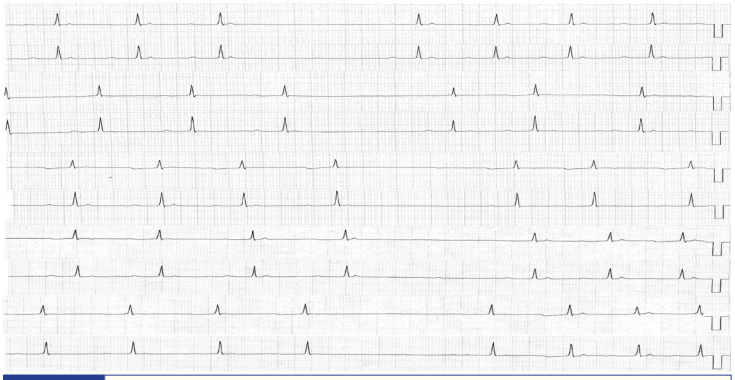

Figure 1: Holter monitoring strips revealing atrio-ventricular conduction block are shown

doses. However, it should be kept in mind that antiepileptic drug therapy may also potentially alter autonomic function or produce proarrhythmogenic effects as in our case.

On several occasions, our case was extensively investigated at an outside hospital for near syncope and atrio-venricular block attacks on Holter monitoring and the cause of the atrio-venricular block remained unexplained, despite investigations. Finally pacemaker insertion was recommended. In hindsight, it was apparent that she was suffering from side effects of valproic acid. This case report reminds us to review our patients' medications meticulously when they present with symptoms that are difficult to explain. We suggest that patients in whom atrio-ventricular block is shown on Holter monitoring valproic acid usage should be checked as illustrated by our case in order to lessen the misdiagnosis, as well as avoid unnecessary pacemaker implantation.

Conclusions

Healthcare providers must be alert to the possibility of side effects of valproic acid when patients suffer from atrio-ventricular block recurrently with symptoms that are difficult to explain.

Conflict Of Interests

None.

Disclosures

None.

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