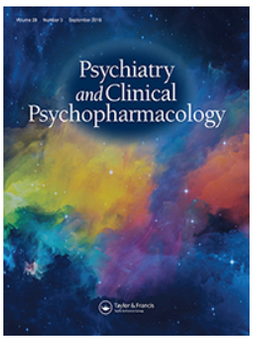

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CASE REPORT

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Treatment of ADHD in a patient with Brugada syndrome: a case report and a brief review

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ABSTRACT

The Brugada syndrome is one of the common causes of sudden cardiac arrest in healthy-appearing adults. The use of drugs in the treatment of this disease may give variable and unwanted results. Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurobehavioural disorder which has begun to be noticed in adults as much as children. In our case, we present a 39-year-old male patient with an ADHD who was diagnosed with the Brugada syndrome during a routine examination and we discuss the treatment of this case. The association of ADHD and Brugada syndrome has not been previously reported in any clinical study. As far as we know, the present case is the first article in the literature to discuss the follow-up and treatment of ADHD in a patient with the Brugada syndrome. We observed all medical and non-medical treatment methods for ADHD treatment and discussed these methods such as psychostimulants, atomoxetine, bupropion, and psychotherapy.

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KEYWORDS
ADHD; Brugada syndrome; cardiovascular adverse events; psychostimulants

Introduction

Attention-deficit/hyperactivity disorder (ADHD), which has been a known childhood disorder, is a chronic neurobehavioural disorder which has begun to be noticed in adults as much as children. It is the most common psychiatric disorder in childhood; however, in 60% of patients, the findings can extend to adulthood [1]. It is a psychiatric disorder which is characterized by symptoms of inattention, hyperactivity, and impulsivity. Despite the fact that the pathophysiology of ADHD is still not fully understood, imbalance of dopaminergic and noradrenergic system particularly in the frontal cortex is thought to be the main neurobiological cause [2]. ADHD consists of a series of characteristic symptoms involving inattention, distractibility, deficient emotional self-regulation, impulsive behaviours, hyperactivity, poor academic performance, diminished family relations, and impaired motor coordination. Furthermore, it has been shown that the incidence of accompanying disorders such as obsessive-compulsive disorder, depressive disorders, anxiety disorders, self-destructive disorders, or substance use disorders are increased in ADHD patients. Although it is known that there are serious side effects such as cardiovascular adverse events, including sudden cardiac death (SCD), myocardial infarction (MI), and torsade's de pointes, stimulant medications are still the first choice in the treatment of ADHD. In addition, the most common, manageable and tolerable side effects of drugs used in the treatment of ADHD are reduced appetite, insomnia, weight loss, and headaches [3].

The Brugada syndrome that is characterized by a pathognomonic ST-segment elevation in leads V1–V3 is an autosomal dominant disorder and was first described in 1992 [4]. Although it can be seen in a wide range of symptoms such as SCD, syncope, and arrhythmia, it can be also asymptomatic [5]. It is one of the common causes of sudden cardiac arrest in healthy-appearing adults [6]. The use of drugs in the treatment of this disease may give variable results. To date, there is no curative treatment. The only effective strategy that prevents SCD is implantable cardioverter defibrillators (ICD) [7].

In our case, we present a male patient with an ADHD who was diagnosed with the Brugada syndrome during a routine examination and discuss the treatment of this case.

Case presentation

The patient was a 39-year-old married man with an academic career who works at a hospital as a medical doctor. He presented to our outpatient clinic with

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complaints such as unable to concentrate, constantly postpone work, drowsiness, difficulty in anger control, difficulty in focusing, disorganization, and inability to make plans. Complaints have been going on since childhood. He could not do the work that needed to be done in a timely manner, and he was living with troubles in his working life. He was unable to concentrate on his business and the people he was addressing, and was living in a disorganized. There were problems in interpersonal relations. When he understood that he cannot control his thoughts and behaviour and his occupational and family life were adversely affected, he became anxious and had presented to the psychiatry department. He and his parents reported no history of psychiatric disorders in the family. After the patient's detailed examination, he was diagnosed with ADHD according to the DSM-5. Adult ADHD Self-Report Scale (ASRS) was performed. His ASRS score was 54. His complete blood count, liver and renal function tests, electrolytes, complete urine examination, thyroid function tests, and PA lung X-ray were unremarkable. There were no specific features in the medical history of the patient. But there was ST elevation at the right precordial leads (V1–V3) in the ECG of the patient, suggesting the Brugada syndrome. The patient was referred for a cardiology consultation. After the detailed examination and genetic tests were performed, the diagnosis of the Brugada syndrome was confirmed. Cardiologists commented that medical treatment would be safer after ICD and there could be a risk of SCD and malignant arrhythmias during psychostimulant or non-psychostimulant treatment. The patient was undecided about the implementation of ICD. Cognitive behavioural therapy (CBT) was initiated until the patient decided for ICD. After six sessions of CBT, the patient observed partial benefits from psychotherapy. Post-therapy ASRS score was 43. The application of the ICD is expected for pharmacological treatment of the ADHD.

Discussion

The association of ADHD and the Brugada syndrome has not been previously reported in any clinical study. But the Brugada syndrome and psychiatric disorders such as anxiety disorder, depressive disorder, and schizophrenia are in the literature. As far as we know, the present case is the first article in the literature to discuss the follow-up and treatment of ADHD in a patient with the Brugada syndrome. We have reviewed all medical and non-medical treatment methods for ADHD treatment and discussed these methods below.

Psychostimulants

Currently, psychostimulants, especially methylphenidate and amphetamine, are preferred as a first-line pharmacological treatment in ADHD. Although psychostimulants are known to be safe, effective, well tolerated and the long history of used drugs, the reliability of these medications has recently begun to come into question due to isolated reports about possible serious cardiovascular side effects including SCD. Previous studies have shown that psychostimulants can cause an increase in heart rate and blood pressure, but that the use of these drugs does not increase the risk of severe cardiovascular events such as SCD and MI [8]. Although no previous studies have been conducted on this topic and no statistically significant increase in cardiovascular side effects has been shown, we believe that patients with a premorbid cardiovascular disease such as Brugada syndrome can carry a greater risk due to an increased number of isolated reports about SCD. In addition, the most common side effects in the Food and Drug Administration's (FDA) Side Effects Reporting System included cardiac arrest, MI, and SCD which caused to stay away from this treatment option [9].

Atomoxetine

Atomoxetine, an antidepressant with the norepinephrine transport inhibitor action mechanism, was approved by the FDA in 2002 as the first non-stimulating agent in the treatment of ADHD [10]. Atomoxetine, no difference in activity when compared to psychostimulants, long duration of action, limited abuse potential, and in comorbid conditions such as tics and anxiety disorder is particularly as a useful alternative in the treatment of ADHD [11]. Although atomoxetine is well tolerated and is an effective non-stimulant drug, cardiovascular side effects are very similar to psychostimulants [12]. Because of this reason and the effects of the drug on the cardiovascular system, the use of atomoxetine in our patients was not appropriate.

Bupropion

Bupropion, which is an antidepressant and a smoking cessation agent, is a dopamine and norepinephrine reuptake inhibitor. It has been used off-label for the treatment of ADHD based on several studies [13]. In addition, ADHD patients with comorbid psychiatric disorders such as depression and smoking cessation may be a good option. It is not as effective as psychostimulants, but being fast acting, no lack of potential addiction risk, and well tolerated are important features of bupropion. Depending on the sympathomimetic activity, bupropion may cause an increase in heart rate and an increase in blood pressure [14]. Due to cardiac side effects of psychostimulants and atomoxetine, we did not use bupropion in our patient.

Other pharmacological treatments

Although not FDA approved, there are some drugs such as clonidine, guanfacine, venlafaxine, and modafinil used for the treatment of ADHD, due to some evidences that are in the literature [15].

Clonidine and guanfacine that are alpha2A-adrenoceptor agonists are used for the treatment of hypertension in clinical practice. Unlike other pharmacological treatments of ADHD, despite having no sympathomimetic system activation as an advantage, bradyarrhythmia and low blood pressure may occur while using clonidine and guanfacine [16]. More importantly, while using these drugs, withdrawal symptoms such as sympathetic hyperactivity possibility may occur [17]. This situation is not warranted for the patients with the Brugada syndrome.

Modafinil that effectively treats excessive sleepiness associated with obstructive sleep apnoea, narcolepsy, shift work disorder, and other related sleep disorders is a novel stimulant agent which is an indirect noradrenergic agonist. In addition to continuing modafinil wakefulness, it has been realized that it enhances cognitive functions, brain activity, and performance. And then it was tried to be used as off-label in ADHD treatment. Low-dependency risk and being effective in comorbid psychiatric disorders such as sleep disorders and depression are important advantages. But the presence of cardiovascular side effects such as high blood pressure and heart rate prevented us from using modafinil in our patients [18].

Venlafaxine and duloxetine that are serotonin and norepinephrine reuptake inhibitors currently are used for the treatment of major depressive disorder in clinical practice. When the current literature reviewed the efficacy and safety of venlafaxine and duloxetine in the treatment of ADHD, they have been shown to be effective in the treatment of ADHD compared to placebo, although not as effective as psychostimulants. Venlafaxine and duloxetine may be a good option for patients who cannot tolerate drugs used in the treatment of other ADHD. These drugs are not preferred in our patients due to cardiovascular side effects such as possible tachycardia and hypertension [19].

Cognitive behavioural therapy

In addition to pharmacological approaches in ADHD treatment, CBT, a non-pharmacological approach, is noteworthy. In patients with ADHD who cannot use medication and comorbidities, CBT emerges as a suitable method for increasing functional fitness. In particular, CBT can help to apply the methods of coping with the underlying symptoms of ADHD in their routine life [20]. We preferred CBT, which is a non-pharmacologic approach in our patient, because it is not a cardiovascular side effect. We also believe that CBT is the most reliable method until ICD implantation.

Conclusion

Because of the sympathomimetic activation of the norepinephrine mechanism of pharmacological agents used in the treatment of ADHD, there is always a potential for cardiovascular side effects. For people without cardiovascular comorbidities such as the Brugada syndrome, these side effects may not be very important. Because research suggests that cardiovascular side effects will not be felt by individuals. However, these side effects, especially in patients with cardiac comorbidities such as the Brugada syndrome, may result in irreversible results. For this reason, we found it more appropriate to avoid pharmacological treatment until ICD implantation in a patient and we implemented CBT to reduce the patient's current complaints and improve their daily functioning.

As a result, we recommend that ECG be taken for possible cardiac side effects of treatment before ADHD patients begin pharmacological treatment. Because, as in our patient, the Brugada syndrome may be asymptomatic and unidentified. Acting together with cardiologists, especially in high-risk patients, would be wise to prevent undesirable consequences. More and longer studies are needed to determine the safety of pharmacological agents used in the treatment of ADHD in patients with the Brugada syndrome.

Implications for future

In our study, a patient with the Brugada syndrome had a literature review on the planning and implementation of ADHD treatment. Working with a cardiologist before and during pharmacologic treatment in ADHD and doing ECG follow-ups will protect clinicians from encountering undesirable outcomes such as SCD. The results of our study may play a guiding role in the treatment of any psychiatric disorder in a patient with the Brugada syndrome. In addition, well-designed clinical trials reinforced at a sufficient level to be made in the future are important to establish the frequency of ADHD in patients with the Brugada syndrome and to demonstrate the results of pharmacological treatment.

Disclosure statement

No potential conflict of interest was reported by the authors.

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