

Accidentally detected asymptomatic Wolff-Parkinson-White syndrome

Wolff-Parkinson-White syndrome in an adolescent with depression

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Summary

Wolff-Parkinson-White (WPW) syndrome is a congenital disorder characterised by a macro-reentrant arrhythmia caused by preexcitation of the ventricles. A significant proportion of cases are detected incidentally in asymptomatic patients during routine checkups. Because little is known about the use of selective serotonin reuptake inhibitors in youths with preexisting cardiac disease, we report here a 15-year-old adolescent with asymptomatic WPW syndrome and severe depressive symptoms. An improvement in depressive symptoms was observed with sertraline therapy and the absence of cardiac adverse effects after 5 months of treatment suggested that sertraline could be used at therapeutic doses in adolescents with preexisting but asymptomatic WPW syndrome.

Key words: adolescent; depression; Wolff-Parkinson-White syndrome; sertraline

Introduction

Depression is reported to affect 6% of adolescents aged from 13 to 18 years [1] with high suicidality, recurrence and chronicity [2, 3]. In adolescents with moderate to severe depression, pharmacological treatment in combination with a psychological therapy is often indicated [4]. As a result of lack of clinical trials in children and adolescents, the off-label use of antidepressant drugs is widespread (about 49% of all antidepressant drugs prescribed) in this population [5]. Among these off-label prescriptions, the use of the selective serotonin reuptake inhibitors (SSRIs) is becoming preferred because of their safer cardiac profiles compared with older medications such as tricyclic antidepressants.

Wolff-Parkinson-White (WPW) syndrome is a macro-reentrant arrhythmia with an estimated prevalence of 2–4 per 1000. A significant proportion of cases are found incidentally in asymptomatic patients presenting for routine checkups [6]. Conduction through an accessory pathway may cause preexcitation of the ventricles leading to supraventricular tachycardia, atrial

fibrillation, ventricular fibrillation and even cardiac arrest [6].

In adolescents with preexisting cardiac disease, depression and anxiety are commonly reported [7]. SSRIs are generally recommended as first-line psychotropic agents for depressed patients with heart failure [8] and improvement in depression was reported to be associated with improved adherence to cardiovascular drug therapy in adults [9]. However, little is known about the use of SSRIs in youths with preexisting cardiac disease, in particular, no cases have been published on the use of SSRIs in adolescents with WPW syndrome.

Case report

We report here the case of a 15-year-old girl who was admitted to our outpatient consultation for a severe depressive episode without psychotic symptoms (F32.2, ICD-10). She had a depressed mood from more than 1 year together with disturbed sleep, loss of energy and of body weight, diminished ability to concentrate and a feeling of worthlessness. Recurrent thoughts of death were present. She scored six on the Clinical Global Impression-Severity (CGI-S) scale, which classified her as “severely ill”. As past medical history, she was born prematurely and had been diagnosed with infantile pyloric stenosis, which is rare in preterm infants according to the literature [10, 11]. She was treated medically at birth during a prolonged hospitalisation of 3 weeks, but no additional information about her initial treatment could be obtained. She later had several standard electrocardiogram (ECG) recordings with normal results, according to the family. As she had no known history of substance use and cardiac disease, cardiac arrest or related risk-factor, antidepressant treatment with sertraline was prescribed. The daily dose was increased gradually every six days from the initial dose of 25 mg to 50 mg, and then to the maintenance dose of 100 mg. The combination of psychologi-

cal and pharmacological treatment resulted in a significant improvement from baseline in depressive symptoms. Her suicidal thoughts almost disappeared. After 3 months of treatment, she scored four on the CGI-S scale (“moderately ill”) and two on the Clinical Global Impression-Improvement (CGI-I) scale (“much improved”).

Six months after starting sertraline, she underwent an endoscopic examination in order to investigate some recurrent gastric symptoms. The endoscopy revealed no anomalies; however, asymptomatic WPW syndrome was found incidentally on ECG monitoring during the examination. She was referred to a cardiologist for a further cardiovascular investigation. Holter monitoring revealed sinus rhythm with no QTc prolongation, and a mean heart rate of 76 per minute but with a range from 42 to 167 leading to variable prolongation of the QRS complex, suggesting a left lateral accessory pathway. A few isolated supraventricular and ventricular arrhythmias were observed. Such isolated paroxysmal arrhythmias did not allow measurement of the more specific anterograde characteristics of the accessory pathway (in order to assess its clinical gravity) with noninvasive evaluation (for example, the shortest preexcited R-R interval on the ECG [SPERRI]). Echocardiography was normal. Electrophysiology studies were scheduled to investigate further the accessory pathway (with a subsequent radiofrequency catheter ablation, if necessary). She received flecainide (100 mg/day) as an antiarrhythmic treatment.

Her residual depressive symptoms did not appear more important with the newly diagnosed cardiac disease. She ruminated a great deal on a theory of fatalism, without any intentional suicidal thought or plan. She became sometimes more anxious, showing intense emotional outbursts. The antidepressant treatment with sertraline was estimated by the cardiologist as unlikely to be a cause for the development and evolution of the asymptomatic WPW syndrome found in this patient. In addition, to our knowledge, WPW syndrome is considered to be a congenital condition and no cases of WPW syndrome induced by an SSRI are described in the literature. Considering her residual depressive symptoms and anxiety symptoms related to the newly diagnosed WPW syndrome, we proposed her to continue her psychological therapy and pharmacological treatment with sertraline (100 mg/day).

Discussion

In this case report, our patient was an adolescent girl presenting severe depressive symptoms before being diagnosed incidentally with WPW syndrome, a macro-

reentrant arrhythmia disorder with an estimated prevalence of 2–4 per 1000. A significant proportion of patients with asymptomatic WPW syndrome are found incidentally when presenting for routine checkups [6]. Population studies yielded variable but very low incidences of sudden death [12]. Various recommendations on the management of asymptomatic young patients with WPW syndrome have been published [12].

The question arises on the choice of antidepressant treatment when psychological treatment alone is not adequate. In the USA, fluoxetine and escitalopram are approved by the Food and Drug Administration (FDA) for treatment of depression in paediatric patients (starting from 8 years and 12 years, respectively). In Switzerland, none of the SSRIs has been approved by Swiss Agency for Therapeutic Products (Swissmedic) for use in children and adolescents with depression. Fluvoxamine was approved by Swissmedic for use in children 8 years and older and sertraline in children 6 years and older, but only for the treatment of obsessive-compulsive disorders. For this reason, but also because of a favourable cardiac safety profile, sertraline appears to be often used for the treatment of adolescent depression in Switzerland (off-label). Of note, although the SSRIs are considered to have generally safe cardiac profiles, SSRI-related QTc prolongation and/or “torsades de pointes” have been reported [13, 14]. However, a recent meta-analysis [14] concluded that QTc prolongation produced by SSRIs (other than citalopram) seemed to be relatively small and was considered to be clinically insignificant for most patients. Sertraline, compared with other SSRI antidepressants, has been found to be safe for use in adult patients with preexisting cardiac disease [15, 16] and no torsades de pointes has been reported to be associated with single use of sertraline [13]. In children and adolescents, the absence of cardiovascular adverse effects has been reported for sertraline use at doses up to 200 mg [17].

It has been recommended that a baseline ECG is performed when the patient has a suspicious medical history or related risk factors for arrhythmia, or when the medication to be prescribed is documented to cause prolongation of the QTc interval at therapeutic doses [13]. Although careful risk-benefit analysis is always necessary when antidepressant treatment is proposed, in particular in infants and adolescents [9, 15], an ECG check is not considered necessary before prescribing sertraline in the absence of a known history of cardiac disease or related risk factors [13]. In addition, persistent depression increases mortality in patients with cardiac disease and improvement in depression was reported to be associated with improved adherence to cardiovascular drug therapy

[9]. The improvement in depressive symptoms and absence of cardiac adverse effects in our adolescent patient after 5 months of antidepressant treatment with sertraline suggests the cardiac safety of sertraline at therapeutic doses in adolescents with preexisting but asymptomatic cardiac disease such as WPW syndrome. This is in accordance with early reports in adults with preexisting heart disease [15, 16]. However, because of this single case, it is important to emphasise necessary caution, in particular when combining psychotropic treatments, which could lead to severe cardiac events as demonstrated recently with sertraline plus mirtazapine [18], although single use of mirtazapine has been reported to be efficient in treating depression in an adolescent with preexisting cardiomyopathy and arrhythmia [8].

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References

- Costello EJ, Erkanli A, Angold A. Is there an epidemic of child or adolescent depression? *J Child Psychol Psychiatr.* 2006;47:1263–71.
- Dunn V, Goodyer IM. Longitudinal investigation into childhood and adolescent-onset depression: psychiatric outcome in early adulthood. *Br J Psychiatry.* 2006;188:216–22.
- Fombonne E, Wostear G, Cooper V, Harrington R, Rutter M. The Maudsley long-term follow-up of child and adolescent depression. 1. Psychiatric outcomes in adulthood. *Br J Psychiatry.* 2001;179:210–7.
- Hopkins K, Crosland P, Elliott N, Bewley S; Clinical Guidelines Update Committee B. Diagnosis and management of depression in children and young people: summary of updated NICE guidance. *BMJ.* 2015;350:h824.
- Dörks M, Langner I, Dittmann U, Timmer A, Garbe E. Antidepressant drug use and off-label prescribing in children and adolescents in Germany: results from a large population-based cohort study. *Eur Child Adolesc Psychiatry.* 2013;22:511–8.
- Liu A, Pusalkar P. Asymptomatic Wolff-Parkinson-White syndrome: incidental ECG diagnosis and a review of literature regarding current treatment. *BMJ Case Reports.* 2011; doi:10.1136/bcr.05.2011.4192.
- Wang Q, Hay M, Clarke D, Menahem S. The prevalence and predictors of anxiety and depression in adolescents with heart disease. *J Pediatr.* 2012;161:943–6.
- Tanidir C, Tanidir IC, Tuzcu V. Treatment of depression in an adolescent with cardiomyopathy and arrhythmia. *Cardiology in the Young.* in press.
- Glassman AH, Bigger JT Jr, Gaffney M. Psychiatric characteristics associated with long-term mortality among 361 patients having an acute coronary syndrome and major depression: seven-year follow-up of SADHART participants. *Arch Gen Psychiatry.* 2009;66(9):1022–9.
- Georgoula C, Gardiner M. Pyloric stenosis a 100 years after Ramstedt. *Arch Dis Child.* 2012;97:741–5.
- Cascio S, Steven M, Livingstone H, Young D, Carachi R. Hypertrophic pyloric stenosis in premature infants: evaluation of sonographic criteria and short-term outcomes. *Pediatr Surg Int.* 2013;29:697–702.
- Cohen MI, et al. PACES/HRS expert consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, ventricular preexcitation) electrocardiographic pattern: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), the American Academy of Pediatrics (AAP), and the Canadian Heart Rhythm Society (CHRS). *Heart Rhythm.* 2012; 9(6):1006–24.
- McNally P, McNicholas F, Oslizlok P. The QT interval and psychotropic medications in children: recommendations for clinicians. *Eur Child Adolesc Psychiatry.* 2007; 16(1):33–47.
- Beach SR, Kostis WJ, Celano CM, Januzzi JL, Ruskin JN, Noseworthy PA, Huffman JC. Meta-analysis of selective serotonin reuptake inhibitor-associated QTc prolongation. *J Clin Psychiatry.* 2014; 75(5):e441–9.
- Jiang W, O'Connor C, Silva SG, Kuchibhatla M, Cuffe MS, Callwood DD, et al. SADHART-CHF Investigators. Safety and efficacy of sertraline for depression in patients with CHF (SADHART-CHF): a randomized, double-blind, placebo-controlled trial of sertraline for major depression with congestive heart failure. *Am Heart J.* 2008;156(3):437–44.
- Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, et al. Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA.* 2002;288(6):701–9.
- Wilens TE, Biederman J, March JS, Wolkow R, Fine CS, Millstein RB, et al. Absence of cardiovascular adverse effects of sertraline in children adolescents. *J Am Acad Child Adolesc Psychiatry.* 1999;38(5):573–7.
- Atmaca M, Mermi O. A case of ventricular tachycardia and cardiac arrest associated with sertraline and mirtazapine combination. *Iranian J Psychiatry.* 2014;9(1):45–6.

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