CJC Open 4 (2022) 240–242

Case Report

Reversible Complete Heart Block in a Pregnant Woman Related to Sertraline Treatment

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ABSTRACT

Complete heart block (CHB) is a serious condition, usually affecting older patients. We report a case of CHB in a 31-year-old pregnant woman treated with sertraline in whom atrioventricular (AV) conduction normalized after discontinuation of sertraline. Results of subsequent genetic investigations for inherited cardiomyopathy and ion-channel disease and a pharmacogenetic study of sertraline pharmacokinetics were negative. Reversible CHB in this younger pregnant patient was temporally related to sertraline. This case underlines the importance of identifying reversible causes when a young patient presents with AV block with unknown trajectory and prognosis, as well as regular recording of electrocardiograms in pregnant patients on psychotropic medications.

RÉSUMÉ

Le bloc cardiaque complet (BCC) est une affection sérieuse, qui touche généralement les patients âgés. Nous présentons un cas de BCC chez une femme enceinte de 31 ans traitée par sertraline chez qui la normalisation de la conduction atrioventriculaire (AV) a été constatée après l'arrêt de la sertraline. Les résultats des examens génétiques subséquents de cardiomyopathie héréditaire et de maladies des canaux ioniques, et d'une étude pharmacogénétique de la pharmacocinétique de la sertraline étaient négatifs. LE BCC réversible chez cette jeune patiente enceinte était temporairement lié à la sertraline. Ce cas montre l'importance de cerner les causes réversibles lorsqu'un jeune patient présente un bloc AV à la trajectoire et au pronostic inconnus, et de faire régulièrement des électrocardiogrammes chez les patientes enceintes qui prennent des psychotropes.

Case

A 31-year-old woman in her 21st week of pregnancy was admitted to our clinic with the experience of palpitations. Physical examination revealed an irregular, slow heart rhythm (59 beats per minute), and hypotension (99/55 mm Hg). Electrocardiography (ECG) showed complete heart block (CHB) with atrioventricular (AV) dissociation (Fig. 1B). A transthoracic echocardiogram showed a structurally normal heart. Results of laboratory tests, including leukocyte blood count, C-reactive protein (CRP), thyroid-stimulating hormone (TSH), Lyme titer, and cardiac troponins, were all normal. The patient had no history of cardiac disease and no family history for cardiomyopathy, intracardiac device, or sudden cardiac death. She was treated for obsessive-compulsive disorder, and, 5 months before, citalopram had been replaced by sertraline 50 mg once daily to be continued during pregnancy owing to its more favourable safety profile. The results of an ECG obtained at that time were normal (Fig. 1A).

Because of the young age of the patient and lack of identifiable causes of CHB, no pacemaker was implanted, sertraline treatment was discontinued, and the patient was kept on telemetry. During the following days, a gradual recurrence of AV conduction was observed. On day 3, some impulses were conducted through the AV node. On day 4, the heart rate had increased to 100 beats per minute, and an ECG showed prolonged PR interval with episodes of second-degree Wenckebach type AV block. The PR interval gradually decreased and reached normal values on day 8 (Fig. 1C). Follow-ups with 48-hour Holter monitor recordings conducted 2 weeks, 4 months, and 6 months after sertraline was stopped showed sinus rhythm, normal PR interval, and no AV block. After giving birth, the patient started paroxetine, and the results of the ECG were normal. Genetic investigations for inherited cardiomyopathy and ion-channel disease were negative. Furthermore, a pharmacogenetic study obtained from Health in Code, La Coruna, Spain (https://pharmahic.com/en/#estudio) showed the following polymorphisms of the sertraline metabolizing genes, which are not known to be

Received for publication July 24, 2021. Accepted September 21, 2021.

Ethics Statement: This research report has adhered to the relevant ethical guidelines.

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See page 242 for disclosure information.

https://doi.org/10.1016/j.cjco.2021.09.021

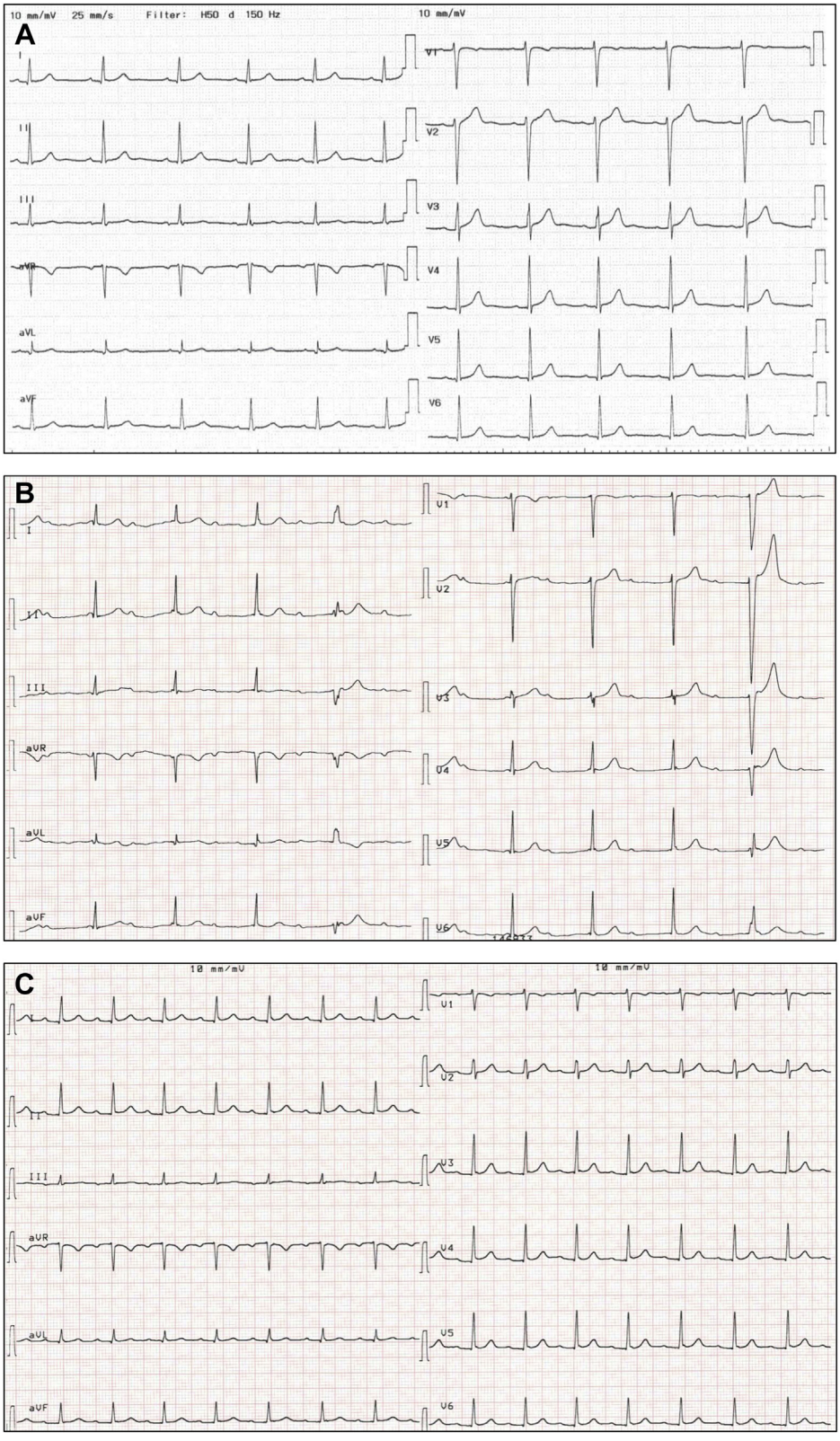

Figure 1. Patient electrocardiogram (ECGs) (25 mm/s). (**A**) Normal ECG recorded after a few days of sertraline treatment and 6 months before onset of symptoms. (**B**) ECG recorded 2 days after hospitalization, showing complete heart block with atrioventricular dissociation, heart rate 59. (**C**) ECG recorded 8 days after cessation of sertraline, showing sinus rhythm and normal PR interval.

Novel Teaching Points

- Sertraline is well known to prolong QT interval and has other cardiac electrophysiological effects, but, to our knowledge, CHB related to sertraline treatment is a novel finding. Whether the cause of disease was attributable to something peculiar to this patient would require further study.
- The case makes an example of the importance of identifying reversible causes of AV block, particularly in younger patients with proximal AV nodal block with unknown trajectory and prognosis. In such a situation, permanent pacemaker implantation may be unnecessary and may pose more risk to the patient than benefit.

associated with slow metabolism of sertraline: CYP3A4 (*1/*1); CYP2B6 (*1A/*1A), CYP2C19 (*1A/*1A), CYP2D6 (*1A/*2A).

Discussion

When a young patient presents with CHB, the physician should always consider drugs as potential contributors, especially if recently prescribed and even if this specific adverse effect has not previously been described in the literature. Our patient received a relatively low dose of sertraline, 50 mg daily, and, to our knowledge, this drug has not been associated with CHB. The unusual course of this patient raises a discussion of the possible underlying mechanisms and contributing factors.

Sertraline is a selective serotonin reuptake inhibitor (SSRI). Sertraline generally is considered safe and well tolerated in therapeutic doses in patients with preexisting heart disease.[1] SSRIs have a wide spectrum of inhibitory effects on various cardiac ion channels, which may induce changes of the cardiac action potential duration and the QT interval. Indeed, sertraline has been reported to induce ventricular tachycardia [2]. However, when the effects of sertraline on the ECG were investigated in an adult population, sertraline had no significant effect on the PR, QRS, or QT intervals.[3] Whether a channel-blocking effect of sertraline was the mechanism of conduction block remains unknown. In the current case, this possible effect should have reversed 3 to 5 half-lives (of approximately 22 to 36 hours) after cessation,[4] which is not incompatible with the 7 days observed.

Pharmacokinetically, sertraline exhibits a high degree of plasma protein binding and extensive tissue distribution. Multiple cytochrome P450 isoforms (CYP) contribute to the metabolism of sertraline, primarily N-demethylation into N-desmethylsertraline. CYP2C19 is probably a major contributing enzyme, and the oral clearance of sertraline is significantly lower in poor metabolizers compared with extensive metabolizers in respect of this specific enzyme.[5] A recent study found that women generally experience a higher incidence of adverse drug reactions to sertraline than men, which was also associated with individual metabolism status of CYP2C19 and CYP2B6.[6] In our case, it remains unknown whether pregnancy-related pharmacokinetic changes caused by altered P450 activity played a role. Some studies have demonstrated a decreased activity of CYP2C19 in pregnancy, but the significance of this finding remains uncertain because of a high degree of overlapping effects of the P450 family.[7]

Following the patient's recovery, a genetic analysis was negative for known variants associated with cardiomyopathy and channelopathies. A pharmacogenetic study found no polymorphisms in the CYP3A4, CYP2B6, CYP2D6, and CYP2C19 genes, indicating normal metabolism of sertraline. Serum sertraline concentrations were not obtained, and reinitiation of sertraline treatment after pregnancy was deemed inexpedient in this patient with obsessive-compulsive disorder. Consequently, a definite causal relation between sertraline and CHB observed cannot be established. Maternal CHB in patients with structurally normal hearts has been reported, suggesting that CHB could be solely associated with pregnancy.[8] Still, in the light of the course of disease with recovery of AV conduction during the week after discontinuation of sertraline, there could be a correlation. Our findings emphasize the importance of recording regular ECGs in pregnant patients on SSRIs rather than recommending drug withdrawal (unless arrhythmia is documented), as such intervention could seriously impair maternal mental health.

In summary, we report a case of reversible CHB in a pregnant 31-year-old patient temporally related to sertraline.

Funding Sources

Funding for this research was provided by Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark.

Disclosures

The authors have no conflicts of interest to disclose.

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