Familial sick sinus syndrome possibly associated with novel *SCN5A* mutation diagnosed in pregnancy

Ichitaro Abe, MD, PhD,[*1] Pu Wang, MD,[†§1] Masaki Takahashi, MD,[*] Seiko Ohno, MD, PhD,[‡] Katsushige Ono, MD, PhD,[†] Naohiko Takahashi, MD, PhD[*]

*From the *Department of Cardiology and Clinical Examination, Faculty of Medicine, Oita University, Oita, Japan, [†]Department of Pathophysiology, Faculty of Medicine, Oita University, Oita, Japan, [‡]Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Otsu, Japan, and [§]Department of Cardiology, The First Hospital of Hebei Medical University, Shijiazhuang, China.*

Introduction

Sick sinus syndrome (SSS) denotes a collection of cardiac arrhythmias associated with dysfunction of the sinoatrial node that commonly lead to disorders in cardiac rhythm and conduction.[1] Mechanisms underlying the pathogenesis for sinus node dysfunction in SSS patients are still not clear. It could occur in healthy people without any evident structural heart disease. Recent studies have identified several gene mutations, including the *SCN5A* gene, in congenital SSS patients.[2,3] *SCN5A* is the cardiac Na channel gene responsible for the generation and rapid propagation of action potentials in the heart. Mutations in *SCN5A* have been linked to a wide range of inherited lethal arrhythmias, referred to as cardiac Na channelopathy, including long QT syndrome type 3,[4] Brugada syndrome,[5] progressive cardiac conduction defect,[6] and SSS. In the present report, we describe a proband (and her family members) with a novel *SCN5A* mutation, who displayed SSS, which was diagnosed during pregnancy.

KEY TEACHING POINTS

- This case highlights a proband with familial sick sinus syndrome (SSS) diagnosed during pregnancy.
- The genetic analysis identified a novel missense mutation in *SCN5A* (M1838V), which was electrophysiologically characterized using patch clamp experiments.
- This is the first report in which heart rate changes during pregnancy with threatened premature labor were precisely evaluated in an SSS patient carrying an *SCN5A* mutation.

Case report

In April 2019, a 30-year-old woman presented to a local hospital with severe nausea and anorexia at 9 weeks of pregnancy. She had a past medical history of pregnancy after in vitro fertilization and had a family medical history of permanent pacemaker implantation for SSS in her maternal grandmother. She had never complained of syncope, dizziness, or other brain ischemic episodes. When she was diagnosed as having severe hyperemesis gravidarum and admitted to the hospital, the 12-lead electrocardiogram (ECG) showed sinus bradycardia with a heart rate of 37 beats per minute (bpm), and the P waves exhibited low voltage and wandering (Figure 1A). The Holter ECG revealed a total of 56,315 beats per day (mean heart rate: 42 bpm), with a minimum heart rate of 25 bpm (Figure 1B). Escape rhythm and atrial tachycardia were also observed (Figure 1B). To examine whether the cause of nausea was hyperemesis gravidarum or bradycardia, she was transferred to our hospital and admitted (first admission).

The heart rate change during pregnancy is shown in Figure 1A and 2B. Following her first admission, on physical examination, the pulses were equally palpable bilaterally. Lung fields were clear, and precordial auscultation noted a normal first heart sound and a single second heart sound without murmur. The Holter ECG showed 51,846 beats per day of total beats (mean heart rate: 36 bpm), with a minimum rate of 22 bpm. Echocardiography showed that the left ventricle ejection fraction measured by the biplane Simpson method was 64% with no structural abnormalities. Although exercise test including treadmill test could not be done because of her pregnancy, there were no apparent symptoms on low-level activity. Her physical status was NYHA functional class

KEYWORDS Familial; Novel mutation; Pregnancy; *SCN5A*; Sick sinus syndrome
(Heart Rhythm Case Reports 2020;■:1–6)

Sources of Funding: None. Conflict of Interest Disclosure for all authors: None. [1]Drs Abe and Wang contributed equally to this work. **Address reprint requests and correspondence:** Dr Ichitaro Abe / Dr Naohiko Takahashi, Department of Cardiology and Clinical Examination, Oita University, Faculty of Medicine, 1-1 Idaigaoka, Hasama, Yufu, Oita 879-5593, Japan. E-mail address: i-taro@oita-u.ac.jp; takanao@oita-u.ac.jp.

https://doi.org/10.1016/j.hrcr.2020.11.016