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Case Report
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# Coexistence of Gitelman Syndrome and Hypertrophic Cardiomyopathy in a Pregnant Woman

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Gitelman syndrome (GS) is transmitted as an autosomal recessive trait and characterized by hypokalemic metabolic alkalosis in combination with significant hypomagnesemia and low urinary calcium excretion. The symptoms and severity of the disease can vary greatly from one person to another and can range from mild to severe. Sudden cardiac arrest has been reported occasionally as well. Here, for the first time, we reported a 34-year-old pregnant GS woman who was diagnosed to have hypertrophic obstructive cardiomyopathy during her cardiac examination for the complaints of palpitation and presyncope.

**Key Words:** Gitelman syndrome • Hypertrophic cardiomyopathy • Pregnant • Presyncope • Sudden cardiac death

## INTRODUCTION

Gitelman syndrome (GS) is a distal renal tubular disorder caused by defective sodium chloride transporters. Biochemically, it presents with hypokalemic metabolic alkalosis, hypomagnesaemia and hypocalciuria. Autosomal-recessive (AR) genetic mutations in the thiazide-sensitive sodium chloride cotransporter (NCCT) which is encoded by the SLC12A3 gene have been reported to cause the disease.[1] The estimated prevalence of GS is 1:40.000,[2] and the reported prevalence of heterozygous GS is 1% in Europeans. The impact of this complex disorder involves cardiovascular, muscular-skeletal and other physiological functions which adversely affect the patient's quality of life. Sudden cardiac death (SCD) has been reported in some cases with GS, however as no electrolyte disorders have been reported in these cases, causes other than hypokalemia could be responsible.[3] Hypertrophic cardiomyopathy (HCM) is an autosomal dominantly inherited cardiac disease which is characterized by increased left ventricular wall thickness without any coexisting loading conditions. HCM is one of the most common causes of SCD, especially in young adults. Herein, we report the case of a 34-year-old woman with GS who presented with palpitations, fatigue and presyncope during pregnancy who was eventually diagnosed as having HCM.

## CASE REPORT

A 34-year-old woman with GS presented at 20 weeks gestation with palpitations, fatigue and presyncope. This was her first pregnancy. Her initial diagnosis of GS was confirmed 4 years previously based on her clinical presentation and laboratory data. She was maintained on oral electrolyte replacement therapy with oral potassium chloride and magnesium citrate for the course of the pregnancy. A physical examination revealed a grade 3/6 systolic ejection murmur maximally heard at the api-

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cal focus of the heart. Her blood pressure was 80/50 mmHg and laboratory tests showed a serum potassium level of 2.5 mmol/L (normal 3.5-5.1), serum calcium level of 10.2 mg/dL (normal 8.6-10.0), and serum magnesium level of 1.4 mg/dL (1.6-2.6). Blood gas analysis showed metabolical kalosis with a pH of 7.495 (normal 7.380-7.460), pCO2 of 35.6 (normal 32-46) and HCO3 of 34.1 mmol/L (normal 22-26). Serum creatinine, urea and remainder ionograms were normal. Electrocardiography (ECG) showed a normal sinus rhythm with a rate of 67 beats per minutes and remarkable ST-T changes at inferior and precordial derivations. There was also a prolonged QT interval (490 ms) (Figure 1). The echocardiographic findings confirmed a hypertrophic obstructive cardiomyopathy (HOCM) with a septal thickness of 2.1 cm and posterior wall thickness of 1.1 cm (Figure 2A) and a resting gradient of 30 mmHg (Figure 2B). Systolic anterior motion was also noted in the mitral valve creating a mild degree of mitral regurgitation (video). The risk of SCD at 5 years was calculated to be 2.93%. Because the patient was pregnant, the cardiology, gynecology and pediatric departments discussed whether the pregnancy should be continued, and reached a consensus that close follow-up and if needed termination should be performed. With follow-up, the pregnancy was continued without any complications, and the patient gave birth to a healthy daughter.

## DISCUSSION

Gitelman syndrome is a rare AR inherited disorder first described by Gitelman et al. in 1966.[1] It is primarily a renal tubular disorder characterized by hypokalemic metabolical kalosis, hypomagnesemia, and hypocalciuria.[1] Simon et al. first demonstrated complete linkage of GS to the SLC12A3 gene on chromosome 16q13, and classified GS as an AR disorder with 99% penetrance.[4] The SLC12A3 gene encodes the NCCT protein, which helps to transport salts through ion channels in the kidneys. Mutations in this gene can cause abnormal functioning of the NCCT protein leading to salt and water excretion from the body through urine. In turn, other electrolytes such as potassium, magnesium and calcium are also affected. These imbalances ultimately result in the various symptoms of GS, which usually become apparent anywhere from late childhood to adulthood. However, the disorder is highly variable, even among individuals in the same family. Some people do not develop any symptoms (asymptomatic), while others can de-

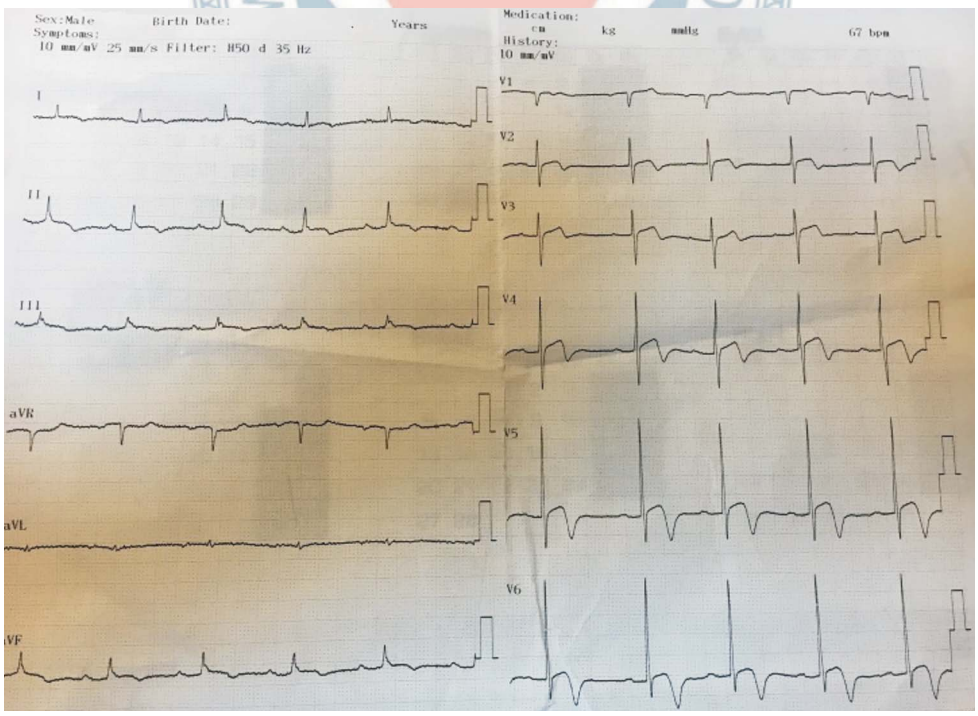


***Figure 1.*** *Electrocardiogram of the patient showing widespread secondary ST-T changes.*

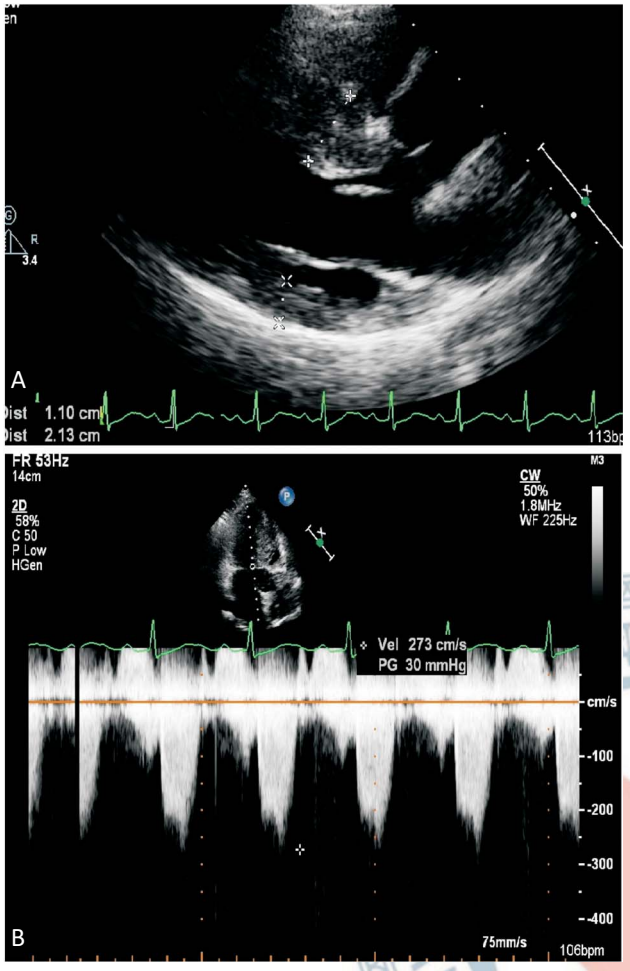


***Figure 2.*** *Transthoracic echocardiography images. (A) Septal and posterior wall thicknesses. (B) Resting left ventricular outflow tract peak gradient.*

velop chronic problems that can impair the quality of life. Muscle weakness, spasms and cramps may occur, and these episodes may also be accompanied by abdominal pain, vomiting, diarrhea or constipation and fever. The severity of fatigue can vary widely, and in some patients symptoms such as presyncope, vertigo, ataxia and blurred vision have also been reported. Despite these symptoms, few studies have reported formal cardiac examinations in these patients.[5] Blood pressure can be abnormally low in comparison to the general population, and cardiac arrhythmias may develop in affected individuals with significant electrolyte imbalance. Although rare, if untreated these cardiac arrhythmias can potentially progress to cause SCD. SCD is a rare but important symptom of GS. Although hypokalemia is the leading cause, cardiac pathologies such as QT prolongation may also cause SCD in patients with GS, as one study reported that patients with GS admitted with aborted SCD had normal electrolyte levels at the time of hospital admission.[3] Pachulski et al. reported a 39-year-old woman with GS who presented with presyncope and long runs of malignant ventricular tachycardia at 230 beats per minute.[6] They also found long QT syndrome on ECG in addition to hypomagnesemia and hypokalemia.

Hypertrophic cardiomyopathy is the most common genetic cardiovascular disorder, with a prevalence of approximately 0.2% (i.e., 1:500) in the general population.[7] It is thought to be caused by autosomal dominant mutations in genes encoding protein components of the sarcomere and its constituent myofilament elements.[8] Intergenetic diversity is compounded by considerable intragene heterogeneity, with > 1400 mutations identified among at least 8 genes. HOCM is generally regarded to be a left ventricular outflow tract pressure gradient of 30 mmHg or more at rest or with provocative maneuvers.[9] Complications of HOCM include SCD, heart failure, and arrhythmias.[10]

Our case was admitted to our clinic with the complaints of palpitations and presyncope at 20 weeks of gestation, and HOCM was diagnosed after a thorough cardiac work-up. In addition, QT prolongation was detected in ECG. The common features of both GS and HOCM are their autosomal transmission and increased risk of SCD and arrhythmias (e.g. ventricular tachycardia). Only a few studies have reported cardiac evaluations in patients with GS,[5,11] and they have suggested that about half of the patients with GS have a prolonged QT interval. Although we did not have the results of genetic analysis in this case and even though there are no clear exclusion criteria for HCM, the rare SCD events in patients with GS may be related to HCM rather than to hypokalemia or QT prolongation. Therefore, it is important to perform comprehensive cardiac tests in all patients with GS in order to evaluate the risk of SCD and accompanying cardiac pathologies. In addition, further investigations focusing on the incidence of HCM in patients with GS should be performed to elucidate the genetic inheritance of these diseases.

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The patient provided a consent form.

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