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Ventricular Tachyarrhythmias in a Patient with Andersen-Tawil Syndrome

Jung Yoon Pyo, MD, Dong Hoo Joh, MD, Jin Su Park, MD, Seung-Jun Lee, MD, Hancheol Lee, MD, Wonjin Kim, MD, and Boyoung Joung, MD

Division of Cardiology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Andersen-Tawil syndrome (ATS), a rare autosomal dominant disorder, is characterized by periodic paralysis, dysmorphic features and cardiac arrhythmias. This syndrome is caused by mutations of KCNJ2 gene, which encodes inward rectifying potassium channel. Here, we report an 18-year-old girl who was presented with life-threatening cardiac arrhythmia and acute respiratory distress. She was diagnosed with ATS, based on dysmorphic features, ventricular arrhythmia, and periodic paralysis. This is the first case to be reported in Korea who experienced a fatal cardiac arrest and respiratory failure caused by ATS. **(Korean Circ J 2013;43:62-65)**

KEY WORDS: Andersen-Tawil syndrome; Ventricular tachycardia; Paralysis.

Introduction

Andersen-Tawil syndrome (ATS) is a long QT syndrome (LQTS) type 7, which is characterized by a triad of periodic paralysis, ventricular dysrhythmias, and dysmorphic features.[1] It is caused by mutations in the gene KCNJ2, located on chromosome 17q23, which encodes Kir2.1, the inward rectifying potassium channel.[2][3] This genetic mutation is found in two thirds of patients.[2][3] Hypokalemic periodic paralysis is common, but potassium level may be low, normal or high.[2][4] Recently, we experienced an 18-year-old girl who presented with coexisting ventriculartachycardia and severe respiratory distress. We made a diagnosis of ATS, based on dysmorphic features, ventricular arrhythmia, and periodic paralysis.

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Correspondence: Boyoung Joung, MD, Division of Cardiology, Department of Internal Medicine, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea
Tel: 82-2-2228-8460, Fax: 82-2-393-2041
E-mail: cby6908@yuhs.ac

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Case

An 18-year-old girl was transferred to our emergency room for post-resuscitated status. She was initially admitted to a local hospital for paralysis and paresthesia of lower extremities, which started 2 days ago. She had experienced recurrent periodic paralysis on both lower extremities for the past 7 months, and it was aggravated after exercise. Each episode lasted for 2 or 3 days. After admission to the local hospital, sudden cardiac arrest developed. Her initial serum potassium level was 3.0 mmol/L, but it rapidly decreased to 1.8 mmol/L at the time of cardiac arrest. She was resuscitated after two minutes of cardiac compression.

When she arrived at our hospital, she was semicomatous. She showed frequent episodes of tachycardia with the heart rate of 200 beats per minutes. She had a short stature as 149 cm (1.5% percentile for her age), broad forehead, small jaw, and clinodactyly on the right fifth finger (Fig. 1A). Interestingly, her mother also had clinodactyly on both fifth fingers (Fig. 1B). However, there was no family history of cardiac disease. The initial neurologic exam revealed grade 0 strength of both lower and upper extremities. Deep tendon reflexes were absent on biceps, triceps, brachioradialis, knee and ankle.

Her initial electrocardiogram (ECG) showed sinus rhythm with prolonged QT interval of 657 ms and frequent premature ventricular contractions (Fig. 2). Her initial laboratory tests showed Na^+ 147 mEq/L, K^+ 2.0 mEq/L and Cl^- 123 mEq/L. Blood gas analysis revealed pH 6.85, pCO_2 126 mm Hg, pO_2 216 mm Hg, and $HCO3^-$ 22.5 mmol/L revealing severe respiratory acidosis, and she was intubated for

acute respiratory difficulty. Other lab findings were not significant, including the thyroid function test. Until the serum potassium was corrected to above 2.5 mmol/L, several episodes of wide and narrow QRS tachycardia were observed (Fig. 3). Interestingly, the wide QRS tachycardia was sometimes changed to narrow QRS tachycardia with the same cycle length of 360 ms. Another ECG, taken after the cardioversion, prolonged QT interval with prominent U wave and right bundle branch block pattern premature ventricalaric contractions are seen at the end of the T wave (Fig. 4).

Dysmorphic features, ventricular arrhythmia, and periodic paralysis made the diagnosis with ATS. During the maintaining of intravenous administration of potassium and bicarbonate, her mental status became alert and she was extubated on the hospital day 3. By hospital day 4, she recovered her motor strength to grade 5/5 on both of the upper and lower extremities, and was able to walk without assistance. After treatment with oral potassium replacement and potassium sparing diuretics, her paralysis symptoms and hypokalemia did not recur during the 2 year follow up period.

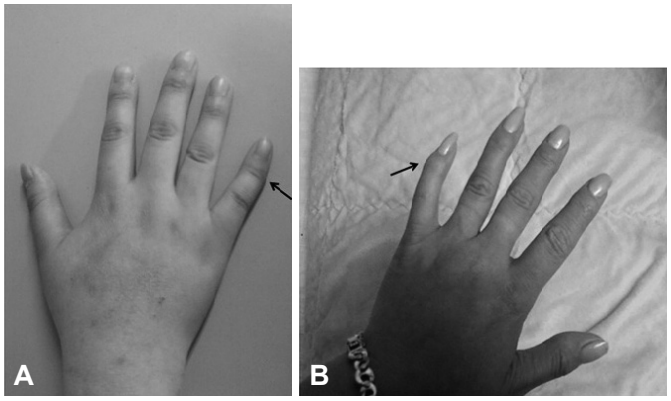

Fig. 1. Characteristic deformity of hand. A: patient's right fifth finger showing clinodactyly (arrow). B: patient mother's left fifth finger also showing clinodactyly (arrow).

Discussion

The LQTS is a disorder of ventricular myocardial repolarization, characterized by a prolonged QT interval, ventricular arrhythmias, and an increased risk of sudden cardiac death. ATS is a rare autosomal dominant disorder, which is characterized by episodes of paralysis, ventricular arrhythmias, and dysmorphic features, such as short stature, clinodactyly, hypertelorism, a broad nose, low-set ears, and a hypoplastic mandible.[1] Subsequent genetic studies identified this disorder as LQTS 7.[2][3] These mutations appear to prolong the terminal phase of the myocardial action potential, and in the presence of low extracellular potassium, it can induce Na-Ca exchanger-dependent delayed afterpotentials.[2]

Genetic testing is available, but such testing has limitations due to congenital LQTS is a complex and heterogeneous condition. Therefore, a negative test result does not exclude the disease. In our patient, mutations for KCNJ2 gene, which encodes Kir2.1, inward rectifying potassium channel, were negative. A mutation in the gene, encoding Kir2.1; it is identified in approximately two-thirds of patients with ATS. There is no genotype-phenotype relationship,[5] and incomplete penetrance and marked intrafamilial phenotypic variation are common. Isolated feature, long QT interval, may be manifested in family members who exhibit no other feature of the disease.[4][6][7] Our patient's mother exhibited such condition that she had dysmorphic features, such as short stature, low set of ears, and fifth-digit clinodactyly, but no other symptoms. Her EKG was normal and she had never experienced periodic paralysis.

This case shows an uncommon cause of cardiac arrhythmia and respiratory failure, which came out to be ATS. Her morphological features, such as short stature, fifth finger clinodactyly, her mother's clinodactyly, periodic paralysis and ventricular arrhythmia resulted in a diagnose of ATS. Kir2.1 channels stabilize the resting membrane

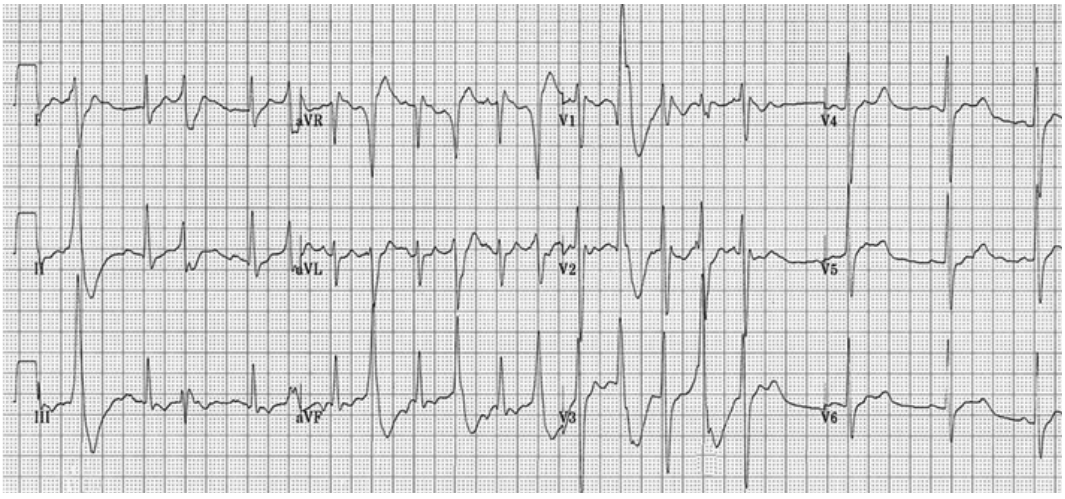

Fig. 2. Initial 12 lead electrocardiogram. Ventricular bigeminy with two different morphologies of QRS, along with long QT interval.

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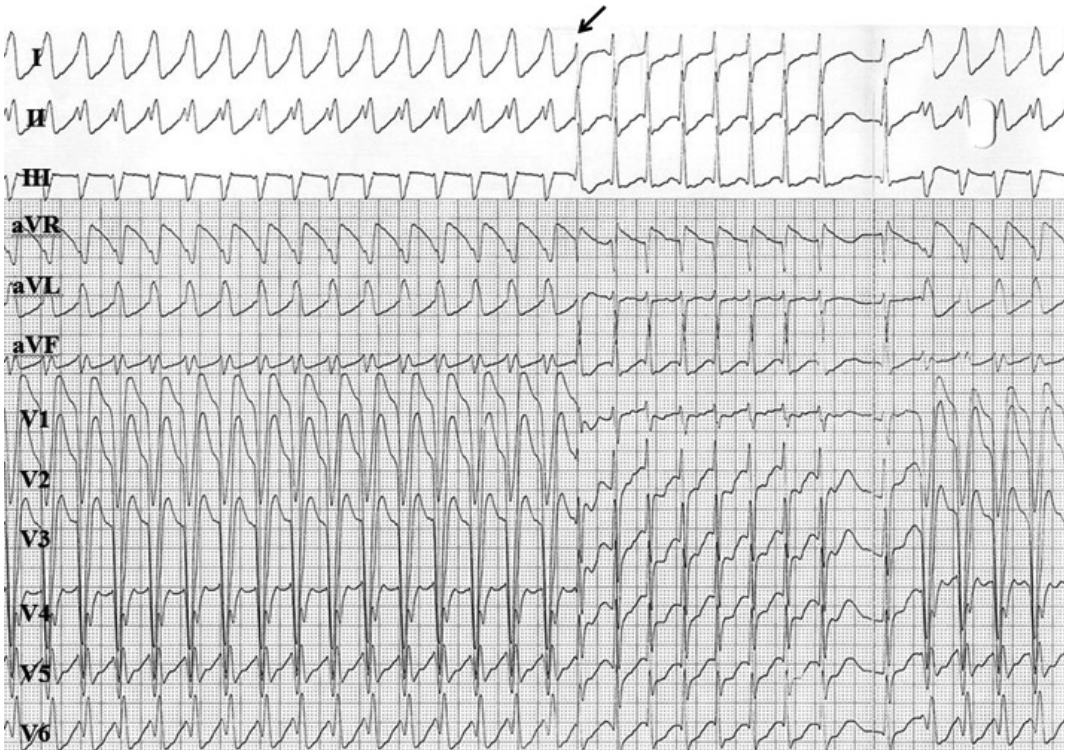

Fig. 3. The 12 lead electrocardiogram of tachycardia. The wide QRS tachycardia was changed to narrow QRS tachycardia (arrow). After the termination of narrow QRS tachycardia, wide QRS tachycardia started. ECG: electrocardiogram.

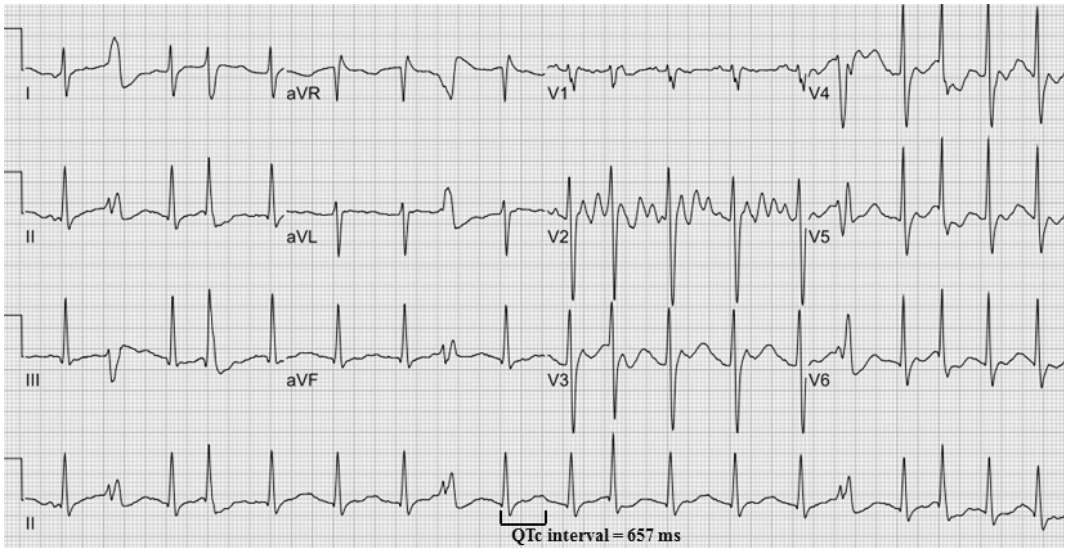

Fig. 4. The 12 lead ECG without wide QRS tachycardia. This ECG shows prolonged QT interval with prominent U wave. And some premature ventricular contractions are presented at the end of T wave, consistent with R on T phenomenon. ECG: electrocardiogram.

potential in skeletal and cardiac muscle, and contribute significantly to the most terminal repolarization phase of the cardiac action potential.[3] The KCNJ2 gene mutation alters potassium channels in such a way that it disrupts the flow of potassium ions in the skeletal and heart muscle. Periodic paralysis and cardiac arrhythmia is easily understood because of the contribution of Kir2.1 to membrane excitability in both tissues.[4]

The most possible mechanism for changes in QRS morphology, from wide to narrow and vice versa in this case (Fig. 3), is the alternation of two tachycardias, caused by increased automaticity from the atrioventricular junction and ventricular focus. Severe hypokalemia may induce cardiac arrhythmia by increasing the automaticity of cardiac tissues.[8,9] The irregular RR interval of tachycardia favors the increased automaticity as the mechanism, rather than re-

entry in this patient. Additionally, the tachycardia was the first episode, and was not observed after the correction of hypokalemia. The patient had no symptom, even during the follow up period of 2 years. Therefore, we did not perform the electrophysiologic study. The possibility of the transition from antridromic to orthodromic circus movement tachycardia is low, because the patient did not show delta wave. The possibility of Mahaim fiber is also low, because the patient showed narrow QRS tachycardia, even at almost the same cycle length of a wide QRS tachycardia.

Treatment of ATS is based upon symptoms, and there is no prospective, randomized therapeutic trial. This case has important implications because our patient's initial presentation was life-threatening, but it was well treated with potassium replacement and recurrence of periodic paralysis or other symptoms did not occur in two years follow up period. Thus, the proper diagnosis and regular follow up, close monitoring potassium levels is very important for the patient's outcome.

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