Long QT Syndrome Associated with Adrenal Insufficiency in a Patient with Isolated Adrenocorticotropic Hormone Deficiency

Kenta Kanamori, Risa Yamashita, Kenta Tsutsui, Masumi Hara and Yuji Murakawa

Abstract

QT prolongation and Torsades de Pointes were observed in a 44-year-old woman who had adrenal insufficiency caused by isolated adrenocorticotropic hormone deficiency. Although she had several risk factors for QT prolongation, we concluded that the adrenal insufficiency contributed to the QT prolongation, because the electrocardiographic changes were improved after steroid replacement therapy. It is known that the QT interval in a patient with adrenal insufficiency tends to be extended. However, reports on adrenal insufficiency in which the QT interval was sufficiently prolonged to cause Torsades de Pointes are rare. Clinicians should consider the possibility of adrenal insufficiency in patients with QT prolongation.

Key words: long QT syndrome, adrenal insufficiency, torsades de pointes, glucocorticoid

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Introduction

Long QT syndrome (LQTS), which is defined as a prolongation of the QT interval on electrocardiograms (ECG), occasionally results in ventricular arrhythmia, such as Torsades de Pointes (TdP). LQTS is classified into congenital LQTS and acquired LQTS.

Isolated adrenocorticotropic hormone (ACTH) deficiency causes secondary adrenal insufficiency. The clinical presentation of the disease includes fatigue, anorexia, low blood pressure, hyponatremia and hypoglycemia. Since these symptoms are nonspecific and manifest only when the physiological demand for adrenal hormones exceeds their production, clinicians often fail to diagnose the disease (1).

Although it is known that QT prolongation is sometimes observed in patients with adrenal insufficiency (2), reports on adrenal insufficiency in which the QT interval was sufficiently prolonged to cause TdP are rare. Moreover, the association between glucocorticoids and the QT interval is poorly understood.

We herein report a rare case of LQTS causing TdP that was associated with adrenal insufficiency in a patient with isolated ACTH deficiency.

Case Report

A 44-year-old previously healthy woman presented at our emergency department complaining of fatigue and nausea. Several minutes after arrival, she went into cardiac arrest. Cardiac monitoring showed polymorphic ventricular tachycardia known as TdP (Fig. 1). The TdP disappeared spontaneously a few minutes later before a defibrillator could be used. She was then admitted to the intensive care unit.

On admission, the ECG showed an inverted T wave and a prolonged QT interval (Fig. 2). The laboratory test results showed mild hypokalemia (3.4 mEq/L) and an elevated C-reactive protein level (11.22 mg/dL). The serum levels of other main electrolytes, such as sodium, calcium and magnesium, were within the normal range (136 mEq/L, 9.0 mg/dL and 2.3 mg/dL, respectively). Contrast-enhanced computed tomography of the chest and whole abdomen revealed only gallstones without cholecystitis. Transthoracic echocardiography revealed diffusely impaired left ventricular wall motion (ejection fraction 44%) and no valvular disorders. Coronary artery stenosis was not seen on angiography. An
Our patient experienced cardiac arrest after her arrival at the hospital. Cardiac monitoring showed polymorphic ventricular tachycardia known as Torsades de Pointes. The arrhythmia suspended spontaneously after a few minutes.

**Figure 1.** Our patient experienced cardiac arrest after her arrival at the hospital. Cardiac monitoring showed polymorphic ventricular tachycardia known as Torsades de Pointes. The arrhythmia suspended spontaneously after a few minutes.

**Figure 2.** An electrocardiogram recorded on admission. The QT interval was prolonged. The corrected QT interval (QTc) increased to 670 msec. Inverted T waves were shown in leads V₁, V₂, V₃ and V₅.

**Figure 3.** An electrocardiogram recorded after the initiation of steroid replacement therapy. The corrected QT interval (QTc) was restored to 540 msec. The inverted T waves were improving.

Our first diagnosis was myocarditis. Conservative treatment, including correcting the hypokalemia, was initiated. Her serum potassium level returned to normal (3.8 mEq/L) on the second day of hospitalization, and then remained in the normal range for the duration of her hospital stay. Although a fatal arrhythmia did not recur, the QT interval remained prolonged and she continued to complain of fatigue and nausea.

On the ninth day of hospitalization, the progression of hyponatremia and a hypoglycemic attack occurred (128 mEq/L and 66 mg/dL, respectively). We therefore suspected adrenal insufficiency and initiated steroid replacement therapy on the same day. Additional laboratory tests showed low baseline cortisol and ACTH levels. A combined stimulation test for corticotropin-releasing hormone (CRH), gonadotropin-releasing hormone and thyrotropin-releasing hormone showed a poor response to CRH stimulation. The other pituitary hormones responded well to their superordinate hormones (Table 1). The basal thyroid-stimulating hormone level was high because of primary hypothyroidism. Anti-thyroglobulin antibodies and anti-thyroid peroxidase antibodies were detected in high titers (272 IU/mL and 295 IU/mL respectively), which indicated autoimmune hypothyroidism. The response to continuous ACTH stimulation was normal, indicating isolated ACTH deficiency (Table 2).

After steroid replacement therapy, the patient’s symptoms disappeared completely, and the electrocardiographic changes were improved (Fig. 3). Echocardiography on the 12th day of hospitalization revealed normal left ventricular wall motion (ejection fraction 64%). The patient was discharged on the 24th day. Thyroid hormone replacement therapy was initiated in the outpatient department after she was discharged from the hospital.

**Table 1.** Combined CRH/GnRH/TRH Stimulation Test

<table>
<thead>
<tr>
<th></th>
<th>basal</th>
<th>30mins</th>
<th>60mins</th>
<th>90mins</th>
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<tbody>
<tr>
<td>ACTH(pg/mL)</td>
<td>20.9</td>
<td>26.8</td>
<td>21</td>
<td>-</td>
</tr>
<tr>
<td>Cortisol(µg/dL)</td>
<td>1.3</td>
<td>1.5</td>
<td>1.1</td>
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</tr>
<tr>
<td>FSH(mIU/mL)</td>
<td>5.35</td>
<td>-</td>
<td>9.63</td>
<td>11.6</td>
</tr>
<tr>
<td>LH(mIU/mL)</td>
<td>3.39</td>
<td>25.57</td>
<td>28.36</td>
<td>-</td>
</tr>
<tr>
<td>PRL(ng/mL)</td>
<td>20.5</td>
<td>133.9</td>
<td>77.67</td>
<td>-</td>
</tr>
<tr>
<td>TSH(µU/mL)</td>
<td>22.5</td>
<td>76.9</td>
<td>59.9</td>
<td>-</td>
</tr>
</tbody>
</table>


**Table 2.** Continuous ACTH Stimulation Test

<table>
<thead>
<tr>
<th>Cortisol in urine (µg/day)</th>
<th>basal</th>
<th>day2</th>
<th>day3</th>
<th>day4</th>
<th>day5</th>
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<tr>
<td>Serum cortisol (µg/dL)</td>
<td>0.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>19.2</td>
</tr>
</tbody>
</table>

ACTH: Adrenocorticotrophic hormone

The QT interval is the time from the start of depolarization to the end of repolarization of the cardiac cells. Ion channels and pumps play a significant role in this process. Genetic mutations that cause ion channel dysfunction have...
been revealed to cause congenital LQTS (3). TdP is often caused by LQTS. The arrhythmia begins with triggered activity that originates from early afterdepolarization (EAD) (4, 5). A reentrant mechanism is considered to contribute to sustaining TdP under circumstances in which a spatial dispersion of the duration of the action potential exists between cardiac cells (4, 6). Although TdP usually resolves spontaneously, as in our case, it sometimes progresses to ventricular fibrillation and sudden death (7).

Acquired LQTS can be caused by drugs, an electrolyte imbalance, bradycardia, intracranial events, cardiac disease and endocrine disorders (4, 8–10). It is known that the QT interval of patients with adrenal insufficiency tends to be extended (2), however the etiology is currently unclear. Takimoto et al. reported that glucocorticoid upregulated Kv1.5K+ channel gene expression in the ventricle of rat hearts. This report suggested that adrenal insufficiency prevented the slowly inactivating K+ current and prolonged the QT interval (11). On the other hand, Narayanan reported that glucocorticoid might play a role in the maintenance of the membrane Ca2+ transport function. Their finding suggested that calcium overload was involved in the prolonged QT interval in patients with a glucocorticoid deficiency (12).

In addition to adrenal insufficiency, our patient had other risk factors for LQTS, including myocarditis, hypothyroidism and hypokalemia. It is reasonable to suppose that the hypokalemia and hypothyroidism had little influence on the QT interval in our case, since correcting the hypokalemia had little effect on the QT interval, and the electrocardiographic changes were improved without the need for thyroid hormone replacement therapy. On the other hand, we could not deny the possibility that the myocarditis influenced the QT prolongation, because the patient’s ventricular wall motion on transthoracic echocardiography was revealed to be normal on the 12th day of hospitalization, when the QT interval was found to be improved. It was unclear whether the adrenal insufficiency or myocarditis was the main cause of the prolonged QT interval. However, we believe that the adrenal insufficiency contributed to the LQTS, because the electrocardiographic changes were improved after the initiation of steroid replacement therapy.

In conclusion, we would like to emphasize that the possibility of adrenal insufficiency should be considered in patients with QT prolongation, particularly when they have unexplained hypoglycemia and hyponatremia. Further studies are needed to clarify the etiology of acquired LQTS induced by adrenal insufficiency.

The authors state that they have no Conflict of Interest (COI).

References