Torsade de Pointes Associated with Recurrent Ampulla Cardiomyopathy in a Patient with Idiopathic ACTH Deficiency

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Abstract. We describe here a patient with torsade de pointes associated with recurrent ampulla cardiomyopathy, who was later proven to suffer from idiopathic ACTH deficiency. A 70-year-old man was admitted to our hospital for bacterial pneumonia. A cardiac examination performed on admission revealed ampulla cardiomyopathy, which improved spontaneously as the pneumonia was cured. Two months after discharge, he was transferred to our hospital for relapse of the pneumonia. After the second admission, the pneumonia subsided with antibiotic treatment and his general condition ameliorated gradually. However, on the 20th hospital day, he was found lying on the floor in a prone position in cardiopulmonary arrest. Cardiac telemetry monitoring showed torsade de pointes worsening to ventricular fibrillation, and immediate cardiac defibrillation was performed. The electrocardiogram after successful defibrillation showed inverted T waves in the chest leads with long QT intervals, and subsequent emergent coronary catheterization revealed the recurrence of ampulla cardiomyopathy. Thereafter, endocrinological examinations for the diagnosis of sustained hyponatremia demonstrated secondary adrenal insufficiency caused by idiopathic ACTH deficiency. The cardiomyopathy resolved promptly after steroid hormone replacement without relapse as did the hyponatremia. Patients with ampulla cardiomyopathy or ventricular fibrillation without apparent etiology should be examined for adrenal function. If begun as soon as adrenal insufficiency is diagnosed, immediate steroid replacement therapy can prevent the deterioration and relapse of cardiac involvement.

Key words: Torsade de pointes, Ampulla cardiomyopathy, Adrenal insufficiency, Idiopathic ACTH deficiency, Hyponatremia

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Case Report

A 70-year-old man was admitted on an emergency basis to the Pulmonary Division in July 2007, for bacterial pneumonia. He had a past medical history of bronchial asthma but received no routine medications including glucocorticoids, and underwent a total gastrectomy for gastric cancer at age sixty. An electrocardiogram obtained upon admission showed inverted T waves in leads II, III, aVL, and V1-V6 (Fig.1), although he had not complained of any chest symptoms. An echocardiogram revealed the left ventricular dysfunction with akinesis of the apex and hyperkinesis of the basal wall, suggesting ampulla cardiomyopathy. Consideration was given to the need for coronary angiography, but the patient refused. The pneumonia was cured by antibiotic treatment, and the follow-up electrocardiogram and echocardiogram during admission demonstrated a spontaneous recovery from the ampulla cardiomyopathy. He was discharged three weeks after admission.

Two months after discharge, he was transferred to our hospital again due to a relapse of bacterial pneumonia. On the second admission, he was awake and alert with a pulse of 80 beats per minute, blood pressure of 130/71 mmHg, and body temperature of 39.9°C. On physical examination, his height was 171.8 cm and he weighed 41.7 kg. His thyroid was not palpable, and a coarse crackle was audible in the left lower chest without no cardiac murmurs or gallops. There was a surgical wound in the abdomen, and he had normal pubic and axillary hair. No abnormal skin pigmentation was observed on his body. He complained of neither chest pain nor abdominal symptoms.

The results of laboratory examinations are shown in Table 1. Peripheral blood tests showed normocytic anemia, and slight increases in white blood cell counts with eosinophilia (10%). Electrolyte abnormalities and hypoglycemia were absent on biochemical analyses. The electrocardiogram showed a reappearance of inverted T waves in V1-V6 (Fig.1), although the disturbance in the left ventricular wall was not apparent on the echocardiogram.

While the pneumonia subsided immediately with antibiotic treatment, the eosinophilia and hyponatremia persisted post-admission (Fig.2). Despite a
suspected allergic reaction to antibiotics, eosinophilia continued even after the discontinuation of medication. On October 11th (the 20th hospital day), he was found lying on the floor in a prone position with cardio-pulmonary arrest. Telemetry electrocardiac monitoring showed torsade de pointes worsening to ventricular fibrillation (not recorded), and immediate cardiac defibrillation was performed with subsequent endotracheal intubation. Spontaneous respiration and cardiac rhythm were recognized after successful defibrillation. Because the electrocardiogram showed deep inverted T waves in the chest leads
He had not received any medications such as antibiotics, antiallergics or antiarrhythmic agents that might induce adverse effect of QT prolongation. He was transferred to intensive care unit and his general condition ameliorated rapidly; the following day he underwent extubation and the discontinuation of intravenous cathecholamines. He regained consciousness and was alert within a few days despite sustained hyponatremia. He was referred to our division with prolonged QT intervals (Fig. 3), urgent coronary catheterization was performed for a possible percutaneous intervention. However, the coronary angiography demonstrated only a non-significant coronary stenosis. Left ventriculography showed akinesis of the left ventricular apex with ballooning during systole (Fig. 4). Blood examination before resuscitation revealed the absence of elevated cardiac enzymes, hypoglycemia, or electrolyte abnormalities except for magnesium (not determined). He had not received any medications such as antibiotics, antiallergics or antiarrhythmic agents that might induce adverse effect of QT prolongation. He was transferred to intensive care unit and his general condition ameliorated rapidly; the following day he underwent extubation and the discontinuation of intravenous cathecholamines. He regained consciousness and was alert within a few days despite sustained hyponatremia. He was referred to our division.
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with GRh (100μg), TRh (100μg), and LhRh (100μg) revealed decreased and delayed response of GH, with almost normal responses of Lh, FSh, TSh and prolactin. Evaluation of the hypothalamic-pituitary-adrenal (HPA) axis showed blunted response of ACTH and cortisol to exogenous cRh (100μg) as well as even after continuous cRh loading (100μg daily for five days), and a markedly decreased response of cortisol: maximum stimulated serum level of 1.2µg/dL to...
exogenous ACTH (250μg). An insulin tolerance test was not performed due to the possibility of severe cardiac involvement. Magnetic resonance imaging of the brain revealed empty sella (Fig. 6).

Given these characteristic endocrinological and imaging findings, we made a diagnosis of secondary adrenal insufficiency caused by idiopathic ACTH deficiency, complicated with impaired GH secretion probably attributable to prolonged hypocortisolism, which has been known to reduce GH responsiveness to several stimuli including GHRH [6]. He was placed on a maintenance regimen of physiological steroid replacement therapy (15mg hydrocortisone daily). The hyponatremia and eosinophilia disappeared promptly after the initiation of replacement therapy (Fig. 2), as did the electrocardiogram and echocardiogram findings of ampulla cardiomyopathy (Fig. 7). At one year after the initiation of steroid replacement therapy, there had been no recurrence of pneumonia, and the patient showed weight gain and a resolution of anemia. He remained free of arrhythmia with normal electrogram and echocardiogram findings. The plas-
Ampulla cardiomyopathy is characterized by transient cardiac dysfunction: akinesia of the apex with systolic ballooning, usually occurring after emotional, psychological, or physical stress. The condition is often misdiagnosed as an acute myocardial infarction due to its similar electrocardiogram findings and chest pain. Several pathogenic mechanisms have been suggested, such as coronary microvascular dysfunction, multivessel coronary vasospasm [7], and catecholamine-mediated cardiotoxicity [8]. However, the precise etiology of this reversible cardiomyopathy remains uncertain.

This cardiomyopathy is commonly regarded as showing a substantial female bias, and the condition generally resolved within a few days to a few weeks without relapse and the development of severe complications (pulmonary edema, cardiogenic shock, or ventricular fibrillation) is rare [9]. The previous literature describes the incidence of relapse as 11.4% [10], while ventricular fibrillation occurs in about 9% of cases [11]. Therefore, this case of a male showing recurrence with ventricular fibrillation is considered to be very rare, probably because the ampulla cardiomyopathy was provoked by adrenal insufficiency in our patient.

There are a small numbers of previous reports that mention ampulla cardiomyopathy secondary to adrenal insufficiency that resolved promptly after physiological steroid replacement therapy [4, 5]. However, it remains unclear in our case whether steroid replacement therapy contributed to recovery in the ampulla cardiomyopathy, since the initial cardiomyopathy resolved spontaneously without replacement. From those previous reports it can be inferred that glucocorticoid deficiency induced reversible cardiomyopathy through hypoglycemia or hyponatremia, followed by a functional disturbance of the cardiac membrane sodium-calcium pumps, although those abnormal laboratory findings were absent at the onset in our case. In terms of hormones, it has been suggested that overt catecholamine production, which is partially regulated by glucocorticoids, induces transient cardiac damage resulting in ampulla cardiomyopathy as shown in pheochromocytoma [12]. In addition, glucocorticoids are considered to play an important role in protecting myocytes from cardiac damage such as infarction, and in maintaining the contraction function of cardiomyocytes [13].

Rarely, ampulla cardiomyopathy is complicated by ventricular fibrillation as mentioned above, presumably provoked by QT prolongation secondary to a deep inverted T wave. Several case reports [14-18] attribute the involvement of torsade de pointes associated with QT prolongation similar to our case, but the incidence of severe arrhythmia is described as very low in comparison with that of QT prolongation [15, 16]. A few reports refer to torsade de pointes secondary to ampulla cardiomyopathy in patients who were later found to suffer from congenital long-QT syndrome [19] or cardiac hypertrophy [20] as pre-existing diseases. Therefore, there is a possibility of unknown factors contributing to the onset of arrhythmia.

Interestingly, adrenal insufficiency itself has been said to cause also abnormal electrocardiogram findings including QT prolongation and deep inverted T waves without apparent dysfunction of the cardiac wall, rarely resulting in ventricular fibrillation [21]. Walter et al first reported adrenal insufficiency producing various abnormal changes in the electrocardiogram: ST depression, inverted T waves and long QT intervals [22]. These alterations are considered to be associated with cellular overhydration [23] or a mineral imbalance between the intra and extra capillaries [24]. Hypomagnesemia is referred to in a previous case report of QT prolongation caused by adrenal insufficiency [25], while a second case, like our patient, showed normal level of serum magnesium. Thus, although the precise mechanism remains to be elucidated, adrenal insufficiency in the present case might have induced ventricular fibrillation either directly or through the onset of ampulla cardiomyopathy. Indeed, patients with adrenal insufficiency, who show torsade de pointes with reversible cardiomyopathy, have been described in a few previous reports [26, 27].

In summary, the present case of a patient suffering from torsade de pointes who developed ventricular fibrillation with short-term recurrent ampulla cardiomyopathy, was subsequently diagnosed with adrenal insufficiency secondary to a diagnosis of hyponatremia. The cardiomyopathy resolved immediately after the start of steroid replacement therapy with no subsequent relapse: therefore, the cardiac dysfunction is considered to have been secondary to adrenal insuffi-
ciency. Ampulla cardiomyopathy is generally referred to improve spontaneously without any treatment, but rarely is complicated by ventricular fibrillation such as in our case. In addition, adrenal insufficiency itself also can induce ventricular fibrillation with or without cardiomyopathy. Therefore, patients with ampulla cardiomyopathy or ventricular fibrillation with no apparent etiology should be examined for adrenal function. In that way, immediate steroid replacement therapy can prevent the deterioration and relapse of cardiac involve-
ments as soon as adrenal insufficiency is diagnosed.

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References


