□ CASE REPORT □

Neurogenic Stunned Myocardium Associated with Status Epileptics and Postictal Catecholamine Surge

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Abstract

A 75-year-old woman developed left ventricular apical ballooning, shortly after recovering from status epileptics. Plasma noradrenaline and adrenaline levels were 2.05 ng/ml and 0.48 ng/ml, respectively. Endomyocardial biopsy disclosed patchy areas of interstitial myocardial fibrosis, atrophy and vacuolization of cardiac myocytes, and some disappearance of myocyte nuclei. Follow-up echocardiography showed that the left ventricular apical ballooning was restored to normal within 25 days. These findings are compatible with neurogenic stunned myocardium. It is important to recognize that patients suffering from intractable seizures may harbor a risk of postictal catecholamine surge and catecholamine-induced myocardial dysfunction.

Key words: neurogenic stunned myocardium, epilepsy, takotsubo cardiomyopathy, catecholamine, sudden unexpected death in epilepsy (SUDEP)

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Introduction

Neurogenic stunned myocardium is reversible myocardial dysfunction associated with neurological disorders such as subarachnoid hemorrhage, Guillain-Barré syndrome, and metastatic brain tumors (1-3). The electrocardiographic abnormalities of neurogenic stunned myocardium resemble those of acute myocardial infarction, but the enzyme elevations are mild. Echocardiography or left ventriculography typically shows left ventricular apical ballooning, which is inconsistent with coronary artery disease. The wall motion abnormality returns to normal within a few weeks. The mechanism of neurogenic stunned myocardium is believed to be due primarily to increased sympathetic activities. We present a case of neurogenic stunned myocardium associated with intractable epileptic seizures and postictal catecholamine surge.

Case Report

A 75-year-old woman was found unconscious with convulsions by her family member in her kitchen. She was taken by ambulance and admitted to the intensive care unit

because of status epilepticus. She began to suffer grand mal epilepsy when she was 20 years old. She had been treated with antiepileptic drugs including valproate 200 mg, phenytoin 200 mg, and diazepam 15 mg. She had remained free from epileptic attacks during the preceding 10 years. She had also been affected with short-term memory impairment for about 30 years.

On arrival, her heart rate was 125 beats/min, and blood pressure was 154/90 mmHg. Because intramuscular administration of diazepam did not relieve repetitive tonic-clonic seizures, continuous intravenous propofol infusion was subsequently administered. The intractable seizures were terminated by 2 hours after admission; however, her systolic blood pressure fell to 80 mmHg. ST-segment elevation in the monitor lead prompted us to obtain 12-lead electrocardiogram, which disclosed ST segment elevations in leads II, III, aVF, and V 2-5 (Fig. 1A). Laboratory findings revealed a white blood cell count of 10,000/mm³ and a positive qualitative troponin T test. Cardiac enzymes remained within normal limits. A chest X-ray film showed no cardiomegaly along with clear lung fields. Echocardiography demonstrated abnormal left ventricular wall motion with apical ballooning and basal hyperkinesis (Fig. 2A). A low dose intravenous nitroglycerin infusion was started. She remained moderately

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Figure 1. A: Initial electrocardiogram showing ST-segment elevations in leads II, III, aVF, and V2-5. B: Serial electrocardiogram showing giant negative T-waves in leads II, III, aVF, and V3-6.

Figure 2. A: Initial echocardiogram demonstrating left ventricular apical ballooning and basal hyperkinesis. B: Follow-up echocardiogram indicating that the left ventricular apical ballooning was restored to normal.

hypotensive, but catecholamine support was not applied because urinary output was well maintained. The propofol infusion was discontinued on the following day, and the patient recovered from unconsciousness. Plasma noradrenaline and adrenaline levels were 2.05 ng/ml and 0.48 ng/ml, respectively immediately after the onset of left ventricular dysfunction. While a 24-hour urinary excretions of noradrenaline and adrenaline were 408 µg and 59.4 µg. Maximum levels of creatine kinase and its MB isozyme were 2,871 U/L and 95 U/L, being observed 22 hours after the onset.

Cardiac catheterization studies were performed on the 12th hospital day. The left ventricular apical ballooning was still evident on left ventriculogram (Fig. 3). Coronary angiography showed normal left coronary arteries and a hypoplastic right coronary artery. Acetylcholine provocation test induced diffuse spasm in the left anterior descending and circumflex coronary arteries (Fig. 4). Endomyocardial biopsy specimens were obtained from the right ventricular

septum. Microscopic findings disclosed patchy areas of interstitial myocardial fibrosis, atrophy and vacuolization of cardiac myocytes, and some disappearance of myocyte nuclei (Fig. 5). ¹²³I- Metaiodobenzylguanidine (MIBG) myocardial scintigram showed decreased accumulation and increased washout in left ventricular apex indicating increased sympathetic activities. Serial electrocardiograms revealed giant negative T-waves in leads II, III, aVF and V3-6 (Fig. 1B). Follow-up echocardiographic examinations demonstrated that the left ventricular apical ballooning was restored to normal within four weeks (Fig. 2B). In accordance with the normalization of left ventricular apical wall motion, the patient gradually recovered from the hypotensive state. She received valproate 1,200 mg per day along with benizipine 4 mg and nicorandil 30 mg per day. She was discharged 27 days after admission, and no recurrence of epilepsy or left ventricular dysfunction was observed afterwards.

Figure 3. Left ventriculogram showing that the left ventricular apical ballooning was still evident on the 12th hospital day.

Figure 4. Coronary angiogram showing normal left coronary arteries (left) and diffuse spasm in the left anterior descending and circumflex coronary arteries induced by acetylcholine provocation test (right). The right coronary artery was hypoplastic.

Discussion

Epileptic seizures have not attracted attention as a triggering cause of neurogenic stunned myocardium (4). The present case demonstrated left ventricular apical ballooning shortly after intractable tonic-clonic seizures. Electrocardiogram revealed extensive ST-segment elevations at the occurrence, and the wall motion abnormality was inconsistent with coronary anatomy. The left ventricular apical ballooning restored to normal within four weeks. These findings are compatible with neurogenic stunned myocardium. Some specific conditions could explain the difficulties of recognizing postictal myocardial dysfunction. The postictal patients are usually unable to complain of chest discomfort because of prolonged disturbance of consciousness. A raised creatine kinase is not helpful, because it may merely reflect skeletal

muscle injury. Although electromyogram artifacts are induced by epileptic seizures, ST-segment elevation on electrocardiogram is an important clue to the diagnosis of neurogenic stunned myocardium. The present case suggests that electrocardiographic monitoring is mandatory, especially in a patient suffering from intractable seizures.

Catecholamine surge has been shown to occur following status epilepticus (5). Simon et al demonstrated that plasma noradrenaline and adrenaline rise sharply within 30 minutes of the seizure and then decline rapidly (6). The noradrenaline response was attributed to generalized sympathetic neural activation, and the adrenaline response was presumed to be due to adrenal activation. A substantial increase in plasma catecholamine levels was also demonstrated in the present case shortly after intractable seizures, the timing of which closely coincided with the development of left ventricular apical ballooning. The transient increase in sympa-

Figure 5. Microscopic findings of endomyocardial biopsy disclosing patchy areas of interstitial myocardial fibrosis, atrophy and vacuolization of cardiac myocytes, and some disappearance of myocyte nuclei.

thetic nervous activity plays an important role in the pathogenesis of neurogenic stunned myocardium. Markedly elevated levels of catecholamines have been noted in patients with SAH or Guillain-Barré syndrome complicating neurogenic stunned myocardium (1, 2). The mechanisms of catecholamine induced myocardial injury include cyclic AMP-mediated calcium overload, oxygen-derived free radicals, and microvascular coronary spasm (7, 8). Both calcium overload and free radicals are associated with decreased responsiveness of contractile filaments to calcium. Furthermore, vasoconstriction of peripheral arteries by catecholamines may further aggravate afterload mismatch. We believe that the elevated plasma catecholamine levels associated with epileptic seizures resulted in the left ventricular apical ballooning in the present case.

Transient left ventricular apical ballooning with basal hyperkinesis is also a distinctive feature of takotsubo cardiomyopathy (9). Other than the left ventricular wall motion abnormality, there are substantial similarities in the clinical presentation between neurogenic stunned myocardium and takotsubo cardiomyopathy. Catecholamine excess triggered by emotional or physical stress is also proposed as a major underlying mechanism in the pathogenesis of takotsubo cardiomyopathy. A systematic review has shown that noradrenaline concentration was elevated in 74.3% of the patients with takotsubo cardiomyopathy (10). The microscopic find-

ings in the present case, such as interstitial myocardial fibrosis, myocyte vacuolization and loss of myocyte nuclei, are comparable to takotsubo cardiomyopathy (11). Some previous reports have recognized that epilepsy was a triggering condition for takotsubo cardiomyopathy (12, 13). Takotsubo cardiomyopathy is characterized by its morphological appearance, whereas neurogenic stunned myocardium is defined by its neurologic etiology. It is not too much to say that these two disorders contain the same pathological conditions of catecholamine cardiotoxicity, as they are merely viewed from a different aspect.

Neurogenic stunned myocardium could be related to sudden unexpected death in epilepsy (SUDEP), which is one of the most important problems in epilepsy patients (14). The incidence of SUDEP has been estimated to be 0.35-9.3/1,000 person-years, and the rate of SUDEP was found to be 23.7 times that of the general population. The risk factors of SUDEP are young age, early onset of seizures, the presence of generalized tonic-clonic seizures, male sex and being in bed. The mechanism of SUDEP is not fully understood. Potential pathological mechanisms include cardiac arrhythmia, myocardial ischemia, dysfunction of autonomic nervous system to the heart, and central or obstructive apnea (14). The microscopic findings of hearts in the SUDEP cases comprise patchy areas of interstitial myocardial fibrosis, myocyte vacuolization, atrophy of cardiomyocytes, leukocytic infiltration, and perivascular fibrosis (15, 16). Some of them were also found in the present case. These lesions are compatible with catecholamine-related myocardial injury, and may be relevant to the phenomenon of SUDEP. For instance, myocardial fibrosis has been implicated as a cause of late lethal arrhythmias (17). Electrocardiographic abnormalities including ST-T changes are not unusual, especially in generalized seizures, but myocardial dysfunction relevant to these changes remains unknown (18). Most of the patients with neurogenic stunned myocardium have a favorable prognosis and rarely experience its recurrence. However, unlike other underlying neurologic disorders, epileptic patients may be repeatedly exposed to catecholamine surge following each seizure episode. Therefore, it is important to recognize that epileptic patients may harbor a risk of postictal catecholamine surge and catecholamine-induced myocardial dysfunction.

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