

**LETTER TO THE EDITOR****To the Editor****Tit for Tat Brain versus Heart: A Case of Status Epilepticus, Cardiomyopathy, and Stroke**

Death from fright was first described in 1942 by Walter B. Cannon.<sup>1</sup> A modern understanding of this phenomenon is based in the fact that the heart and other viscera function in an interdependent manner. Excessive stress experienced by the nervous system exerts an unusual influence over the function of other viscera causing neurovisceral injury.<sup>1</sup> “Cerebral T waves,” which were originally thought to be artifactual in nature, are known to represent neurovisceral injury and a true alteration in cardiac function.<sup>1</sup> The principal cardiac manifestations seen secondary to acute neurological injury are electrocardiogram (ECG) abnormalities, cardiac arrhythmias, and neurogenic cardiomyopathy. These occur on a continuum and share a common pathophysiology. We report a case of neurological insult resulting from status epilepticus (SE) associated with an acute cardiomyopathy, which culminated in a devastating left middle cerebral artery cardioembolic stroke.

A 46-year-old right-handed woman with a history of bilateral temporal lobe epilepsy presented to a peripheral hospital with SE (discrete seizures without return of consciousness in between and lasting >30 minutes) and no cardiovascular risk factors. There had been a recent interruption in the dosing of her antiepileptic medication (lacosamide 300 mg/day) and the seizures abated with reintroduction of lacosamide. After resolution of SE, the patient was alert, obeyed commands, and moved all four extremities normally without any abnormalities on neurological examination. On day 3, the patient developed tachycardia, agitation, and hypoxemia requiring intubation. Chest radiograph showed diffuse bilateral infiltrates. Rhabdomyolysis was evident with creatine kinase 30,000 IU/L and oliguric acute kidney injury (creatinine, 400 µmol/L). Computed tomography of the brain was normal. An ECG showed new-onset left bundle branch block. Transthoracic echocardiography (TTE) showed mild dilation of the left ventricle, severely reduced left ventricular (LV) systolic function (LV ejection fraction 20%) with akinesis of the septum, anterior wall, and lateral wall. The wall motion abnormalities extended beyond a single coronary arterial territory.

On day 4, the patient was transferred to our hospital. On arrival, the patient was mechanically ventilated with stable vital signs. Neurological examination demonstrated a new inability to obey commands despite appearing alert, a right visual field deficit, a right-sided hemiplegia, and an extensor plantar response on the right side. Creatine kinase was 10,000 IU/L and troponin-T was 569 µg/L. An ECG showed nonspecific T-wave abnormalities and prolonged QT interval. A repeat TTE showed persistent functional and structural abnormalities (Figure 1). Coronary angiography was normal with no occlusive disease. An electroencephalogram demonstrated an asymmetry of cerebral potentials with lower voltage and increased delta activity over the left hemisphere, suggestive of a structural abnormality. There were no epileptiform discharges. Magnetic resonance imaging of the brain

demonstrated a large acute and complete left middle cerebral artery territory infarct. There was no evidence of carotid stenosis or other abnormality of the anterior circulation. The patient was managed with aspirin, bisoprolol, and ramipril.

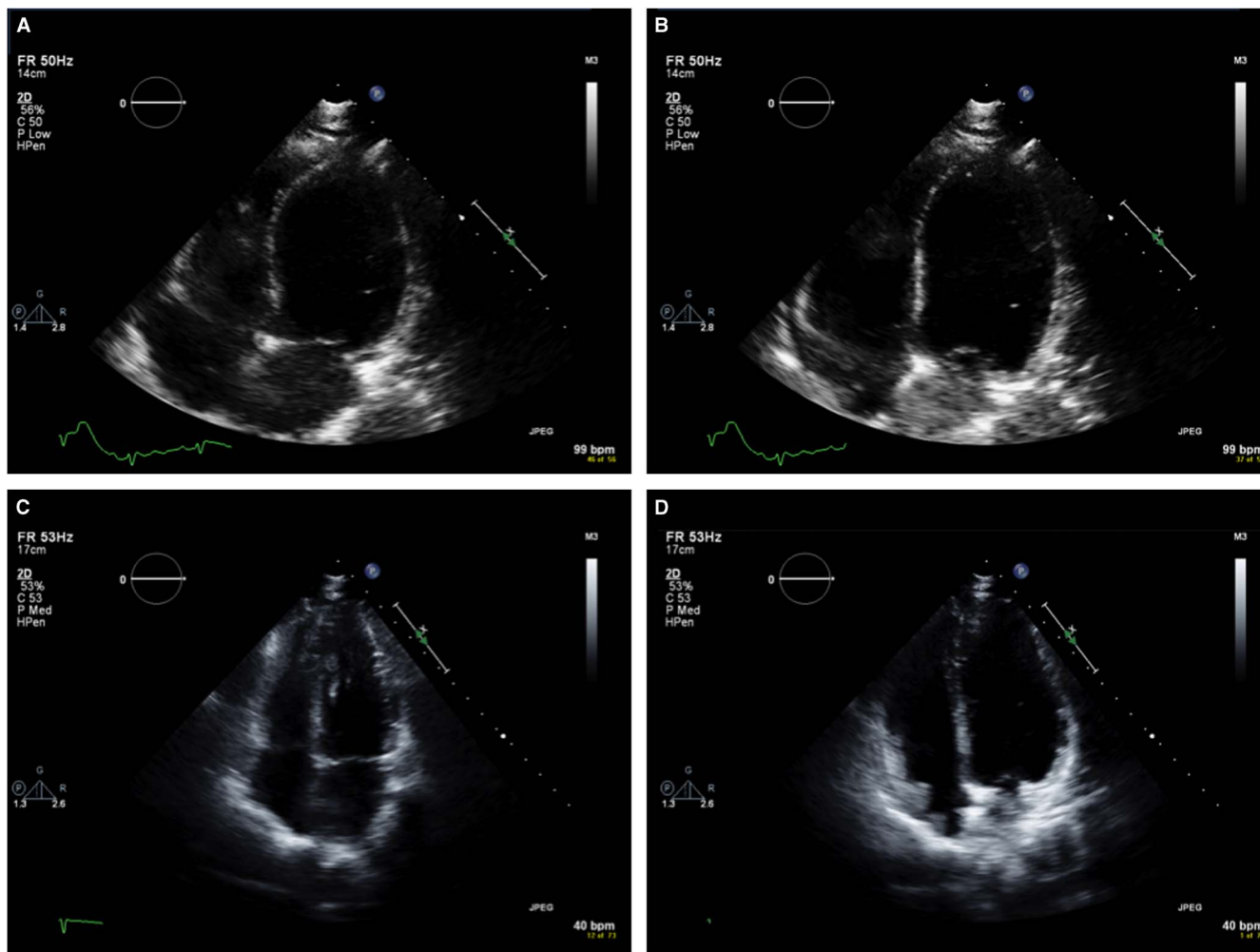
The patient has persistent aphasia, a right homonymous hemianopsia, right hemiplegia, and right hemianesthesia. The acute kidney injury resolved and cardiac status also improved. A repeat TTE 3 months later revealed normal wall motion (Figure 1C, D).

In this case, the precipitating event for cardiac dysfunction was believed to be SE. The patient fulfilled the Mayo Clinic diagnostic criteria for neurogenic/takotsubo cardiomyopathy:<sup>2</sup> transient akinesis or dyskinesis of LV mid-segments with or without apical involvement; regional wall motion abnormalities extending beyond a single epicardial vascular distribution; and associated new ST-segment or T-wave abnormalities on ECG or elevated cardiac troponins, mimicking acute myocardial infarction, with absence of obstructive coronary disease or evidence of plaque rupture on coronary angiography. The patient’s stroke was likely a consequence of embolization of a LV thrombus generated during the acute event of global cardiac dysfunction. The intracardiac thrombus was not visualized because it had either completely embolized or because the TTE had insufficient sensitivity for detection of a small ventricular thrombus. Coronary angiography was normal, and wall motion abnormalities on echocardiography resolved over time. An alternative explanation for the etiology of cardiomyopathy could be that it occurred in response to the stroke. However, evidence of cardiac dysfunction before the onset of neurologic deficits and absence of preexisting stroke risk factors supports the theory of stress-induced cardiomyopathy preceding and indeed being responsible for the stroke.

Neurogenic cardiomyopathy has been reported with various psychological and physical stressors.<sup>3</sup> Precipitants include subarachnoid hemorrhage, ischemic stroke, transient ischemic attacks, intracerebral hemorrhage, traumatic brain injury, and seizures or status epilepticus; with rare case reports associated with less common neurological illnesses. Neurogenic cardiomyopathy associated with generalized seizures or SE are increasingly being recognized and it is thought that it may play a role in sudden unexpected death in epilepsy.

Neurogenic cardiomyopathy leading to cardioembolic stroke has been reported rarely. In two recent reviews of seizure-associated neurogenic cardiomyopathy, there were only two cases reported in which epilepsy was associated with a subsequent stroke.<sup>3-5</sup> Few case reports exist that describe cerebrovascular thromboembolization secondary to neurogenic cardiomyopathy precipitated by SE.

LV thrombus formation has been reported in approximately 2.5% of all patients with documented takotsubo syndrome, with cardioembolic complications occurring in fewer than 1%.<sup>5</sup> Reported embolic events include peripheral embolizations (renal artery embolism, popliteal artery embolization, stroke). Few cases of LV apical thrombus in the setting of neurogenic cardiomyopathy caused by seizures have been reported<sup>6</sup>; neither of these resulted in cardioembolic stroke. Case reports have concluded that neurogenic/takotsubo cardiomyopathy could be both the cause and effect of stroke. The “chicken or egg” question regarding



**Figure 1:** Transthoracic echocardiogram at the time of the acute stroke presentation. (A, B) Diastole systole during acute hospitalization. The images demonstrate mild dilation of the left ventricle with severely reduced left ventricular systolic function and severe global hypokinesia of the left ventricle. There are multisegmental wall motion abnormalities, with relative preservation of the basal lateral and apical segments. (C, D) Normal wall motion during diastole and systole 3 months after discharge.

etiology is difficult to resolve. In this case, there was clear evidence of cardiac abnormality, consistent with the Mayo Clinic diagnostic criteria<sup>2</sup> for neurogenic/takotsubo cardiomyopathy after resolution of SE, with normal neurological status before the onset of stroke.

Although animal and human data are suggestive of cerebral lateralization and a cortical representation of cardiac function, the so-called “cardunculus”—the neuroanatomic pathways for cardiac control, are poorly understood. Catecholamine excess may play a role; inducing calcium channel activation, cell membrane damage, and coronary vasospasm that lead to myocardial stunning.<sup>3</sup> Temporal lobe epilepsy may cause autonomic function and neurogenic cardiomyopathy<sup>4</sup> because of the influence of the nearby insular cortex. Whether significant laterality exists and which side modulates parasympathetic versus sympathetic function is less clear. In this case, we postulate that the seizures led to excessive excitation of the insular cortex, leading to a surge in autonomic activity.

In some institutions, the practice is to treat with anticoagulation once an LV thrombus or a low ejection fraction has been

identified.<sup>7</sup> There is little evidence base to support this, likely because of the rare occurrence of neurogenic cardiomyopathy. In this case, it is unlikely that anticoagulation would have prevented the stroke, because the ventricular dysfunction was not identified until after the stroke had occurred.

We describe a case in which a “tit-for-tat” strategy of heart and brain seems evident: SE led to excessive excitation of the autonomic nervous system causing a neurogenic cardiomyopathy with LV hypokinesia, which in turn resulted in a cardioembolic stroke. Once the diagnosis of neurogenic cardiomyopathy is suspected or diagnosed, it is important to look for LV thrombus formation. Identification of an LV thrombus may help to prevent the potentially devastating consequences of stroke or other systemic embolization.

#### DISCLOSURES

SSB and PR have no disclosures to report. PT has been a speaker for, tutored as a health expert for, and received honoraria from AstraZeneca, and has lectured, participated in sponsored

programs, taught, researched, and received honoraria from Metronic. TG has served as an examining neurologist for the SURTAVI study and received honoraria from Metronic.

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