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Case Study

Hyperperfusion of amygdala contributing to Takotsubo syndrome in a case of lacunar stroke: CNS scintigraphic evidences

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ABSTRACT

The largely well-known causes of Takotsubo syndrome highly associated with brain disorders are seizure, infection-related encephalitis/meningitis, migraine, head injury, metastatic brain tumors, and stroke, such as brain infarction, subdural hematoma, and subarachnoid hemorrhage. Takotsubo syndrome is characterized by varying short systolic/diastolic wall-motion impairment, e.g. apical ballooning, in the left ventricle. Amygdala has also been confirmed as an indirect cause of Takotsubo syndrome. Findings of single photon emission tomography with hyperperfusion of amygdala after stroke associated with Takotsubo syndrome have not been previously reported. We herein report an unusual case of Takotsubo syndrome correlated with obvious hyperperfusion in the bilateral amygdalae due to prior stroke was assessed with brain perfusion scintigraphy is described.

Keywords: Takotsubo syndrome, Hyperperfusion, Brain lesion, Amygdala, Limbic system, Scintigraphic rehabilitation

Background

Takotsubo syndrome, also called Takotsubo cardiomyopathy, is characterized by temporary systolic/diastolic left ventricular disfunction with varying wall-motion defects, including left ventricular apical ballooning [1]. The condition is often initiated by emotional and/or physical stimuli and shows electrocardiographic changes without coronary artery disease, even predominantly affects elderly women, but improves within weeks in most cases [2]. Most patients with Takotsubo syndrome improve in a few weeks, except some patients with poor outcomes due to a severe cardiac event, such as cardiac rupture [3]. Differential diagnosis with acute myocardial infarction should be careful [4].

Disorders of central nervous system diseases are common generators of Takotsubo syndrome [5]. A lot of neurological disorders, such as brain infarction, subdural hematoma, subarachnoid hemorrhage, and metastatic brain tumors, have been associated with Takotsubo syndrome [6-10]. Amygdala has also been reported as a cause of Takotsubo syndrome [11-13].

Brain nuclear scintigraphy with findings of hyperperfusion of amygdala after stroke associated with Takotsubo syndrome has not been previously reported. Here we report an unusual case of Takotsubo syndrome associated with hyperfunction of the amygdala due to prior stroke.

Case presentation

A 68-year-old man presented to our outpatient clinics with apathy. He showed with easy dizziness and weakness of left lower limb secondary to prior minor stroke 1 year ago. He was independent in his daily life and had hypertension, type 2 diabetes mellitus, dyslipidemia, or coronary artery disease in the past years. He suffered from lacunar stroke 1 year ago, and diagnosis of Takotsubo syndrome was made 6 months ago, based on the ventriculography findings of left ventricle with akinesia in the middle part and hyperkinesia in the apical/basal parts. His family history was unremarkable. His sister reported poor emotional control with his manners, for instance, if the rehabilitation vehicle arrives even slightly late, he will keep muttering. He often scolds others for well-intentioned reminders. His memory is disordered. He sometimes cries, and laments why he did not die sooner. He just wants to stay at home and doesn't want to go out, indicating early stage of dementia. Neural examinations showed instant recall loss with better long-term memory maintenance with MMSE score 23. He showed no symptoms of motor or sensory functions.

Brain computed tomography showed old lacunar infarcts in basal ganglia (Fig. 1). The Tc-99m ethyl cysteinate dimer (Tc-99m ECD) single photon emission computed tomography (SPECT) disclosed peculiar hyperperfusion in bilateral amygdalae (Fig. 2). Three-D stereotactic surface projections [14] of the ECD-SPECT images, in which the regional cerebral blood flow of the patient was compared to those of the control database using the z -test, obviously revealed hypoperfusion in bilateral anterior cingulate cortex and prefrontal cortex (ACC/PFC) (Fig. 3). The results of the ensuing tests of blood items were all within normal limit: leukocyte count, erythrocyte sedimentation rate, hs C-reactive protein, anti-nuclear

antibody, anti-ds-DNA, SS-A, rheumatoid factor, anti-streptolysin O titer and human leukocyte antigen-B27.

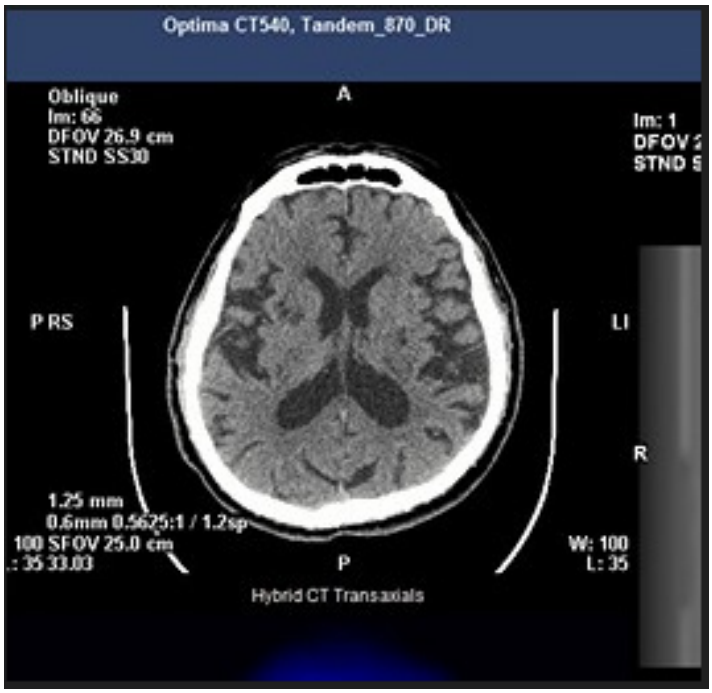

Figure 1. Brain computed tomography showed old lacunar infarcts in basal ganglia.

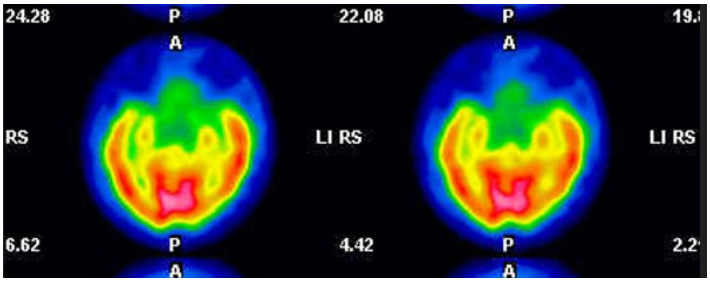

Figure 2. ECD single photon emission computed tomography (ECD-SPECT) of this patient. discloses peculiar hyperperfusion in bilateral. SPECT findings showing the abnormal bilateral hyperperfusion of the amygdalae.

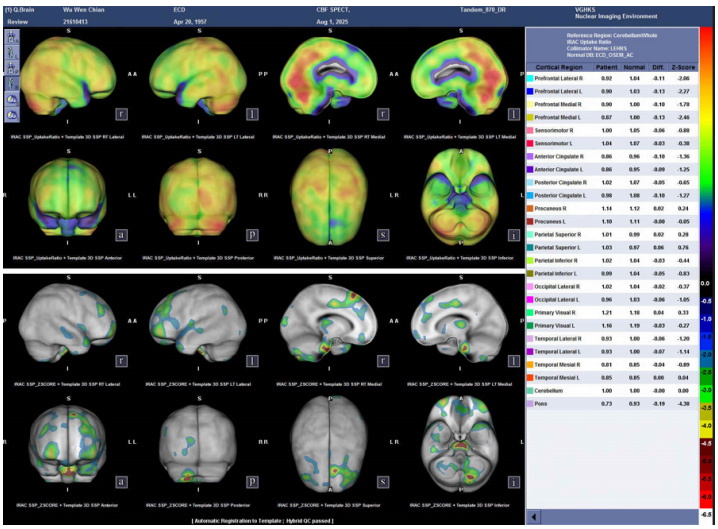

Figure 3. 3D stereotactic surface projections of the ECD-SPECT images, in which the regional cerebral blood flow of the patient was compared to those of the control database using the z -test, obviously revealed hypoperfusion in bilateral anterior cingulate cortex and bilateral prefrontal cortex, and left posterior cingulate cortex, as well as pons. Significant difference is made if Z-score ≤ -1.25.

Discussion and conclusions

A patient with Takotsubo syndrome showing obvious hyperperfusion in the bilateral amygdalae due to prior stroke was assessed with SPECT is described. Based on the present findings and past medical information, including disorientation of place and vulnerable emotion implied that Takotsubo syndrome may have been initiated by increased activity of amygdala. This is the first case of Takotsubo syndrome probably initiated by hyperactivity of amygdala after a prior stroke.

The largely well-known causes of Takotsubo syndrome highly associated with brain disorders are seizure, infection-related encephalitis/meningitis, migraine, head injury, metastatic brain tumors, and stroke, such as brain infarction, subdural hematoma, and subarachnoid hemorrhage [5,15]. Those with Takotsubo syndrome responsible for brain disorders have discouraging prognosis, whereas those with Takotsubo syndrome related to emotional stress only appeared the most encouraging outcome [16-18]. Hence, it is clinically worthy to justify if pathologies of the limbic system actually bring out cause Takotsubo syndrome. If head MRI showed no acute brain pathology, cerebral perfusion SPECT can show hyperperfusion in the left temporal cortex instead [11]. Brain scintigraphy elucidates the issue precisely [19,20].

Regarding the SPECT survey, brain activity has been shown to be altered in Takotsubo syndrome [12]. A prior study has mentioned that patients with limbic encephalitis show abnormal hyperperfusion in associated areas on SPECT, which corresponds to hyperintense corresponding lesions on images of MR [21]. A recent report showed an unusual case of Takotsubo syndrome secondary to autoimmune limbic encephalitis [13]. Our patient also revealed hyperperfusion in the bilateral amygdalae on SPECT (Fig. 2), which findings were highly evocative of Takotsubo syndrome indirectly caused by prior minor stroke for our case.

Overexerting stimulation of sympathetic function has been hypothesized as the fundamental source of Takotsubo syndrome [22]. The limbic interneural network, e.g. the insula, amygdala, cingulate cortex, and hippocampus, has been demonstrated to contribute to the feasible organizing of the autonomic nervous system [23]. A previous functional MR study has disclosed less connectivity of the central brain areas coupled with autonomic integration, including the limbic system, in cases of Takotsubo syndrome [24]. Contemplating this fact, it is reputed that dysfunction occurred in the limbic system owing to prior stroke is linked with overexerted sympathetic stimulation, and Takotsubo syndrome took place.

With respect to pathophysiology of Takotsubo syndrome, Takotsubo syndrome that was related to brain infarction at or near the insular cortex and limbic encephalitis has been thought to be caused by alterations in central autonomic function because of the affected insular cortex [10,15,25]. Those results might advise that not only catecholamine release due to the stress but also stimulation of the central limbic system, for instance, amygdala, might cause Takotsubo syndrome.

Although the precise mechanism of Takotsubo syndrome is unknown, it appears to be a toxic effect of excessive endogenous catecholamine [26,27]. Takotsubo syndrome may be caused by catecholamine-induced myocardial stunning and has been associated with intense physical or psychological stresses [26,27]. The intense physical stress caused by frequent emotional fluctuation due to increased activity of amygdala might contribute Takotsubo syndrome.

Another possible mechanism by which exacerbated sympathetic stimulation provokes Takotsubo syndrome might be owed to its involvement with the flooding of stress-related neuropeptides [28]. The pathophysiology of Takotsubo syndrome is schematized in Figure 4. It has been known that a complex integration between neocortical and limbic system is secondary to stress by way of triggering the noradrenergic cells in brainstem and neuropeptide Y (NPY), a stress-related neuropeptide, of the hypothalamic arcuate nucleus [29]. NPY and norepinephrine located in the presynaptic terminals of the postganglionic sympathetic system, and acute spillage of both at the myocardial level may clarify the dominant theory of neurogenic-modulated mechanism of myocardial staggering. Scintigraphic scrutiny is worthy of survey of various brain disorders. Further studies are expected to clarify the pathophysiology and mechanism of Takotsubo syndrome linked with the brain–heart axis.

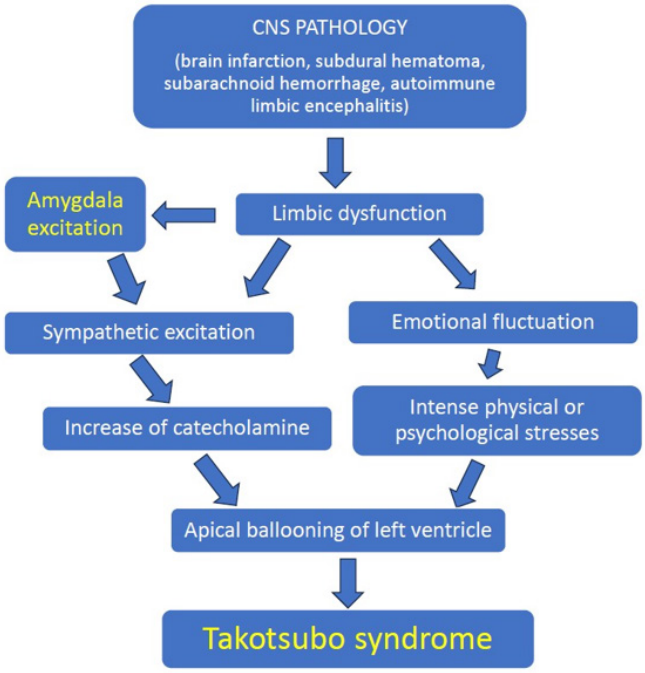

Figure 4. The pathophysiology of Takotsubo syndrome is schematized.

Conclusions

It is assumed that the dysregulation of limbic system due to autonomic limbic disorder is associated with overexerted stimulation of sympathetic function, which fact likely resulted in Takotsubo syndrome like our patient. When we encounter a patient with heart disease who is in a bad mood and irritable after a stroke, we need to arrange a cerebral perfusion examination immediately to investigate the activity of their amygdala.

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