Tako-tsubo syndrome as a consequence and cause of stroke

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Summary

Since tako-tsubo syndrome (TS) frequently appears soon after stroke (usually stroke involving the insular cortex), it is believed to be a consequence rather than a cause of stroke.
Herein, we describe a 70-year-old woman presenting with a left middle cerebral artery stroke (involving the insular cortex) who developed a further contralateral ischemic stroke with concomitant detection of a transient intracardiac mural thrombus attributable to TS. It can reasonably be maintained that that in our patient insular stroke triggered the TS, which in turn became the embolic cause of a further stroke.
Given the association between TS and the risk of embolic stroke, congestive heart failure and sudden death, stroke physicians need to promptly detect and appropriately manage this condition.

KEY WORDS: cardioembolic, insular stroke, stroke, stroke cause, Tako-tsubo syndrome

Introduction

Tako-tsubo syndrome (TS) is a new diagnostic entity, consisting of acute cardiomyopathy which mimics acute myocardial infarction, but without evidence of obstructive coronary artery disease (Prasad, 2007). The acute apical dilatation characterizing this condition gives the heart the appearance of a *tako-tsubo*, the Japanese word for octopus trap. TS is considered a benign and reversible cardiomyopathy; its precise incidence is unknown, although it is believed that up to 2.5% of all patients with an initial primary diagnosis of an acute coronary syndrome may have TS (de Gregorio et al., 2008; Nef et al., 2007; Gianni et al., 2006). Chest pain or dyspnea, ischemic electrocardiographic findings including ST-T segment changes, transient left ventricular dysfunction and limited release of cardiac injury markers, in the absence of epicardial coronary artery disease, characterize the acute phase of TS (Gianni et al., 2006; Biteker et al., 2010; Mayer et al., 1995). Even though TS is generally regarded as an isolated clinical entity, it may also complicate other structural heart diseases, including dilated cardiomyopathy. Although the precise cause of this syndrome is still unclear, a mechanism of catecholamine-induced myocardial stunning has been hypothesized, since TS was found mainly in postmenopausal women and was frequently associated with emotional or physical stress, including surgical interventions or subarachnoid hemorrhage (de Gregorio et al., 2008; Yalta et al., 2010; Lee et al., 2006; Sharkey et al., 2005; Bybee and Prasad, 2008). TS probably favors intracardiac mural thrombus formations (Gianni et al., 2006; Yalta et al., 2010; Bybee and Prasad, 2008; Parodi et al., 2007), which are responsible for thromboembolic complications in about 0.8% of cases.
Yoshimura et al. (2008), in a consecutive series of stroke patients, first identified and systematically examined seven stroke patients who developed an unusual cardiomyopathy diagnosed as TS. The fact that the phenomenon frequently appeared soon after stroke and the stroke frequently involved the insular cortex or adjacent areas, known to be associated with dysautonomic and cardiovascular symptoms (Cereda et al., 2002; Ay et al., 2006), suggested that TS is a complication rather than a cause of stroke.
Herein, we describe a 70-year-old woman presenting with a left middle cerebral artery (MCA) stroke (involving

the insular cortex) who developed a further contralateral ischemic stroke with concomitant detection of a transient intracardiac mural thrombus attributable to TS.

Case report

In June 2010 a 70-year-old woman was hospitalized due to sudden onset of aphasia. The neurological examination performed in the emergency department showed a predominantly motor aphasia associated with right hemineglect, hemianopia and hemiparesis. Her NIHSS score was 12. The patient's past medical history was unremarkable except for a recent (one week earlier) hospitalization due to pneumonia and previous work-related mental stress. The CT scan performed in the acute phase revealed a temporoparietal infarction in the MCA territory. Neck and intracranial angio-CT scan and carotid ultrasound examination did not reveal any arterial stenosis. Continuous cardiac monitoring and Holter ECG did not detect atrial fibrillation at any time during the disease course. Two days later the patient presented sudden-onset left hand weakness with sensory disturbances related to a new right temporoparietal stroke. Given the hypothesis of a cardioembolic source we performed a transthoracic echocardiography (TTE) which showed an ejection fraction (EF) of 40% in the left ventricle and an extensive large inferoseptal akinetic area with ballooning associated with a round hypoechogenic lesion (20x16 mm) consistent with an intracardiac thrombus (Fig.1, right side). The ECG performed at that time showed ST-T segment elevation associated with increased levels of troponin (up to 0.63; normal value, n.v. <0.09 ul) and brain natriuretic peptide (BNP) up to 979 (n.v. <100 ng/l). Intravenous anticoagulation using sodium heparin was promptly started followed by orally administered dicumarolic drugs. A cardiac CT scan did not reveal any coronary disorders. On two follow-up TTEs, performed respectively two days and one week later, the intracardiac thrombus was no longer visible and the EF was found to have increased to 55% (Fig.1, left). At the same time troponin and BNP levels progressively fell to normal. TS syndrome was diagnosed according to the criteria proposed by Bybee et al. (2004). The patient underwent physiotherapy and speech therapy and progressively recovered.

Discussion

Tako-tsubo syndrome has already been reported in 19 stroke patients (Yoshimura et al. 2008; Jabiri et al., 2010), mostly in the Japanese population. In line with previously reported cases, our patient was a postmenopausal woman. Like most previously described TS patients, she presented with stroke involving the insular cortex. Insular cortex infarction has been described to be associated with decreased heart rate variability and with an increased incidence of complex arrhythmias and sudden death (Cereda et al., 2002; Ay et al., 2006).

Interestingly, in all the previously described cases stroke seemed to precede TS, suggesting that TS is a consequence rather than a possible cause of stroke. In these cases, a mechanism of stroke-induced abnormal catecholamine release was hypothesized. However, Jabiri et al. (2010) published the first report of a patient presenting with a clinical syndrome (chest pain, ECG abnormalities, large apical akinetic area at echocardiography with normal coronary angiography) consistent with TS, who developed an MCA stroke a few days later, raising the question of whether TS might itself be a cause rather than a consequence of stroke.

In our patient, although a TTE was performed only after the first cerebrovascular event, stroke preceded the ECG changes and detection of hypokinesia and

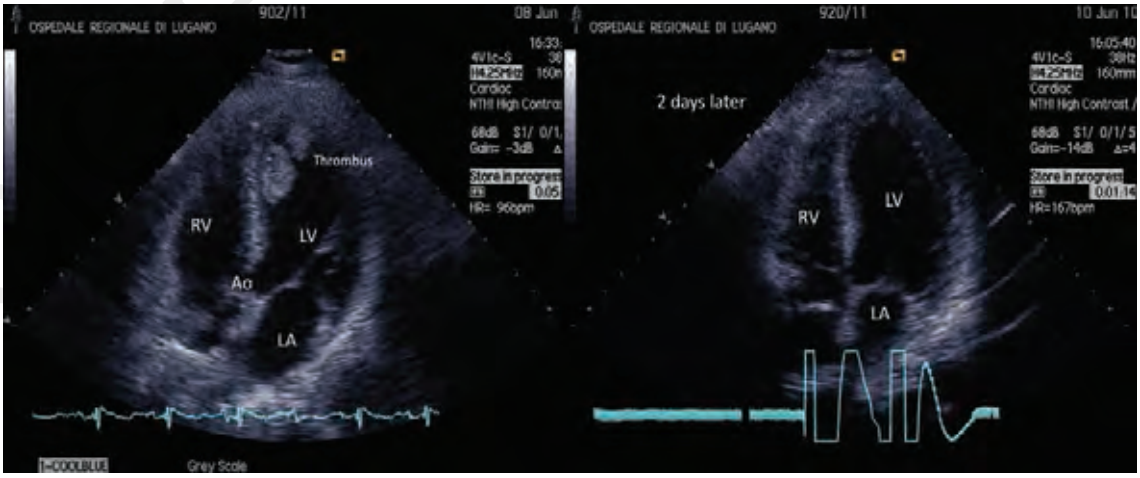

Figure 1 - Acute phase and two-day follow-up transthoracic echocardiography.
Right. LV= left ventricle with akinetic apex and thrombus. LA=left atrium; RV=right ventricle; AO=aorta.
Left. After only two days complete resolution of the thrombus under anticoagulation therapy.

intramural thrombus. Thus, it can reasonably be maintained that in our patient the insular stroke triggered the TS, which in turn became the embolic cause of a further stroke.

Thus, our report underlines the association between TS and ischemic stroke and the role of this entity as a potential cause of mural thrombus formation in the left ventricle, thereby contributing to a better understanding of the intricate pathophysiology and the clinical issues of this relatively rare disease.

Tako-tsubo syndrome usually has a favorable prognosis and recurrences are rare, in the absence of significant underlying comorbid conditions (Elesber et al., 2007). Cardiac wall motion abnormalities are usually transient and resolve completely within days or a few weeks. Treatment with beta-blockers is currently recommended for the majority of TS cases, given the hypothesis of a catecholamine-induced myocardial injury.

Given its association with risk of embolic stroke, congestive heart failure and sudden death, stroke physicians need to promptly detect and appropriately manage this condition,

Thus, ECG, long-term ECG monitoring, as well as repeated ultrasound examinations and ischemic myocardial markers, including creatine kinase, troponin-T and BNP levels, are recommended in all stroke cases, particularly in elderly female patients with insular infarcts.

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