


Mortal consequences of a cooperative action between Takotsubo syndrome and increased intracranial pressure

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Abstract

An elderly patient with head injury was registered to the emergency room. Because the patient arrived to the hospital unconscious, her cranial, cerebrovascular, and cardiac function was studied. The cardiac function measurements were (i) heart rate, (ii) blood pressure, (iii) oxygen saturation level, (iv) electrocardiogram (ECG), (v) coronary angiogram, (vi) chest computerized tomography (CT), and (vii) echocardiogram. The head damage was studied by cerebral CT and magnetic resonance imaging (MRI). The serum ischemia and inflammatory biomarkers were analysed. For the immediate treatment, the patient received cardiovascular system supporting medication. The cardiac diagnostic results were (i) the ECG suggested an elevation in the left ventricular systolic function, (ii) the blood test showed neutrophilia, increased creatine and increased troponin I kinase values, and (iii) the coronary angiogram and ECG analysis demonstrated a lack of a myocardial infarction but identified apical akinesia. The patient did not have previous symptoms of cardiovascular disease. The brain imaging demonstrated (iv) an acute ischemia in the left occipital area and (v) increased intracranial pressure. Brain MRI indicated (vi) aqueductal stenosis and (vii) multiple gliomatotic foci demonstrating hydrocephalus caused by gliomatosis cerebri. A chest CT indicated (viii) chronic obstructive pulmonary disease (COPD). One week later, the patient died because of cardiac arrest. The diagnosis was Takotsubo syndrome enforced by gliomatosis cerebri and COPD. To our knowledge, this is the first reported case in which the cardiac dysfunction of the patient is associated with gliomatosis cerebri-derived hydrocephalus and increased intracranial pressure that together with COPD may have enhanced the negative clinical outcome.

Keywords Acute brain ischaemia; Cardiomyopathy; Chronic obstructive pulmonary disease; Gliomatosis cerebri; MRI; Takotsubo syndrome

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Introduction

Brain ischaemia can induce a secondary disease, Takotsubo syndrome,¹ in the heart that causes a mild temporal injury, although more severe and permanent cardiac damage, and even death, have been reported. Characteristically, the symptoms of Takotsubo syndrome mimic an acute myocardial infarction suggesting electrocardiogram abnormalities and a slight elevation of cardiac biomarkers, although patients do not display obvious coronary artery disease.²

The criteria for suspected Takotsubo syndrome include (i) transient hypokinesia, akinesia, or dyskinesia in the left ventricular mid-segments with or without apical involvement; (ii) regional wall-motion abnormalities that extend beyond a single epicardial vascular distribution; (iii) often, but not always, a physical or emotional stressful trigger; (iv) an absence of obstructive coronary disease or angiographic evidence of an acute plaque rupture; (v) electrocardiogram abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin; and (vi) an absence of

pheochromocytoma and myocarditis.^{3,4} The triggering events that cause this syndrome include trauma injuries, sepsis, pancreatitis, post-surgical pathology, thyroid disease, rhabdomyolysis, poisoning, emotional stress, pheochromocytoma crisis, acute respiratory failure, anaphylaxis, hypothermia or hyperthermia, and neurological conditions,⁴ which suggests that large-scale stress-related conditions are stimulants. The probability of developing the syndrome can be further predicted using Takotsubo Intetak diagnostic score values (www.takotsubo-registry.com) that are based on a combination of clinical variables including the female gender, emotional and physical stress, a lack of ST-segment depression, an acute former/chronic psychiatric/neurological disorder, and a prolonged QTc time.⁵ However, the exact mechanisms that induce the syndrome are not completely understood. Here, we report a case of an elderly patient with Takotsubo syndrome that was induced by the cooperative action of an acute brain ischaemia and gliomatosis cerebri-derived intracranial pressure.

Case report

An 82-year-old unconscious female patient was registered to our hospital in the late evening with a fall-derived head injury and a laceration in the left occipital area with intense

sweating. The falling incident was preceded by a progressive cognitive decline during the previous 6 months that consisted of repeated temporary loss of consciousness and spatial disorientation that occurred during the previous 3 to 4 days, as reported by her family. The patient was taken to the emergency unit for a cerebral computerized tomography (CT) scan that showed a lack of haemorrhage or acute cerebrovascular ischaemia, but identified diffuse and confluent hypodensity of the periventricular white matter and the bilateral and symmetrical semioval centres from chronic hypoperfusion, as well as the ventricular system in a wide location.

According to the emergency department's diagnosis, the patient had increased blood pressure (160/100 mmHg), a heart rate of 84 b min⁻¹, a 96% oxygen saturation level without oxygen support, and a low respiratory rate of 15 per minute. The electrocardiogram indicated a significant ST tract elevation in the anterolateral leads that suggested cardiac dysfunction and a severe global reduction in left ventricular systolic function (a left ventricular ejection fraction of 35%) with apical akinesia ('apical ballooning') (Figure 1). There was no evidence of coronary artery disease or cardiac ischaemia after a coronary angiogram and ventriculography (Figure 2) and an echocardiogram of the carotid arteries confirmed a lack of occlusions. For the immediate treatment, the patient received aspirin (100 mg) once a day; ramipril (Triatec) (10 mg), an angiotensin-converting-enzyme (ACE) inhibitor, once a day; a beta-blocker (Cardicor) (3.75 mg) once a day; atorvastatin

Figure 1 Electrocardiogram at admission. The electrocardiogram showed a significant ST segment elevation in the anterolateral leads (I, aVL, and V2-6)

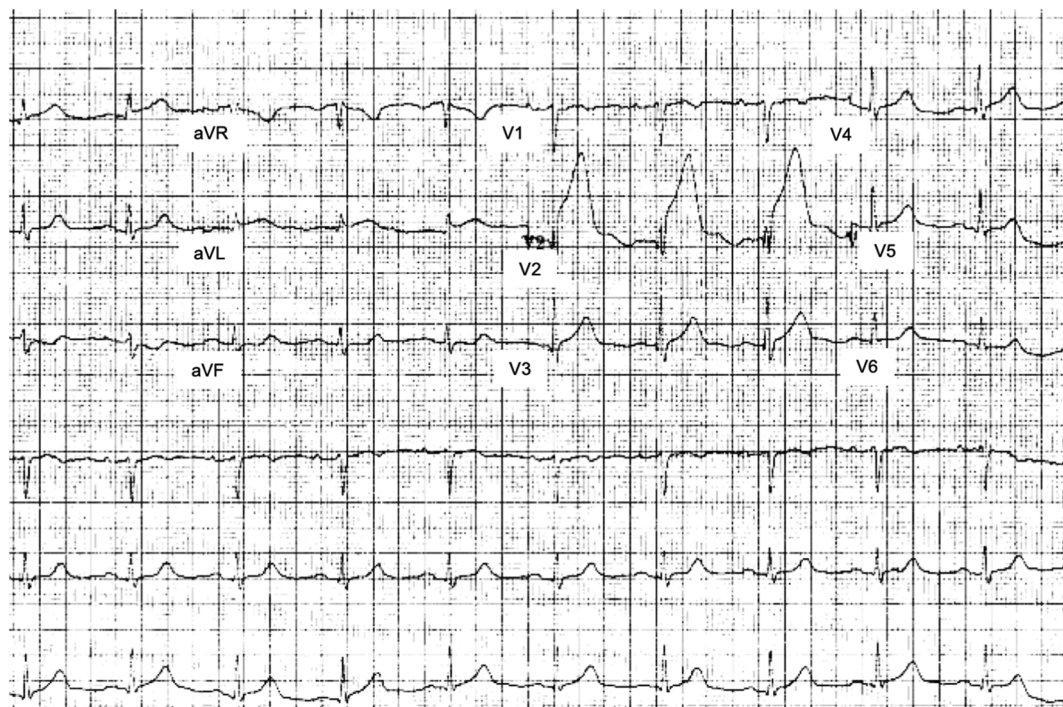
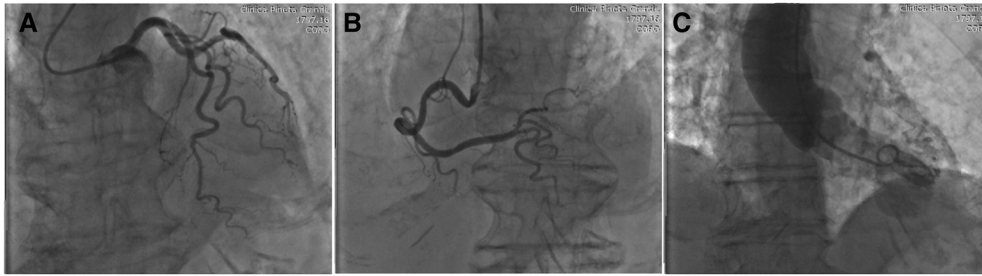


Figure 2 Patient cardiac catheterization results. (A) Right coronary angiogram. (B) Left coronary angiogram. (C) Ventriculography with a typical pattern of apical ballooning. No significant coronary stenosis was found in the patient



(Torvast) (20 mg) once a day; and pantoprazole (Pantorc) (20 mg) once a day to inhibit gastric acid secretion.

The day after the patient was registered to the hospital, she developed a mild neurological status that consisted of involuntary eye blinking and limb movement. As a result, the brain CT scan was repeated and confirmed a diffuse hypodensity that involved the midbrain and the nuclei of the base that was compatible (in the first hypothesis) with an acute ischaemic injury and the symmetrical ventricular system, and showed increased dimensions of the ischaemic-malacic area in the left occipital, and increased amplitude of the periencephalic liquor spaces (Figure 3).

A magnetic resonance imaging (MRI) with (Figure 4B) and without (Figure 4A) contrast medium (gadolinium) was performed to confirm the presence of the lesions in the left cerebral occipital globe and to detect regions of hypodensity. The MRI found multiple gliomatotic foci at the intraparenchymal and ependymal sites, a pattern that is compatible with gliomatosis cerebri.

In particular, the brain MRI images indicated the presence of aqueductal stenosis (Figure 5A, arrow), while the

width of the periencephalic fluid space that determines transependymal transudation was indicative of obstructive hydrocephalus (Figure 5B,C, arrows), and the CT hydrocephalus observation was highlighted by several parameters that were suggesting the intracranial pressure increase (Figure 5D–F).

The blood test analysis (Table 1) performed at admission showed neutrophilia and lymphocytopenia, increased creatine kinase myocardial band (3.55 mg/dL; normal value 0.5–1.1 mg/dL), which further increased at 12 h after admission (32.04 mg/dL). Troponin I value was recorded at 12 h after admission being 3.232 ng/mL (normal value <0.04 ng/mL). Catecholamine levels were not measured. The patient had a prior history of cholecystectomy, femoral fracture, generalized osteoarthritis, and systemic arterial hypertension (without therapy at home). A chest CT indicated severe chronic obstructive pulmonary disease (COPD) with marked thickening of the axial and of the peribronchial interstitium.

The patient died because of cardiac arrest 7 days after being registered at the hospital without showing any improvement in the cardiac function. The cause of death

Figure 3 Brain computerized tomography (CT) scan comparison. Displaying the increased dimensions of the ischaemic-malacic area in the left occipital (arrows). (A) Brain CT taken at the time of admission. (B) Brain CT repeated 48 h after hospital admission

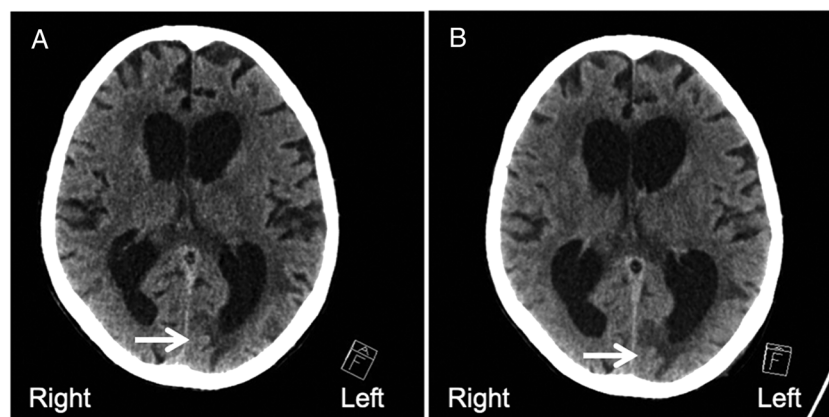


Figure 4 Patient magnetic resonance imaging indicating gliomatosis cerebri. (A) Axial section without contrast medium. (B) Axial section with contrast medium. The magnetic resonance imaging shows a signal and widespread alterations at the thalamus and subthalamus level (arrows) with involvement of the truncus encephalicus, the mesencephalon, and the left occipital cortex. This image is compatible with a case of gliomatosis cerebri

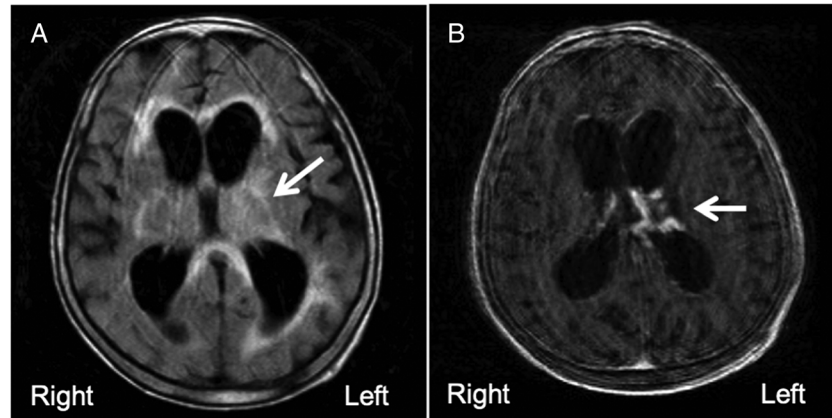
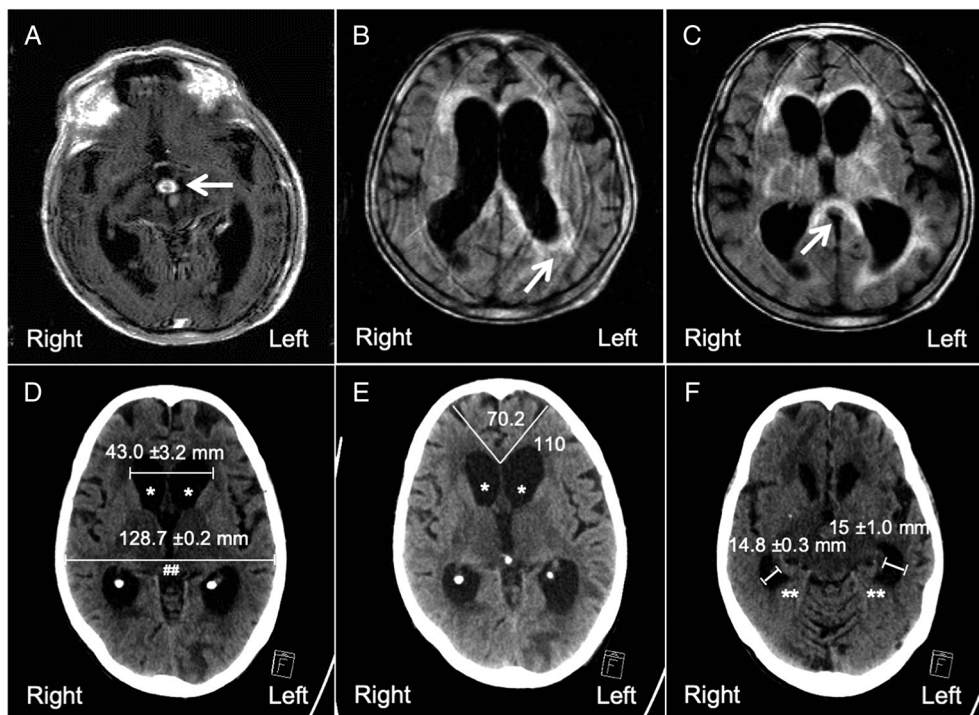


Figure 5 Magnetic resonance imaging (MRI) and computerized tomography indications of hydrocephalus. (A) MRI findings with gadolinium contrast medium suggest aqueductal stenosis (arrow). (B and C) MRI without contrast medium suggests hyperintensity on the fluid-attenuated-inversion recovery that is contiguous to the ventricular wall by transependymal resorption (arrows). (D) Computerized tomography observation of Evans' index, which is the ratio of the maximum width of the frontal horns of the lateral ventricles and the maximal internal diameter of the skull at the same level, suggested a border line value of 0.33 (normal value less 0.30) (one asterisk (*) indicates frontal horn; symbol '##' indicates average bi-parietal diameter). (E) The angle between two frontal horns was 110 mm (normal value 120 mm). (F) The diameter of the temporal horns (***) was dx 14.8 ± 0.3 mm, sx 15 ± 1.0 mm (normal values less than 2 mm)



was diagnosed as Takotsubo syndrome based on the diagnosed apical akinesia, the lack of cardiac ischaemia, and no reports of previous symptoms of cardiovascular disease.

Gliomatosis cerebri-derived cranial hypertension and COPD enforced the lethal consequences of Takotsubo syndrome.

Table 1 The laboratory test analysis

Blood test result	Range	Value 0 h	Value 12 h	Value 1 day	Value 2 days	Value 3 days	Value 4 days
White blood cell count ($\times 10^3$ /mL)	4.8–10.8	7.66	6.41	6.34	5.95	8.13	6.88
Neutrophils (%)	40–70	—	81.1	82.4	83.0	82.3	80.5
Lymphocytes (%)	20–45	—	9.5	7.3	10.2	8.8	10.9
Monocytes (%)	0–10.0	—	7.7	8.0	6.5	7.0	6.9
Eosinophils (%)	0–6.0	—	0.3	0.3	0.3	0.2	0.4
Basophils (%)	0–1.5	—	0.2	0.2	0.1	0.2	0.2
Red blood cells ($\times 10^6$ /mL)	4.0–5.4	5.39	5.32	4.94	5.35	5.29	5.0
Haemoglobin (g/dL)	12.0–16.0	15.4	15.3	14.2	15.3	15.1	—
Haematocrit (%)	35–48	44.5	43.9	41	44.5	43.7	41.3
Red blood cell distribution (%)	11.6–14.4	16.4	16.2	16.3	16.3	16.4	16.4
Platelets ($\times 10^3$ /mL)	150–400	160	149	153	132	181	149
Platelet volume (fl)	9.0–13.0	7.3	7.2	7.8	7.7	7.7	7.6
Procalcitonin (%)	0.19–0.38	0.12	0.11	0.12	0.1	0.14	0.11
Creatine kinase MB (mg/dL)	0.5–1.1	3.55	32.04	21.67	—	—	—
Lactate dehydrogenase (U/L)	140–280	—	667	591	—	—	—
Troponin I (ng/mL)	<0.04	—	3.232	2.471	1.366	0.527	—

Discussion

Takotsubo syndrome is generally benign but may occasionally lead to the death of the patient depending on the nature of the triggering event, the magnitude of the consequential myocardial injury, and other pathologies of the patient. A general practice for the clinical treatment of patients with Takotsubo syndrome has still not been established, likely because of the difficulty of organizing controlled clinical studies for the syndrome. β -Blockers have been used during the acute phase to reduce basal cardiac hypercontractility and subsequent obstruction, but this alone may not reduce patient mortality.⁶ Recently, it has been suggested that a combination of β -blockers with ACE inhibitors can reduce the recurrence of the syndrome.⁷ Other therapeutic options include using anticoagulant therapy to attenuate the possible development of a left ventricular thrombosis⁸ and the use of an implantable cardioverter defibrillator.⁹

In the current case, an 82-year-old patient with gliomatosis cerebri and acute ischaemic lesions in the left occipital area that were caused by accidental falling developed a significant cardiac dysfunction and died after 7 days because of cardiac arrest despite a combined β -blocker-ACE inhibitor-aspirin therapy. The severity of the case may have been exacerbated

by, COPD, increased gliomatosis cerebri-derived hydrocephalus, and consequential intracranial pressure.

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Conflict of interest

All authors declare no conflict of interest.

Ethics approval and consent to participate

The consent for publication was provided by the patient's son. The patient's identification has been protected and any information that could potentially be used to reveal the identity of the patient has been removed.

The blood sample was taken immediately after the registration (0 h) and after 12 h, 1, 2, 3, and 4 days from the registration.

MB, myocardial band.

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