Early Endovascular Treatment of Aneurysmal Subarachnoid Hemorrhage Complicated by Neurogenic Pulmonary Edema and Takotsubo-Like Cardiomyopathy

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SUMMARY – *Aneurysmal subarachnoid hemorrhage (SAH) may be associated with acute cardiopulmonary complications, like neurogenic pulmonary edema (NPE) and Takotsubo-like cardiomyopathy (TCM). These dysfunctions seem to result from a neurogenically induced overstimulation of the sympathetic nervous system through the brain-heart connection and often complicate poor grade aneurysmal SAH. The optimal treatment modality and timing of intervention in this clinical setting have not been established yet. Early endovascular therapy seems to be the fitting treatment in this particular group of patients, in which surgical clipping is often contraindicated due to the added risk of craniotomy. Herein we describe the case of a woman admitted to the emergency department with aneurysmal SAH complicated by NPE-TCM, in which early endovascular coiling was successfully performed. Our case, characterized by a favorable outcome, further supports the evidence that early endovascular treatment should be preferred in this peculiar clinical scenario.*

Introduction

Cardiopulmonary dysfunctions, in particular neurogenic pulmonary edema (NPE) and Takotsubo-like cardiomyopathy (TCM), may complicate aneurysmal subarachnoid hemorrhage (SAH)^{1,2}. NPE is appreciated in 2-29% of SAH patients and is more frequently associated with poor grade SAH².

TCM is reported to complicate 4-15% of SAH³. It is still debated in literature whether TCM should be considered a distinct clinical entity or a manifestation of neurogenic stunned myocardium⁴, so we use the term “Takotsubo-like cardiomyopathy” to differentiate it from the idiopathic form, that by definition should not have an extracardiac cause.

Although NPE and TCM have been considered separate entities in the past, a shared common pathophysiologic mechanism was

recently demonstrated⁵. A neurogenically induced overstimulation of the sympathetic nervous system through the brain-heart connection may cause endothelial damage, increased pulmonary vascular permeability and a characteristic myocardial injury through an excitotoxic mechanism⁵.

No evidence-based guidelines indicating the optimal modality and timing of treatment for SAH patients complicated with NPE-TCM have been developed yet. However, endovascular therapy was recently recognized as the preferable treatment in these patients⁶. Moreover, medical treatment, performed to prevent and attenuate cerebral vasospasm, is crucial in these patients. Currently, triple-H therapy represents the most widely adopted strategy. However, implementation of this therapy in patients with neurogenic pulmonary edema and Takotsubo-like cardiomyopathy is contraindicated.

Figure 1 Unenhanced brain CT shows SAH involving the interhemispheric fissure and right sylvian fissure; hemorrhage into the left lateral ventricle is associated.

Figure 2 CT angiogram demonstrates an aneurysm (maximum diameter: 6 mm, neck: 3 mm) of the M1 segment of the right middle cerebral artery.

Figure 3 Left ventriculography reveals the ampulla-shaped morphology of the left ventricle, a characteristic sign of Takotsubo-like cardiomyopathy.

Hence, prompt endovascular treatment to minimize the risk of secondary SAH and treat active vasospasm is beneficial in these patients.

Herein we describe a case of aneurysmal SAH complicated by NPE-TCM, in which early endovascular treatment was performed with a favorable outcome.

Case Report

A 42-year-old woman was admitted to the emergency department with loss of consciousness (grade 6 on the Glasgow Coma Scale). Her relatives reported she had been suffering from headache for two days.

Unenhanced brain CT, performed on a 64 slice scanner (Aquilion, Toshiba), showed SAH involving the right frontal and parietal sulci, the interhemispheric fissure, the right sylvian fissure, pre-pontine and peri-mesencephalic cisterns, along with left lateral intraventricular hemorrhage (Fisher scale grade 4) (Figure 1). CT angiogram revealed a ruptured aneurysm of the right M1 segment with a maximum diameter of 6 mm and a neck of 3 mm (Figure 2).

Two hours later the patient developed dyspnea and was found to be hypoxemic; a chest radiograph revealed pulmonary edema and tracheal intubation was performed. On ECG, atrial fibrillation was present and severe systolic dysfunction (EF 25-30%) along with akinesis of the apex and of the distal left ventricular walls were demonstrated on echocardiography. Troponin I and BNP were found to be 1.25 ng/ml (nv < 0.06 ng/ml) and 777.6 pg/ml (nv < 100 pg/ml), respectively. Consequently, acute heart failure was diagnosed. Medical management was started (ACEi, β blockers, diuretics and vasopressin) and the patient's cardiac output progressively improved. On the second day of admission, her vital parameters were made stable, so coronarography could be performed to exclude an acute myocardial infarction. Coronary arteries were found to be unharmed, while left ventriculography demonstrated the typical ampulla-shaped morphology of the left ventricle (Figure 3), leading to a diagnosis of Takotsubo-like cardiomyopathy. Immediately afterwards, endovascular embolization of the ruptured aneurysm with detachable coils could be performed (Figures 4 and 5). An unenhanced head CT, performed on the first postoperative day, revealed the success of the procedure without any complications. An echocardiographic control, performed four days after the intervention, showed a complete recovery of her cardiac function (EF 65%), and a chest radiograph, obtained on the same day, revealed an evident reduction of the signs of pulmonary edema. She was finally discharged on the 14th postoperative day with a favorable outcome.

Discussion

SAH-induced cardiopulmonary complications are thought to result from an increased central sympathetic activity.

In particular, neurogenic pulmonary edema (NPE) seems to originate from a lesion around

the medulla oblongata: compression of the dorsal and solitary tract nuclei suppressing sympathetic activity may cause acute changes in pulmonary vascular permeability². Indeed, NPE is more frequently associated with poor grade SAH patients with ruptured posterior circulation aneurysms⁷.

Takotsubo-like cardiomyopathy (TCM), characterized by reversible left ventricular dysfunction producing a typical ampulla-shaped morphology on the ventriculogram, ECG abnormalities, mildly increased cardiac markers and an absence of coronary artery disease⁴, may result from a neurogenically induced overstimulation of the sympathetic nervous system through the brain-heart connection⁵. The severe stress induced by SAH may promote the release of corticotropin releasing factor from the hypothalamus, causing an increase in plasma catecholamines and a cardiac hypersensitivity to sympathetic stimulation⁸. Myocardial contraction band necrosis is the characteristic anatomopathological result of this overstimulation, been the proof of a sympathetic discharge.

As a consequence of the common pathogenesis, i.e. neurogenic overstimulation of the sympathetic nervous system, SAH patients complicated with NPE tend to develop concomitant TCM more frequently².

Whether the treatment for SAH patients complicated with NPE-TCM should be surgical or endovascular and if the intervention should be performed in the acute stage or should be delayed, is not still clear. Aneurysm clipping versus coiling does not have a differential effect on the risk of troponin release and left ventricular dysfunction after SAH, so the choice of the modality of aneurysm treatment does not affect the risk of developing cardiac injury⁹.

Yabumoto et al. have insisted on the early surgical management of the ruptured aneurysm and symptomatic treatment of NPE, claiming that NPE should not be an obstacle to radical intervention when cardiorespiratory control can maintain the minimal anesthetic limit¹⁰. However, several recent reports indicated an early endovascular procedure as the treatment of choice in these patients, who are often considered poor surgical candidates, reporting a good prognosis^{2,6,11}.

The advantages of endovascular treatment are the minor invasivity, the immediate possibility of performance after the diagnostic angiogram and the shorter duration of the procedure. The timing of the intervention is related to the patient's cardiopulmonary sta-

Figure 4 Digital subtraction angiography (DSA) (oblique projection) confirms the aneurysm of the right M1, well demonstrating its size, orientation and neck.

Figure 5 DSA (same projection) testifies the success of the embolizing procedure, showing complete obliteration of the lumen of the aneurysm by detachable coils.

tus; the procedure should be delayed until hemodynamic stability is achieved. If patients considered unfit for endovascular therapy may be treated with surgery immediately or if the intervention should be deferred for at least two weeks remains unclear⁶.

This clinical scenario is complicated further by the fact that in approximately half of the patients with NPE-TCM neither surgical nor endovascular intervention in the acute phase may be feasible⁶. Medical treatment is based on the prevention and control of cerebral vasospasm, which is estimated to complicate up to 70% of all SAH and remains a major cause of morbidity and mortality. However, much controversy exists generally over the prevention and pharmacological treatment of this fearful complication. A general consensus exists only for the oral administration of nimodipine (a calcium channel blocker) to all patients suffering from SAH to improve the neurological outcome, without an effect on cerebral vasospasm¹².

The use of triple-H therapy (hypertension, hypervolemia and hemodilution) in the prevention and treatment of cerebral vasospasm is still controversial¹². This strategy is intended to increase cerebral blood flow through the expansion of intravascular volume and the reduction of blood viscosity and is performed after the aneurysm treatment. Hypertension may be achieved by volume expansion alone or with

the addition of vasopressor medications, such as phenylephrine or dopamine. Hemodilution is based on the achievement of a hematocrit goal of 30-35%, which is considered an optimal balance between oxygen-carrying capacity and blood viscosity¹³. Recent American Heart/Stroke Association guidelines suggest maintenance of euvolemia for vasospasm prevention and recommend induced hypertension for patients with active cerebral vasospasm with a normal cardiopulmonary status¹³. Indeed, this therapeutic strategy is contraindicated in patients with SAH and cardiopulmonary dysfunction, as the cardiocirculatory status may be worsened by induced hypertension. Indeed, cardiogenic shock with stunned myocardium may be induced by triple H therapy even in patients with normal cardiopulmonary function¹⁴. Consequently, balloon angioplasty is considered the fitting treatment of cerebral vasospasm in this particular clinical scenario¹³.

In our case, the early recognition and treatment of NPE-TCM was crucial for correct planning of the endovascular procedure, successfully performed after the improvement in cardiac function. We suggest that if SAH-related, reversible cardiopulmonary abnormalities are promptly detected, an early endovascular procedure should be preferred once a stable hemodynamic function or initial signs of recovery are demonstrated, leading to the best prognosis.

Conclusions

NPE and TCM represent possible complications of aneurysmal SAH.

An early diagnosis and prompt treatment of these reversible disorders are essential for

a good prognosis and for the correct planning of the aneurysmal treatment. We suggest early endovascular embolization as the most appropriate procedure in SAH patients complicated with NPE-TCM, reporting an excellent prognosis in our case.

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