



## Large Intracranial Hemorrhage after Dobutamine Stress Echocardiography

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### Abstract

We report the case of a fatal intracranial hemorrhage after dobutamine stress echocardiography for chest pain in a 63-year-old female with no previous vascular risk factors. The patient experienced severe headache during stress testing and became clinically unresponsive 2-3 hours afterward. Imaging demonstrated a large 7.9 cm × 6.7 cm intracerebral hemorrhage (ICH) with subfalcine herniation. This is the first reported of a fatal ICH after dobutamine infusion. In large reviews of dobutamine use for cardiac stress testing, the agent has been proven to have a generally safe risk profile. However dobutamine may rarely produce life-threatening events in susceptible patients. Physicians should be aware of cerebrovascular complications, due to agent's hypertensive effects, as another rare, but possible complication of dobutamine infusion.

**Keywords:** Dobutamine; Echocardiography; Intracerebral hemorrhage

### Case Presentation

We report the case of a fatal intracranial hemorrhage after a dobutamine stress echocardiography. The patient was a 63-year-old female who initially presented to our institution for acute-on-chronic back pain unrelated to her eventual vascular pathology. She had a multi-year history of back pain exacerbated by a recent episode where she fell on her back while walking. She was admitted for control of her low back pain radiating to left lower extremity. Her low back pain and left S1 radiculopathy remained refractory to high dose narcotic pain medication, epidural steroid injection, and physical therapy. The patient, therefore, was scheduled for left L5-S1 hemilaminectomy and discectomy later that week. However, on the morning of her scheduled surgery, the patient experienced substernal chest pressure. The pressure was aggravated by anxiety and relieved spontaneously within minutes. Although cardiac enzymes and the EKG were within normal limits the hospitalist service deemed her to be at intermediate risk for the surgery due to the episode and her history of mitral regurgitation. They requested the surgery to be postponed until a stress test could be performed and she was started on aspirin and metoprolol.

The patient underwent pharmacologic dobutamine stress echocardiography the following day. Before initiation of the test, the patient had no neurological symptoms, such as headache. The test lasted for approximately 12 minutes and 7.1 mg of Dobutamine was administered. Patient's baseline heart rate and blood pressure were 78 bpm and 141/85 mmHg, respectively. The patient reached a peak heart rate of 148 bpm, and a peak blood pressure during the exam of 190/32 mmHg. During testing, the patient developed a severe headache upon initiation of infusion, which she rated 10/10. On discontinuation of dobutamine, the headache mildly improved to an 8/10. The test demonstrated no significant findings for cardiac disease or abnormal segmental wall motion. Upon returning to her room, the patient continued to complain of headache and was given hydrocodone and hydromorphone for pain relief. The pain was mildly alleviated by the pain medication. As the patient was in general medicine floor as opposed to a general neurology unit, the neurosurgery team was not informed of the headache and so a thorough evaluation was not performed.

Within three hours, the patient was found unresponsive, obtunded in her bed, and incontinent. On exam, she was unable to open her eyes, was non-verbal, and produced no motor response, thus, demonstrating a Glasgow Coma Scale (GCS) of 3. On exam, the patient had asymmetric pupils with a dilated right pupil of 7 mm in size and the left pupil measuring 1mm. The patient

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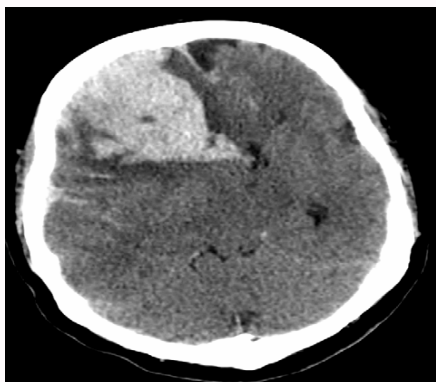
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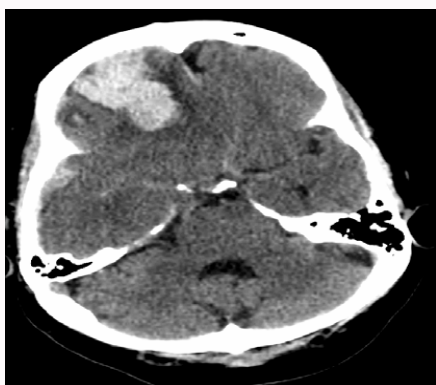
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**Figure 1:** A non-contrast axial CT head showing a right frontal hematoma measuring 7.9 cm in the AP dimension and 6.7 cm in the transverse dimension with a 2 cm leftward transtentorial herniation.



**Figure 2:** A non-contrast axial CT head at the level of the basilar cisterns showing no subarachnoid hemorrhage to indicate the hemorrhage was caused by a ruptured aneurysm.

also demonstrated upward bilateral Babinski responses. She was emergently intubated and underwent computed tomography (CT) scan which demonstrated an acute 7.9 cm x 6.7 cm hematoma extending from the right frontal lobe with multiple foci of loculated hemorrhage, and a significant right-to-left subfalcine herniation of 2.3 cm (Figure 1). An aneurysmal rupture was thought to be less likely as there was no blood in the subarachnoid spaces and the basilar cisterns (Figure 2). She was hypertensive with blood pressure of 220/110 mm Hg requiring multiple doses of labetalol and hydralazine for management of her acute hypertensive crisis. She was immediately taken to the operating room for an emergent right frontal craniotomy and hematoma evacuation within 1 hour since the neurological decline was noted. Post-operative CT of the head showed improved mass-effect with decrease subfalcine herniation now measuring 0.7 cm (Figure 3).

The patient's clinical condition did not improve after surgery except for her pupils became equal 3mm and briskly reactive. Her highest post-operative GSC score was 4; she remained non-verbal, was unable to open her eyes, and her greatest level of motor activity consisted of decerebrate posturing of her upper and lower extremities to pain. Subsequent post-operative CT scans demonstrated reduction of transtentorial herniation from 2.3 cm to 1.5 cm and changes consistent with hematoma evacuation and resection cavity measuring 5 cm x 8 cm. Over the next five days, the patient's post-operative CT did not show any significant changes. Additionally, a craniectomy was performed the fifth day after the initial craniotomy for progressively



**Figure 3:** A non-contrast axial CT head on post-operative day 1 showing the evacuation of hematoma as well as improved transtentorial herniation now measuring 0.7 cm.

worsening edema and further subfalcine herniation. The patient remained comatose without any clinical improvement. At the request of the patient's family, she was placed on comfort measures over the subsequent days and transferred to hospice where she eventually passed away on post-operative day 10.

## Discussion

Pharmacologic stress echocardiography is a commonly used method of evaluation for coronary artery disease in patients who do not tolerate or are unable to perform exercise stress echocardiography. Dobutamine is a synthetic catecholamine that binds to  $\beta$ -1 and  $\beta$ -2 receptors, causing augmentation of both heart rate and contractility, resulting in increased myocardial oxygen demand [1]. Multiple studies have demonstrated a very low reported rate of life-threatening complications. This case is the second reported instance of intracranial hemorrhage as a complication of the dobutamine stress test, and is the first reported case of dobutamine stress echocardiography leading to intraparenchymal hemorrhage and eventual death.

Complications from dobutamine stress test are rare. An early study from Indiana University reviewing the safety profile of dobutamine stress echocardiography in 1118 patients, detailed noncardiac side effects to include nausea in 8%, anxiety in 6%, headache in 4%, and tremor in 4% of the study population [1]. Among methods commonly used for stress echocardiography, dobutamine infusion causes the highest rate of life-threatening events [2]. A multi-center registry of 35,103 studies of dobutamine stress echocardiography documented fatal or near-fatal events in 63 patients, equaling an event rate of 1 in 557 [2]. These events included ventricular tachycardia or fibrillation, myocardial infarction, severe hypotension, asystole, cardiac rupture, stroke, and death [2]. No previous reports in the literature have listed intraparenchymal hemorrhage as a life-threatening complication from dobutamine infusion.

In a small proportion of patients, dobutamine has been noted to induce a marked hypertensive response [3]. The risk of severe hypertension, defined as systolic blood pressure >200 mm Hg and/or diastolic blood pressure >110 mm Hg, has ranged from 0.8% - 2% in multiple studies [4,5]. Although, our patient did not meet this definition of severe hypertensive response, her blood pressure was

markedly elevated during testing, coinciding with the development of severe headache. Furthermore, dobutamine has been demonstrated to augment arterial pressure and middle cerebral artery flow velocity in a small study among septic patients [6]. When comparing patients with hypertensive response from dobutamine stress echocardiography to those without a hypertensive response, the former were more likely to have a history of systemic hypertension and to be on  $\beta$  blocker medication at the time of the test [3]. Our patient had neither of these risk factors.

To our knowledge, there has been only one case report in the literature of intracranial hemorrhage subsequent to dobutamine stress test. In that report, the patient did not have any predisposing risk factors for hemorrhage, but did have a supratherapeutic INR at the time of hemorrhage. Additionally, the patient in that report demonstrated three small foci of intraparenchymal hemorrhage and was eventually discharged from the hospital with no neurologic deficit at 1 month follow-up. This is in stark contrast to our healthy patient who presented with a large hemorrhage requiring decompression via craniotomy and eventually expired due to her illness.

According to the International Classification of Headache Disorders (ICHD) 3<sup>rd</sup> edition guidelines, identification of the etiology of headache and associated neurologic symptoms requires only clinical signs. As per the ICHD guidelines, when attributing a headache to an underlying vascular condition, assessing the temporal relationship between events is crucial [7]. The absence of other possible sources of headache and the timing of the patient's symptoms support dobutamine infusion to be the immediate cause of our patient's acute neurologic change. The patient was without any neurological symptoms before the initiation of dobutamine administration, and the headache initiated with dobutamine infusion and slightly dissipated only after discontinuation. Generally, in cases of non-traumatic intracerebral hemorrhage, headaches present usually in acute onset accompanied by focal neurological signs. In this patient, the headache was the only initial symptom. No focal neurological deficits were noted by the bedside nurse until the patient was found unresponsive.

In summary, dobutamine is a commonly used pharmacologic agent used to perform stress echocardiography with a low documented

risk profile. Large studies of dobutamine stress echocardiography have documented rare life-threatening events to occur in patients. This paper introduces the possibility of intracranial hemorrhage as a very rare complication of dobutamine stress echocardiography mediated through a hypertensive response. We would also like to emphasize the importance of close neurological monitoring in patients who complain of severe headache after undergoing dobutamine stress echocardiography.

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