症　例

Perioperative Management of a Patient with Pheochromocytoma Complicated with Hypertrophic Obstructive Cardiomyopathy- Hemodynamic Control Using Transesophageal Echocardiography

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Pheochromocytoma is often associated with catecholamine-induced cardiomyopathy[1~4], but this condition frequently disappears after removal of the tumor.[5,6] For this reason, surgery is preferred in most cases. Hypertrophic cardiomyopathy with left ventricular outflow obstruction, however, may be related to repid changes associated with stimulation during manipulation of the tumor at surgery, aggravation of the left ventricular outflow obstruction, a marked decrease in cardiac output, and even cardiac insufficiency and myocardial infarction. Therefore, an important aspect of the anesthetic management of these patients is the early detection and prevention of these signs. Transesophageal echocardiography (TEE) is considered to be useful in the diagnosis of myocardial infarction and cardiomyopathy[7]. We adopted this modality as an intraoperative monitor, and found that imaging and quantitative determination by this method enable us a reliable anesthetic control, especially circulatory management. We describe here the anesthetic management, together with the follow-up postsurgical echocardiographic findings until the patient regained normal cardiac function.

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Case Report

A 38-year-old woman weighing 50 kg, who was 155 cm tall had a history of recurrent chest discomfort. Two years before the present admission, the patient developed severe hypertension but did not receive any antihypertensive therapy. She was later transfered to a physician by an ambulance with major complaints of chest pain, headache, and left abdominal pain. Severe hypertension (220/120 mmHg) was noted, and a tumor was detected in the left abdominal region using by abdominal echography. She was subsequently referred to our hospital where a more detailed evaluation revealed the presence of pheochromocytoma of the left adrenal gland (norepinephrine secretion-dominant type). The patient was scheduled for surgical removal of the pheochromocytoma. During the preoperative cardiac function testing, electrocardiography (ECG) indicated left ventricular hypertrophy and sinus tachycardia. During treadmill-loaded ECG, the development of chest pain and increasing blood pressure (252/148 mmHg) necessitated that exertion loading be interrupted after only 6 min. Immediately after the test, frequent ventricular premature beats of multiple origins were noted. Transthoracic echocardiography indicated asymmetrical hypertrophy (ASH) of the left ventricular wall, incomplete closure of the aortic valve at mid-systole,

and a left ventricular outflow tract pressure gradient (PG) of 20 mmHg, suggesting the presence of hypertrophic obstructive cardiomyopathy (HOCM) (Fig. 1). Administration of 10 μg.kg^{-1} of phentolamine under transthoracic echocardiography reduced her blood pressure from 168/88 to 118/70 mmHg, but increased heart rate from 82 to 130 bpm. The patient complained of increased chest pain, while echocardiography indicated an increase in
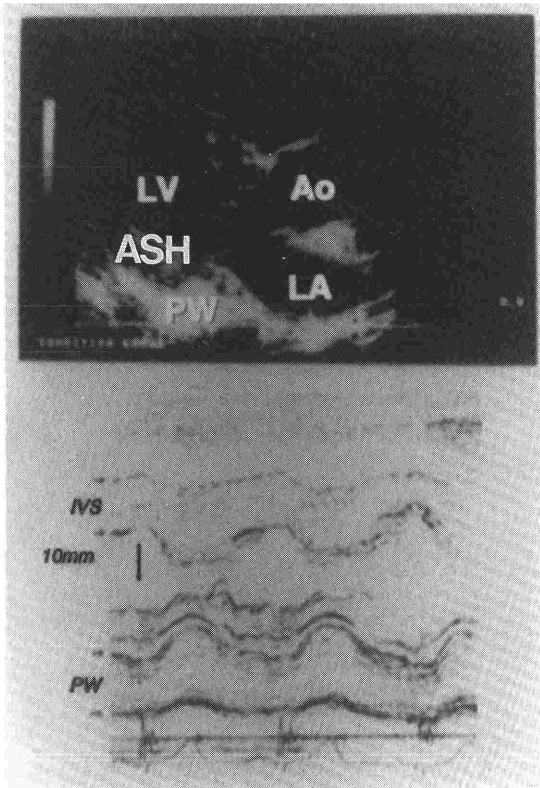

Figure 1 Transthoracic echocardiography displays the following features:

(upper) Echocardiography demonstrates asymmetrical hepertrophy (ASH) of the ventricular wall.

(lower) M-mode echocardiography reveals thickening of IVS and PW. The ventricular cavity is narrowed.

Abbreviations : RA = right atrium, RV = right ventricle, LA = left atrium, LV = left ventricle, LVOT = left ventricle outflow tract, MV = mitral valve IVS = intraventricular septum, PW = posterior wall,

ASH, a PG of 68 mmHg, and systolic anterior movement (SAM) of the apex of the mitral valve, indicating exacerbation of HOCM. Intravenous administration of propranolol 2 mg at this time reduced her blood pressure to 120/80 mmHg and heart rate to 98 bpm, and eliminated her chest pain within 1 min. The pressure gradient was also restored to that before loading with phentolamine, and the clinical symptoms disappeared. The results of preoperative blood and urine biochemical tests were as follows: plasma epinephrine, 0.58 ng·ml^{-1}; plasma norepinephrine, 8.7 ng·ml^{-1}; dopamine, 0.20 ng·ml^{-1}; urinary epinephrine, 70.5 μg·day^{-1}; urinary norepinephrine, 610 μg·day^{-1}; urinary dopamine, 370 μg·day^{-1}; and urinary vanilmandelic acid, 16.5 mg·day^{-1}. Except for the norepinephrine secretion-dominant rise in the catecholamine levels and a slight increase in the blood renin level, all were within normal ranges. To improve the hemodynamics, oral administration of propranolol (15 mg·day^{-1}) was initiated which controlled blood pressure within the range of 120-140/70-90 mmHg and heart rate to around 100 bpm.

Anesthetic Course

The patient was premedicated intramuscularly with scopolamine 0.4 mg, butorphanol, 1 mg and hydroxyzine 25 mg 45 min before induction of anesthesia. In the operating room, an epidural catheter was inserted via the T 10-11 interspace and advanced 8 cm cranially. Anesthesia was induced by intravenous administration of diazepam 10 mg. After tracheal intubation following vecuronium 8 mg i. v., a probe for transesophageal echocardiography (TEE) was inserted for continuous monitoring. To maintain anesthesia, 1.5 % mepivacaine was administered at the rate of 8 ml·hour^{-1} through the epidural catheter for sustained epidural anesthesia in combination with general anesthesia using oxygen, nitrous oxide, and isoflurane (0-3.0 %). At the time of anesthetic induction, intravenous infusions of propranolol 0.5 μg·kg^{-1}·hour^{-1}, nitroglycerin 0.5 μg·kg^{-1}·min^{-1}, and diltiazem 5 mg·hour^{-1} were started to stabilize blood pressure in

the range of 166-139/71-94 mmHg and heart rate at 89-112 bpm. When the tumor was manipulated, however, blood pressure and heart rate transiently increased to 228/152 mmHg and 149 bpm. Combined single intravenous administration of propranolol 1 mg and phentolamine 2 mg immediately stabilized blood pressure amd heart rate. TEE monitoring revealed that mild PG (4.5-9 mmHg) and ASH were detected; the cardiac index (CI) remained at 2.6-3.6 1. min^{-1}·m^{-2}, and hypertrophy of the cardiac wall became evident with the rise in blood pressure at the time of tumor manipulation. Narrowing of the ventricular spece, rise in CI (4.5 1·min^{-1}·m^{-2}), and an increase in PG (21 mmHg) were also observed (Fig. 2). A single intravenous injection of phentolamine and propranolol given immediately after these reactions developed the reduced PG to 9 mmHg and blood pressure to the previous levels. After tumor resection, transient hypotension was noted, and was adequately controled by lactated Ringer's solution, transfusion, and intravenous infusion of a small amount of norepinephrine (0.1 μg·kg^{-1}·min^{-1}). TEE showed satisfactory maintenance of CI, ASH remained unchanged, and PG was reduced below 1 mmHg.

Figure 2 Transesophageal echo four-chamber imaging shows the following : during manipulation of pheochromocytoma, the peak left ventricular outflow tract pressure gradient (PG) was 21 mmHg.

The postoperative course was uneventful. The blood and urinary catecholamine levels were returned to the normal range and clinical symptoms disapeared wihtin 1 week postoperatively. Cardiac function was followed up with periodic echocardiography. Approximately 3 months after surgery, ASH was not observed and echocardiographic findings were normal. No findings suggestive of HCM were noted in a phentolamine provocation test during echocardiography that was conducted 6 months after surgery.

Discussion

Pheochromocytoma[1,2,4] secreted catecholamines produces various complications, in particular, serious cardiovascular symptoms including arrhythmia, myocardial infarction, cardiomyopathy, cerebrovascular disturbance, and dissecting aortic aneurysm. The following factors are involved in the development of these conditions: the release of catecholamines from the tumor and the resultant increase in myocardial oxygen consumption; reduction in myocardial energy effeciency; development of regional myocardial degeneration and hypertrophy enhanced by increased in myocardial protein synthesis; vascular contraction; and hyperplasia and excessive lipid deposits in the arterial endothelium[4,8].

In the present case, catecholamine-induced cardiomyopathy characteristics of HOCM was diagnosed by preoperative tests. For both hemodynamic and pharmacological evaluation, a phentolamine loading test was conducted under echocardiography. Consequently, it was found that administration of phentolamine was associated with hypotension. At the same time, however, a rapid increase in PG and echocardiographic presentation of SAM were noted together with chest pain, all of which were immediately eliminated by administration of a beta-adrenoceptor antagonist. These phenomena were controlled by an alpha-adrenoceptor antagonist before and after loading, indicating that the relative beta-activity-dominant state was responsible for obstruction of the left ventricular outflow tract.
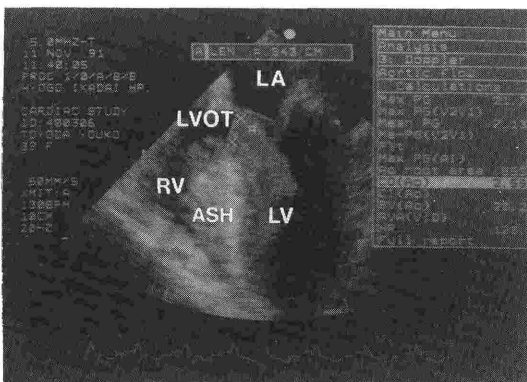
The important considerations in the anesthetic management of pheochromocytoma during surgical removal include maximal suppression of catecholamine secretion from the tumor, real-time observation of the effects of catecholamines on the cardiovascular system, especially the marked changes in hemodynamics during tumor manipulation and immediately after tumor removal, and swift and appropriate management of such hemodynamic responses[9]. There are many reports on anesthetic management[10,11], and on the efficacy of agents which act on the circulatory system (such as calcium antagonists and alpha-and beta-adrenoceptor antagonists)[12~16] and on circulatory monito-ring. [17,18]

In general, echocardiography is useful for qualitative as well as quantitative evaluation of cardiomyopathy.[19,20] We conducted real-time monitoring by 2DE-TEE during surgery. As shown in Fig. 2, stenosis of the left ventricular outflow tract became evident concomitantly with the rise in blood pressure and the increase in heart rate caused by the marked rise in catecholamine secretion during tumor manipulation. However, these changes were corrected immediately and hemodynamic variables were normalized by an intravenous injection of phentolamine and propranolol. It is also noteworthy that continued observation of the movement of the ventricular wall by TEE enabled us to diagnose myocardial ischemia and detect left ventricular dysfunction before any abnormalities were apparent on pressure wave patterns of pulmonary artery pressure[21].

Previous studies have described the reversal of catecholamine-induced cardiomyopathy after normalization of the plasma catecholamine levels following tumor removal[5,6]. However, the findings vary with respect to the timing of the disappearance of clinical symptoms of cardiomyopathy, heart murmurs, electrocardiographic features, and echocardiographic findings. The TEE findings in the present case were generally normal during and immediately after surgery with the exception of ASH, which persisted for approximately 3 months.

Mohamed et al[22]. reported a case of pheochromocytoma complicated with HCM with echocardiographic features of ASH, SAM, and incomplete closure of the aortic valve at the mid-systole phase. They found that despite normalization of the catecholamine level within 10 days of tumor removal, echocardiography 3 months later revealed presistence of the preoperative features, and, that 23 months after surgery the findings were almost normal except for very slight SAM and incomplete closure of the aortic valve at mid-systole. Although the reason for the differences in the timing of the disappearance of these signs is not clear, it is thought that catecholamines enhance myocardial protein synthesis, thus causing regional myocardial degeneration and myocardial hypertrophy[4,8]. Thus, myocardial degeneration is likely to show irreversible changes, and these changes appear to be proportional to the time lag between tumor development and tumor removal and to the blood catecholamine levels. Therefore, as soon as a diagnosis of pheochromocytoma is confirmed, echocardiographic examination should be performed to detect cardiovascular complications, and then the tumor should be excised. Echocardiographic examinations should be conducted periodically during and after surgery to evaluate cardiac function.

In summary, we employed TEE to aid in the circulatory management during anesthesia and surgery in a patient with pheochromocytoma complicated with HOCM. Intraoperative TEE monitoring facilitated visualization of left ventricular contractile function and the LV outflow tract. This technique was found to be more useful than pulmonary artery pressure. We also confirmed that the myocardium does not return to the normal state immediately after surgery but requires a long time for recovery. Accordingly, postoperative follow-up of catecholamine-induced cardiomyopathy by echocardiography is essential.

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