REVERSIBLE LEFT VENTRICULAR WALL MOTION IMPAIRMENT CAUSED BY PHEOCHROMOCYTOMA

—A Case Report—

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Excessive catecholamine levels can cause myocardial damage in experimental animals. Similar observations have been made in humans following autopsy for pheochromocytoma. However, whether catecholamine crises are reversible or not remains uncertain. We report here a case in which pheochromocytoma manifested as acute pulmonary edema during an operation. Serial echocardiograms revealed that the depressed motion of the left ventricular wall was reversed after tumor removal. The plasma catecholamine level was extraordinarily high during the episode of acute pulmonary edema, and it seems that catecholamines in high concentration can directly damage the myocardium.

Acute pulmonary edema is a rare complication of pheochromocytoma. It is not yet clear whether the etiology of the pulmonary edema is depressed myocardial contractility (due either to coronary or metabolic factors), afterload mismatch or increased permeability of the pulmonary vascular bed, or a combination of these factors.1-4

In a patient with pheochromocytoma, we obtained serial echocardiograms during episodes of pulmonary edema. The possible causes of depressed left ventricular motion are also discussed.

CASE REPORT

The patient was a 44-year-old woman for whom an elective oophorectomy had been scheduled on Feb. 20 1986 because of adnexal tumor. Electrocardiogram (ECG) and chest films taken before the operation were normal, and there was no history of hypertension. Spinal anesthesia was performed in a routine manner, using 2 ml dibucaine access at L3-L4. As the systolic blood pressure fell to 70 mmHg, ephedrin and chlorpropamide were injected intravenously. Soon after, the blood pressure increased to 200/100 mmHg and signs of acute pulmonary edema developed. The patient coughed up copious amounts of foamy sputum, was promptly intubated and transferred to the intensive care unit. The mean pulmonary arterial pressure was around 15 mmHg and cardiac output was markedly decreased to 1.8 L/min. An intra-aortic balloon pump was inserted because of cardiogenic shock. Echocardiography revealed a diffusely and severely hypokinetic left ventricle without chamber enlargement (Fig. 1). Chest films documented the changes occurring typical of pulmonary edema (Fig. 2). Dopamine and dobutamine did not produce an increase in the blood pressure and her general condition deterio-
rated. The hematocrit was abnormally high (55%), so a large amount of normal saline was infused. Nine hours after the start of this episode, the patient’s hemodynamic condition stabilized and the motion of the base of the left ventricle was noted to improve. The peak creatine kinase (CK) value was 3520 U and the MB fraction was 6%.

Serial ECG changes are shown in Fig. 3. On Feb 21 elevation of the ST segment was seen in leads V2 to V6, very similar in appearance to acute anteroseptal infarction.

An abdominal CT scan revealed a right adrenal mass. Since the plasma catecholamine levels were high, a diagnosis of pheochromocytoma was made. Propranolol and prazocin were administered and tumor resection was scheduled to be performed as soon as the left ventricular wall motion returned to normal. However, on March 20 acute pulmonary edema developed suddenly after the patient had been straining. Several doses of phenoxybenzamine and propranolol

were injected without benefit. Although the patient coughed up foamy sputum, the pulmonary arterial pressure was not high (see clinical course in Table I). Poor left ventricular wall motion was again evident on echocardiography. While the tumor remained in situ we could not expect hemodynamic improvement, so the operation was performed the next day. The histological appearance of the excised adrenal tumor confirmed the diagnosis of pheochromocytoma (Fig. 4). After surgery, the left ventricular wall motion returned to normal very rapidly, except for a hypokinetic area at the apex.

Cardiac catheterization one month after the operation showed normal coronary arteries (Fig. 5) and a normal left ventricular ejection fraction (67%). Right ventricular biopsy showed moderate fibrosis with a slight mononuclear cell infiltration.

**DISCUSSION**

Various myocardial lesions have been reported in experimental animals and in humans who received catecholamines for long periods. Van Vliet et al. reported 26 autopsies of pheochromocytoma patients. Of the 26 patients, 15 had active myocarditis and was the cause of death in 11 of the 15. James examined 3 cases of fatal myocarditis associated with pheochromocytoma, reporting the widespread prevalence of small foci of damage throughout the myocardium. Platelet aggregates were seen plugging the lumens of the small coronary arteries. McManus et al. reported diffuse infiltration of the myocardium by mononuclear cells and the presence of contraction band necrosis in one autopsy case. They stated that if the tumor could have been resected before catecholamine crisis, the patient would not have died. Once catecholamine crisis...
## TABLE I CLINICAL COURSE OF THIS PATIENT

<table>
<thead>
<tr>
<th>Date</th>
<th>NE (pg/ml)*</th>
<th>E (pg/ml)*</th>
<th>DA (pg/ml)*</th>
<th>Acute Pulmonary Edema (1st)</th>
<th>Acute Pulmonary Edema (2nd)</th>
<th>Resection of Tumor</th>
<th>Acute Pulmonary Edema (3rd)</th>
<th>Oophorectomy</th>
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### Plasma Catecholamine Levels

*Plasma catecholamine levels were slightly elevated before oophorectomy; extraordinarily high levels of catecholamines were seen during the 3rd episode of acute pulmonary edema."

**Abbreviations:** NE = norepinephrine; E = epinephrine; DA = dopamine; Dd = left ventricular end-diastolic dimension; Ds = left ventricular end-systolic dimension; %FS = percent fractional shortening; PA = pulmonary artery (s: systolic, d: diastolic, m: mean); AO = central aorta; CO = cardiac output

* = normal range

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Our case was characterized by the sudden onset of acute pulmonary edema, a high hematocrit value and severely impaired left ventricular wall motion. Episodes of acute pulmonary edema developed twice more while the patient was a waiting surgery, each on occasion accompanied by markedly elevated plasma and urinary catecholamine levels. No drugs, including propranolol and phenoxybenzamine, were able to alter the clinical course. During the third episode of pulmonary edema, the plasma catecholamine levels were extraordinarily high, and despite the prior administration of alpha-and beta-blockers acute pulmonary edema developed with a low pulmonary arterial pressure. Deterioration of left ventricular wall motion, however, was less severe than during the first episode.

After removal of the tumor, left ventricular wall motion improved rapidly; such impairment had clearly been dependent on plasma catecholamine levels.

Depressed contractility due to coronary events, metabolic disorders, or afterload mismatch can lead to decreased left ventricular wall motion. Initially, in this patient acute extensive anteroseptal myocardial infarction with shock was suspected because of the ECG changes, the echocardiogram and the increased CK level. The serial ECG changes were similar to those of acute myocardial infarction, as previously reported; but new Q waves did not develop. The hemodynamic status became stable 9 hours after this episode and left ventricular wall motion improved gradually on echocardiography.

Although excessive catecholamines can induce coronary vasoconstriction in rabbits, we think...
Fig. 4. Coronary angiograms. There was no significant stenosis.

Fig. 5. Histology of adrenal tumor; The cells are arranged in either large trabeculae or in small alveoli, each surrounded by fibrovascular stroma. Cellular and nuclear pleomorphism are noted. (Hematoxylin/Eosin staining, original magnification x 500)
the above findings mitigate against spasm of the major coronary arteries as an explanation.

During the third attack of acute pulmonary edema, we obtained accurate hemodynamic data: systolic pressure was not high and the left ventricular cavity size was normal, indicating a normal afterload. Afterload mismatch might have been an initiating factor in this case but it was not a major cause of the pulmonary edema. Increased permeability of the pulmonary vascular bed due to excessive catecholamines may be one possible explanation of the low pulmonary arterial pressure concurrent with the pulmonary edema.

In retrospect, it was evident from the clinical course that the plasma catecholamine levels and left ventricular wall motion were strongly interdependent.

Characteristic echocardiographic findings in pheochromocytoma, such as reversible dynamic outflow obstruction,\textsuperscript{13} have been reported. The majority of pheochromocytoma cases, however, have had normal echocardiograms.\textsuperscript{14} Concentric hypertrophy, which seems to be a process of adaptation to long-standing hypertension, is seen in a small percentage of cases of pheochromocytoma.\textsuperscript{15} Extraordinarily high doses of catecholamines can damage the myocardium directly. This so-called “catecholamine cardiotoxicity” is a phenomenon very different from other reported cases.

REFERENCES
5. KLINE IK: Myocardial association with pheochromocytoma. \textit{Am J Pathol} 38: 539, 1960
9. JAMES TN: De Subitaneis Mortibus XIX. On the cause of sudden death in pheochromocytoma, with special reference to the pulmonary arteries, the cardiac conduction system, and the aggregation of platelets. \textit{Circulation} 54: 348, 1976