Case reports

A rare cause of cardiogenic shock: catecholamine cardiomyopathy of pheochromocytoma

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Pheochromocytoma is a rare catecholamine secreting tumor that accounts for about 0.04% of cases of hypertension. Other less common cardiovascular manifestations such as arrhythmias, angina pectoris, acute myocardial infarction, dilated cardiomyopathy, acute heart failure, and cardiogenic shock have occasionally been reported. We describe the case of a 32-year-old previously healthy male patient who died of cardiogenic shock within 10 hours of admission. *Postmortem* examination showed a catecholamine cardiomyopathy and a pheochromocytoma of the right adrenal gland. Pheochromocytoma with predominant epinephrine or dopamine secretion may take a hypotensive course. Sudden excessive catecholamine release can, as in the described case, cause cardiogenic shock.

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Introduction

Pheochromocytoma is a rare neuroendocrine tumor derived from the enterochromaffin cells that usually causes paroxysmal or sustained hypertension. Other less common cardiovascular manifestations have occasionally been documented: acute heart failure, myocardial infarction, angina pectoris, arrhythmias, and dilated cardiomyopathy[1].

We describe the case of a patient with no previous specific symptomatology who died of cardiogenic shock. Dilated cardiomyopathy was diagnosed at echocardiography. At autopsy a pheochromocytoma of the right adrenal gland was found.

Case report

A 32-year-old man with a history of palpitations and headache since 15 days was admitted to the emergency unit of our hospital. At the time of admission, he was tachycardic (heart rate 130 b/min) and tachypneic (respiratory rate 36/min). His blood pressure was 170/110 mmHg. Heart and lung examination was unremarkable. The electrocardiogram showed sinus tachycardia with no evidence of ischemia or left ventricular hypertrophy. Immediately after admission, the patient developed acute pulmonary edema and his blood pressure fell to 70/undeterminable. A new S3 gallop was noted and there were widespread crepitations in both lung fields. His respiratory and heart rates were respectively 38/min and 170 b/min. Arterial blood gas analysis revealed pO_2 35 mmHg, pCO_2 38.5 mmHg, pH 7.3. At pulse oximetry, the oxygen saturation was found to be 59%. One hundred percent oxygen was immediately administered via a non re-breathing mask and his blood pressure again rose to 160/120 mmHg. An echocardiogram showed left ventricular dilation, a normal thickness of the left ventricular wall and septum and a severely impaired systolic function (ejection fraction 20%). He was intubated and transferred to the medical intensive care unit.

Mechanical ventilation and dobutamine infusion were started and during the early hours the patient's conditions transitorily improved. Nevertheless, his blood pressure was labile and hypertensive and hypotensive crises continuously alternated. The white cell count (14.7 × 10.9/l) and the serum levels of creatine kinase (CK 711 IU/l, normal < 200 IU/l), CK-MB (53 IU/l, normal < 6% CK), lactic dehydrogenase

(534 IU/l, normal < 440 IU/l), troponin I (6.72 ng/l, normal < 0.50 ng/l) and myoglobin (590 ng/l, normal < 92 ng/l) were increased. Viral antibody determination was within normal limits; the urinary concentrations of norepinephrine, epinephrine and vanilmandelic acid were also assayed.

Chest tomography was normal but a computed tomography of the abdomen revealed a solid mass (9 cm in diameter) of the right adrenal gland with a pericapsule and a retroperitoneal hematoma (Fig. 1).

In the meantime the patient's conditions progressively deteriorated because of persistent hypertensive-hypotensive crises with acute pulmonary edema, despite continuous infusion of dobutamine and nitroprusside. The urinary catecholamine levels were: norepinephrine 277 μg/die (normal 12.0 to 85.0 μg/24 hours), epinephrine 717 μg/die (normal 2.0 to 25.0 μg/24 hours), vanilmandelic acid 51.2 mg/die (normal 1.5 to 7.0 mg/24 hours), and dopamine 86 μg/die (normal 120 to 420 μg/24 hours).

The patient was transferred to the operating room but despite full cardiopulmonary support he died of cardiogenic shock within 10 hours of admission.

At necropsy the heart weighed 330 g (normal 250-400 g) and left ventricular dilation and hypertrophy (the thickness of the left ventricular wall was 2.1 cm) were confirmed. No significant lesions were found in the coronary arteries and histological examination of the heart revealed focal lymphocytic infiltration (Fig. 2), foci of myocardial necrosis with features characteristic of contraction bands (Fig. 3), and some areas of fibrosis (Fig. 4). Both lungs were edematous. A tumor measuring 8 × 9 cm was found in the right adrenal gland. Histology confirmed the diagnosis of a pheochromocytoma with hemorrhagic and necrotic areas (Fig. 5).

Discussion

The commonest manifestations of pheochromocytoma are paroxysmal or sustained hypertension or symptoms of paroxysmal adrenergic stimulation, such as palpitations, headache, anxiety, sweating, and tremors. Rarer presentations, such as acute abdomen, cerebrovascular events, myocardial infarction, acute heart failure and cardiogenic shock, have also been reported[1].

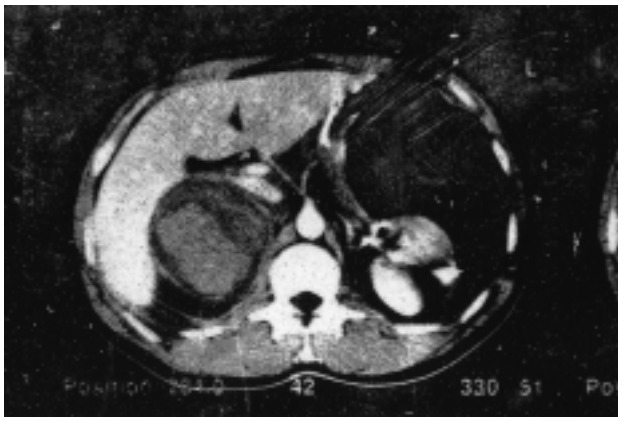

Figure 1. *Pheochromocytoma of the right adrenal gland at the abdominal computed tomographic scan.*

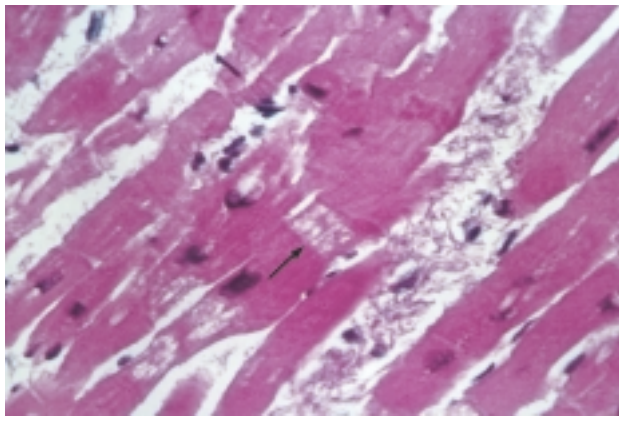

Figure 3. *Hematoxylin-eosin stained section. The* arrow *indicates focal myocardial necrosis with the features characteristic of contraction bands.*

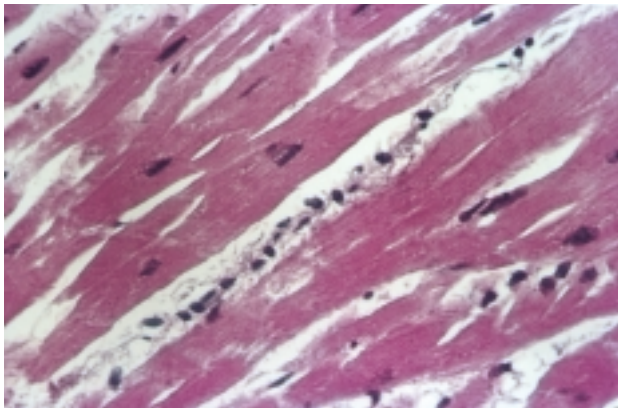

Figure 2. *Hematoxylin-eosin stained section showing focal lymphocytic infiltration surrounding normal myofibers.*

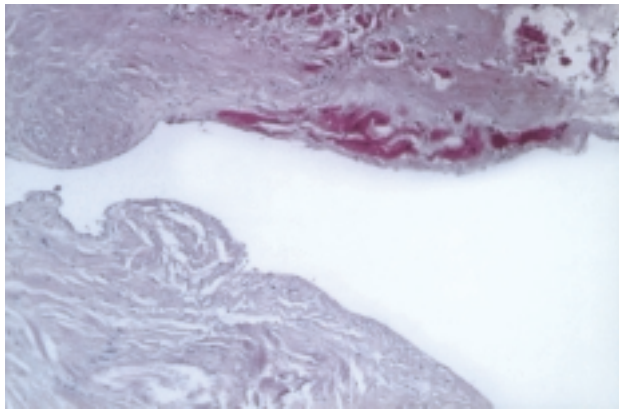

Figure 4. *Hematoxylin-eosin stained section. Subendocardial areas of fibrosis were present.*

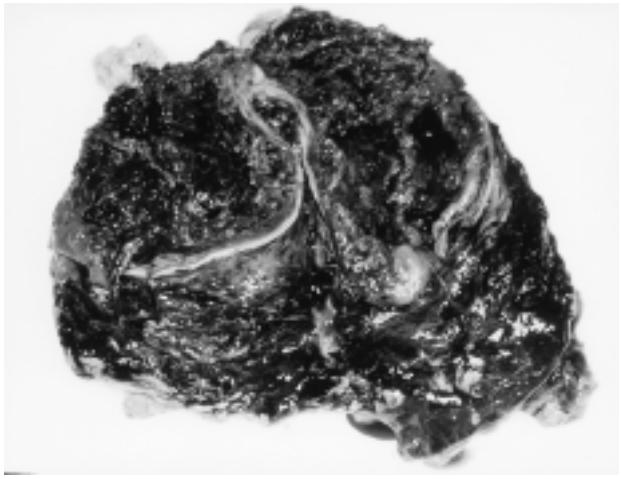

Figure 5. *The tumor (8 × 9 cm in diameters) contained areas of hemorrhage and necrosis.*

Pheochromocytoma accounts for about 0.04% of cases of hypertension, but there is a distinct group of patients with pheochromocytoma who remain normotensive (30% of cases) despite active metabolite secretion[2]. Sometimes the high blood pressure may fall back to normal values because of myocardial damage[3]. On the other hand, normotensive patients who do not have paroxysmal symptoms are more likely to die as a result of catecholamine-induced cardiomyopathy because the presence of the tumor is not suspected[4]. Although rarely, the clinical manifestations of pheochromocytoma may include hypotension and shock, particularly when epinephrine or dopamine are secreted[5].

It is some time that cardiovascular injury by sympathomimetic amines has been demonstrated in both human and experimental studies[6]. The histologic pattern of the initial lesions includes foci of myocardial necrosis with the features characteristic of contraction bands and surrounding lymphocyte infiltration; more advanced lesions have more replacement fibrosis[7].

Studies relating to catecholamine-induced cardiomyopathy have shown a global reduction in myocardial pump function caused by a combination of down-regulated β receptors and a net reduction in viable myofibrils[8]. The pathogenesis of catecholamine-induced cardiomyopathy is probably multifactorial.

Some observations have suggested that the cardiotoxicity of catecholamines is mediated by α_1-adrenergic receptor stimulation[9] with vasospasm of the coronary vessels causing ischemia[10]. In fact, as confirmed at histology, prior treatment with the α-blocker prazosin reduces the extent of the cardiac lesions[9].

On the other hand, a different hypothesis has suggested that the increased norepinephrine concentrations also induce changes in the permeability of the sarcolemmal membrane leading to increased calcium influx. This excess intracellular calcium has a direct toxic action giving rise to cellular necrosis[11,12]. Furthermore, there is evidence that the oxidized products of catecholamines[12] and other free radicals may contribute to the cardiac lesions[13].

In the literature there are many case reports of pheochromocytoma-induced cardiomyopathy. In patients presenting with acute heart failure the prognosis can be very poor because of extensive or irreversible focal myocardial necrosis[1]. On the basis of this observation an early diagnosis is very important since surgical removal of the tumor is associated with a reversal of the myocardial damage[14]. Conversely, the reversibility of a catecholamine-induced cardiomyopathy with medical treatment has been only rarely reported[15]. Our case may be added to the foregoing reports, but we believe that it has some peculiar characteristics.

While it is known that the first manifestation of pheochromocytoma may be acute congestive heart failure, a series of 6 such patients had morphologically normal hearts at necropsy[1]. On the contrary, our patient had a markedly dilated and impaired left ventricular function since the onset of symptoms.

We believe that hemorrhagic necrosis of the tumor resulted in a massive release of catecholamines which led to the patient's initial hypertension and subsequent hypotension and cardiogenic shock[16]. Furthermore, as in our case, the outcome with hypotension and shock has been particularly reported in the presence of an epinephrine-secreting tumor (717 μg/24 hours)[5,17]. Our experience indicates that pheochromocytoma can cause a clinically relevant catecholamine-induced cardiomyopathy and acute heart failure with cardiogenic shock. In patients presenting with heart failure without any obvious cause, the diagnosis of pheochromocytoma should be always taken into consideration.

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