Pheochromocytoma associated with apical-sparing left ventricular dysfunction due to acute afterload mismatch: A novel clinical entity?

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The case of a patient with pheochromocytoma who presented with an unusual pattern of left ventricular dysfunction not previously described is reported. Although a triad of headaches, sweating attacks and palpitations is generally recognized as the classic mode of presentation of this pathology, this patient first presented with shock and pulmonary edema. Moreover, both echocardiography and angiography showed severe basal and mid-ventricular left ventricular dysfunction but preserved apical contractility. This hitherto unidentified finding was interpreted as being due to an afterload mismatch, rather than to an intrinsic myocardial injury, as is usually reported in such cases.

Key Words: Catecholamines; Cardiomyopathy; Shock

CASE PRESENTATION

A 46-year-old man presented at a general hospital for a screening colonoscopy because of a positive familial history of colorectal cancer. His past history included glucose intolerance (managed with diet), dyslipidemia and high blood pressure. He had no history or symptoms of coronary artery disease. Before the colonoscopy, he received small doses of midazolam and fentanyl. At the end of the procedure, he developed cough and hemoptysis. Oxygen saturation was 90% to 92% and blood pressure 85/50 mmHg; jugular venous pressure was high and there were bilateral pulmonary rales.

Electrocardiography showed sinus tachycardia (110 beats/min), with no signs of ischemia; chest x-ray did not show bilateral alveolar infiltrates. A quick-look, bedside echocardiogram showed diffuse left ventricular (LV) dysfunction. The examination was repeated at Laval Hospital (Sainte-Foy, Quebec) and showed severe dysfunction of the base and middle portions of the LV, but surprisingly, apical contraction appeared to be spared, and the ejection fraction was 18%. Emergent coronary arteriography was performed and showed 90% stenosis of the distal third of a dominant right coronary artery (RCA) and nonsignificant irregularities on the left anterior descending coronary artery. During the procedure, arterial blood pressure dropped markedly; an intra-aortic balloon pump was inserted, and treatment with intravenous

Phéochromocytome associé à un dysfonctionnement ventriculaire gauche avec épargne apicale, dû à un déséquilibre aigu de la postcharge : Nouvelle entité clinique ?

Voici la description d'un cas de phéochromocytome chez un patient présentant une forme inhabituelle de dysfonctionnement ventriculaire gauche jamais décrit jusqu'à maintenant. Bien que la triade : céphalées, sudation et palpitations, soit généralement reconnue comme le tableau classique de l'affection, c'est en état de choc accompagné d'œdème pulmonaire que s'est présenté le patient. De plus, tant l'échocardiographie que l'angiographie montraient un dysfonctionnement ventriculaire gauche basal et médio-ventriculaire important mais une bonne contractilité apicale. Le tableau jusqu'alors inconnu a été interprété comme un signe de déséquilibre de la postcharge plutôt que comme une lésion myocardique intrinsèque, ce qui est généralement noté en pareil cas.

Figure 1) Left ventricular angiography showing severe left ventricular dysfunction with preserved contractility of the apex, which was hyperkinetic. **A** End-diastolic view; **B** Mid-systolic view; **C** End-systolic view

dobutamine and norepinephrine was instituted. Consistent with the echocardiogram, LV angiography showed severe LV dysfunction but with preserved contractility of the apex, which was actually hyperkinetic (Figure 1). Because of the hemodynamic instability, angioplasty with stent deployment was performed on the RCA. Nonetheless, given the disproportion between the coronary lesions and the status of LV function, the working diagnosis became fulminant myocarditis.

Twenty-four hours after admission, the patient's status improved significantly; surprisingly, a repeat echocardiogram showed near-normal LV systolic function, with an ejection fraction of 50%. However, a few hours later and within minutes after

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the final tapering of the intravenous inotropic drugs, the patient's blood pressure became very unstable (systolic blood pressure up to 290 mmHg and as low as 45 mmHg), and he complained of general discomfort, palpitations and shortness of breath; there were five such episodes lasting approximately 5 min each. Pheochromocytoma was then suspected, and treatment consisted of multiple boluses of 0.9% sodium chloride (up to 4 L) and an intravenous phentolamine infusion. Prazosin (1 mg twice daily) was also introduced as a bridge to phenoxybenzamine (10 mg twice daily). Abdominal computed tomography showed a 4 cm left suprarenal mass. An iodine-131-meta-iodobenzylguanidine scan demonstrated uptake by a left adrenal mass. Urine epinephrine and total catecholamines levels were 1285 nmol/day (normal less than 175 nmol/day) and 1812 nmol/day, respectively (normal less than 975 nmol/day), while urine metanephrine and normetanephrine levels were 40,236 nmol/day (normal less than 15,000 nmol/day) and 14,995 nmol/day respectively (normal less than 2600 nmol/day). The patient was weaned from the phentolamine infusion, and propranolol (10 mg three times daily) was introduced. On day 20, the patient underwent successful resection of the tumour without interruption of clopidogrel, and pheochromocytoma was histologically confirmed. A third echocardiogram performed three days after surgery showed normal LV systolic function.

DISCUSSION

Although a triad of headaches, sweating attacks and palpitations is generally recognized as the classic mode of presentation of pheochromocytoma, our patient first presented with shock and pulmonary edema. Schifferdecker et al (1) have reviewed the pathophysiology of pheochromocytoma-induced shock, which includes decreased cardiac output and intravascular hypovolemia. The decrease in cardiac output is deemed to be due to catecholamine-induced myocardial injury with systolic dysfunction, myocardial stunning, leukocyte cardiac infiltration, fibrosis, necrosis or vasospasm (1). The myocardial injury may mimic that of myocardial infarction (2).

Our patient, however, presented with a very different pattern of LV dysfunction, that is, with severe basal and mid-ventricular hypokinesia but preserved apical contractility. Moreover, contrary to impaired function due to myocardial injury, this pattern of dysfunction was rapidly reversible. To our knowledge, there is only one report in the literature reporting such a pattern of LV dysfunction in a case of pheochromocytoma (1); as a possible explanation, the authors proposed a subarachnoid hemorrhage cardiomyopathy-like physiology.

Indeed, regional LV wall motion abnormalities, including the apical-sparing pattern, may be present in up to 57% of patients

after subarachnoid hemorrhage (3). Such anomalies are thought to be due to high levels of catecholamines released locally from myocardial sympathetic nerve fibres, and the physiopathology proposed to explain the apical sparing is based on a reduced norepinephrine content and decreased sympathetic nerve terminals at the cardiac apex (3-5). Moreover, it is reported that there is no relationship between the extent of myocardial injury and serum levels of circulating catecholamines (6). This has been corroborated by animal models showing that neurocardiogenic injuries are caused by direct release of marked local levels of catecholamines from the myocardial sympathetic nerve endings, rather than by adrenal release of catecholamines into the systemic circulation (7). Hence, this type of explanation is very unlikely in a case of pheochromocytoma, whereby the increased catecholamines at the cardiac level are due to high circulating levels and not to a release by local fibres. Moreover, it should be emphasized that the pattern of myocardial injury reported in patients with high levels of circulating catecholamines, such as in those with Takotsubo cardiomyopathy, is totally the opposite (ie, apical and mid-ventricular dysfunction, with sparing of the basal segments) (8).

Given that the aforementioned mechanisms are unsatisfactory explanations for the mode of presentation of our patient, a more likely explanation is that the observed anomaly was due to an acute afterload mismatch, rather than to myocardial injury. The fact that the LV anomaly was rapidly reversible would be consistent with this hypothesis. Moreover, McConnell et al (9) have described a similar pattern of dysfunction in the case of the right ventricle. The authors found that patients with acute pulmonary embolism and a severe increase in pulmonary arterial pressures exhibited severe dysfunction of all segments of the right ventricle except for the apex. The proposed explanation for this observation was that the acute increase in pressures results in a more spherical shape of the ventricle and, in view of Laplace's law, to an important afterload mismatch, except at the apex, where the radius of the curvature of the ventricle remains smaller, which allows better shortening of the myocardial fibres at that level. Indeed, we think that the same physiological mechanism was operational in our case, and that the rapidly reversible anomaly we observed was due to an acute afterload mismatch, rather than intrinsic myocardial injury. The initial episode, resulting in shock and pulmonary edema, was most likely triggered by an acute increase in blood pressure (measurements of up to 290 mmHg were recorded during the patient's other episodes of instability). To our knowledge, this is the first description of this type of physiopathology observed on the left side of the heart, and such an observation may be useful in future cases for earlier diagnosis.

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