Cardiac involvement may be the main clinical manifestation of a pheochromocytoma. The prognosis of catecholamine-induced cardiomyopathy associated with a pheochromocytoma depends on its early identification and medical and surgical treatment. In addition, recognition of catecholamine-induced cardiomyopathy, particularly in patients with a pheochromocytoma, is important not only because the myocardium returns to normal within a few months of treatment, but also to avoid factors that may trigger a catecholaminergic crisis.

When a pheochromocytoma is suspected, there is no agreement as to what the most accurate diagnostic test is. A multicenter study concluded that the most sensitive parameter is plasma metanephrine level (99%), followed by fractionated urinary metanephrines (97%), with statistically significant differences versus all other parameters (urinary catecholamines, 86%; plasma catecholamines, 84%; total urinary metanephrines, 77%; and vanilmandelic acid, 64%). The most specific test is measurement of vanilmandelic acid (95%), followed by levels of total urinary metanephrines, plasma metanephrines (89%), urinary catecholamines (88%), plasma catecholamines (81%), and fractionated urinary metanephrines (69%)[9]. To confirm diagnosis, hormone levels should be at least twice the upper normal limit.

A pheochromocytoma is a very serious clinical condition and, based on these results, measurements of plasma metanephrine and fractionated urinary metanephrine levels are considered to be the most sensitive biochemical tests, and are therefore the tests of choice for diagnosis in order to avoid false negative results. Measurement of fractionated urinary metanephrines was sufficient for diagnosis of our patient. However, plasma catecholamine and plasma and urine metanephrine levels were measured to compare the sensitivity and specificity of the procedure at our laboratory.

Surgery is the treatment of choice for a pheochromocytoma. Preoperative drug preparation is a key factor for mortality reduction. While it has been suggested that long-term use of alpha-adrenergic blockade with drugs such as phenoxybenzamine is not always required for surgical preparation, the effectiveness of other types of treatment such as calcium channel blockers or captopril has not been investigated in patients with coexistent pheochromocytoma and catecholamine-induced cardiomyopathy[10].

To sum up, we report a case of a pheochromocytoma with an atypical clinical presentation in which cardiac involvement with an acute coronary syndrome led to diagnosis.

Conflict of interest

The authors state that they have no conflict of interest.

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Carcinoid tumor and patent foramen ovale

Tumor carcinoide y foramen oval permeable

Carcinoid tumors are derived from neuroendocrine cells. They are uncommon (2-5 cases per 100,000 inhabitants/year)[1], but their incidence has increased in recent decades, partly as the result of increasingly perfected diagnostic procedures. Locally invasive or metastatic tumors usually cause a carcinoid syndrome. Once this is established, symptoms of heart involvement (carcinoid heart disease), generally affecting the right valves, occur in more than half of all cases[2].

We report the case of a 73-year-old male patient who attended for diarrhea and episodes of flushing and hot flashes. He had a history of smoking, arterial hypertension, diabetes mellitus, and clinically stable ischemic heart disease. Physical examination revealed facial telangiectasis,

generalized pulmonary hypoventilation, systolic murmur due to tricuspid regurgitation, splitting of the second heart sound, and non-tender nodular hepatomegaly at 10 cm from the costal margin. A complete blood count showed iron-deficient microcytic anemia, normal coagulation times and liver function, and elevated levels of tumor markers Ca 19.9 (44.5 U/mL [0.1-35]) and neuron-specific enolase (24.4 ng/mL [0.1-13]).

An abdominal ultrasound examination revealed multiple space-occupying liver lesions. Computed tomography (CT) of the chest and abdomen characterized these as solid lesions suggesting metastasis, some of them with central necrosis, but the primary tumor could not be identified. Gastroscopy and colonoscopy were unremarkable. Fine needle aspiration of liver lesions revealed cells of a neuroendocrine origin with immunohistochemistry positive for synaptophysin. Ki-67 was normal (less than 2%). Urinary 5-hydroxyindoleacetic acid levels were elevated (urinary 5-HIAA/creatinine ratio, 297.4 mg/g creatinine [0.1-10]), as were plasma levels of gastrin (244 pg/mL [13-115]) and chromogranin A (348 ng/mL [< 100])

An intestinal neuroendocrine tumor was suspected, and video capsule endoscopy (Fig. 1A) was thus performed. This showed a submucosal lesion in jejunum which did not occlude intestinal lumen and with superficial vascularization consistent with a carcinoid tumor. Disease extent and the presence of somatostatin receptors were assessed using a whole body scan and SPECT-CT with ^{111}In-DTPA-D-Phe-octreotide (Fig. 1B), which showed significant radiotracer activity in multiple areas of the liver parenchyma. This finding was highly suggestive of metastatic involvement with no evidence of extrahepatic involvement.

The patient was diagnosed as having a stage IV low-grade carcinoid tumor, based on the clinical signs and supplemental tests performed, and was prescribed treatment with somatostatin analogues to control carcinoid syndrome.

The patient had dyspnea, particularly in the standing position, which partially improved in a supine position. Arterial blood gas tests with environmental oxygen showed severe hypoxemia (pO2 47 mmHg) which did not respond to administration of 100% oxygen (pO2 70 mmHg). This suggested a right to left shunt. A CT scan of the lung and a ventilation-perfusion scan ruled out the presence of pulmonary thromboembolism. A transthoracic echocardiogram (Fig. 2A and B) showed moderate tricuspid insufficiency, moderate tricuspid stenosis, and moderate dilation of the right cardiac chambers. The left cardiac chambers were not affected. Bulging of the interatrial septum was also suggested. Transesophageal echocardiogram (Fig. 2C and D) showed a patent foramen ovale (PFO) 2 cm in diameter which allowed for a right to left intracardiac shunt.

Right cardiac catheterization ruled out the existence of pulmonary hypertension, but showed significantly increased diastolic pressures in the right chambers after balloon inflation through the PFO.

Median sternotomy and extracorporeal circulation were used to replace the tricuspid valve by a biological prosthesis and to close the PFO. The postoperative outcome was satisfactory and uneventful.

Carcinoid heart disease is due to the thickening and deformity of the heart valves, predominantly on the right side, and is one of the main causes of morbidity and mortality from right heart failure[2]. Current evidence supports the concept that heart disease is not due to direct metastatic involvement, but to the release of vasoactive substances which induce endomyocardial fibrosis[2,3]. The development of carcinoid heart disease requires the presence of liver metastases that prevent the metabolic inactivation of such substances by liver metabolism.

As regards treatment, control of humoral secretion has not been shown to induce the regression of cardiac lesions. Surgery of the primary tumor or metastases has not been shown to be curative either, once endomyocardial fibrosis is established. The treatment of choice for carcinoid heart disease is valve replacement, which improves overall patient quality of life and survival[2].

The persistence of a PFO in adults is common, with a prevalence of up to 25% in the general population. PFO is in most cases a finding with no clinical impact, but when associated with another heart condition it may cause platypnea-orthodeoxia syndrome[4], in which the patient experiences dyspnea on standing. In carcinoid heart disease it may also contribute to the occurrence of valvular and endomyocardial changes in the left cardiac chambers due to the passage of vasoactive substances through the PFO. Left involvement is exceptional in conditions other than with a PFO, and is limited to bronchial carcinoids, pulmonary metastases, or intense endocrine secretion exceeding lung clearance capacity[3,5]. The presence of a PFO has therefore even been considered as a marker of the progression of carcinoid heart disease, and some authors have suggested that is should routinely be searched for in patients with carcinoid syndrome[6].

The "bubble test" using transthoracic echocardiography is recommended for this purpose[6]. But if there is a high clinical suspicion, e.g. because of the presence of platypnea-orthodeoxia syndrome, as occurred in our patient, and transthoracic echocardiography is not conclusive, some authors suggest using more sensitive techniques such as transesophageal echocardiography, which provided the diagnosis in this patient, or transcranial Doppler[7].

When a PFO and carcinoid heart disease coexist, PFO closure may improve dyspnea and hypoxemia if associated with tricuspid valve replacement. This avoids progressive right atrial dilation, resolves the PFO, and prevents increased pulmonary hypertension. If this dual intervention is not performed, right ventricular filling restriction, and thus left heart failure, could worsen. In addition, left ventricular preload could decrease and cause an additional low-output left heart failure[8].

The few series reported to date state that in patients with carcinoid heart disease and a PFO, dyspnea significantly improves after the dual intervention described. This also occurred in our patient. However, some authors suggest that there may be some residual intracardiac shunt, so that the possibility of left heart involvement in the future cannot be ruled out[9].

Thus, although carcinoid tumors are diagnosed in advanced stages when extensive systemic involvement has

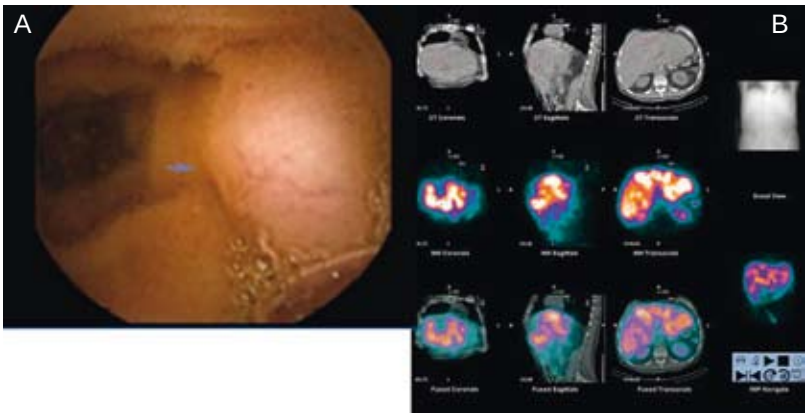

Figure 1 A) Video capsule endoscopy. B) SPECT-CT with ^{111}In-DTPA-D-Phe-octreotide.

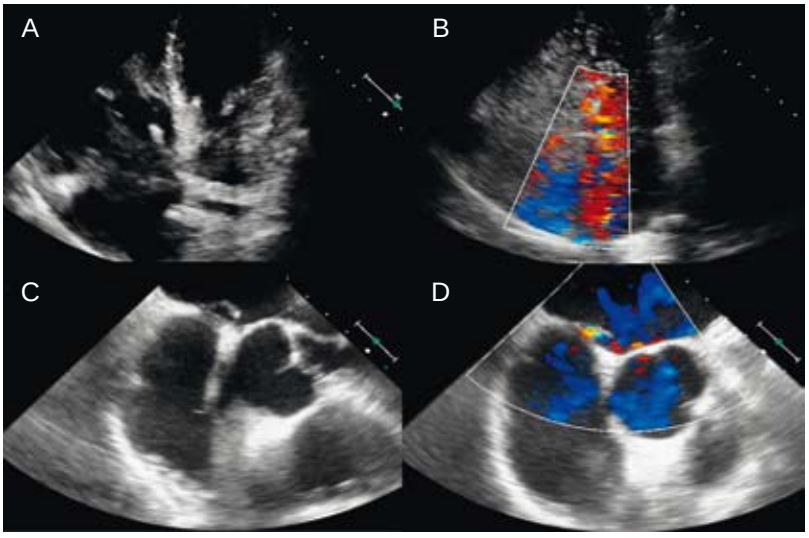

Figure 2 A and B) Transthoracic echocardiogram. C and D) Transesophageal echocardiogram.

already occurred, as in the case here reported, medical treatment should be maintained because it improves the symptoms of carcinoid syndrome[10]. Carcinoid heart disease should also be resolved, but the presence of a PFO, highly prevalent in the general population, should mandatorily be ruled out first. Current clinical guidelines recommend the use of transthoracic echocardiography[6]. However, when this is not conclusive and there is a high clinical suspicion, we suggest using other, more sensitive procedures such as those previously mentioned. Thus, if there is a PFO, closure of this together with valve replacement will be required to achieve a higher overall survival rate. Failure to identify the PFO and valve surgery alone may impair patient prognosis.

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