Cardiac Paraganglioma: Advantages of Cardiovascular Multimodality Imaging

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INTRODUCTION

Primary cardiac tumors are very rare. The reported prevalence ranges from 0.001% to 0.03%. Cardiac paragangliomas are among the most infrequent tumors, making up <1% of all primary cardiac tumors.[1] They are chromaffin cell tumors that produce and secrete catecholamines and are located in the adrenal medulla in 90% of cases and in the mediastinum in <2%.[2]

CASE PRESENTATION

We present a case of cardiac paraganglioma with left coronary artery involvement.

The patient was a 22-year-old woman with a clinical history of recurrent episodes of palpitations, diaphoresis, and headache. She was found to have high blood pressure and, because of her age, several studies were done looking for secondary hypertension. Results of transthoracic echocardiography and renal Doppler imaging were normal, and plasma and urine metanephrine levels were within normal limits. Ambulatory blood pressure monitoring found severe hypertension, and the patient started treatment with angiotensin receptor blockers. After 2 years, she continued to have the same symptoms, but at this time, a mesocardial systolic murmur with back irradiation was found on auscultation. New transthoracic echocardiography showed high velocities in the pulmonary artery and a mass with intermediate echogenicity located at the base of the heart in close relation to the aorta and the pulmonary artery, extending into the left atrioventricular groove (Figure 1, Videos 1 and 2). Free metanephrines in plasma (noradrenaline 4,886.67 pg/mL) and urine (noradrenaline 1,426.9 μg/24 h) were high.

To obtain better characterization, cardiac magnetic resonance was performed and showed a middle mediastinal mass located in the left atrioventricular groove, extending posteriorly to the left atrial roof and almost surrounding the pulmonary artery anteriorly. The mass was closely associated with the aortic root, but the emergence and path of the left coronary artery and its branches were not adequately visualized (Figure 2). Tissue characterization sequences showed a mass with a heterogeneous appearance on T2-weighted sequences and slightly hyperintense on T1-weighted and T2 with fat saturation sequences (Figure 2). Important mass vascularization was demonstrated with the perfusion sequence, which showed rapid uptake of contrast shortly after its administration. We also found focal late gadolinium enhancement at the periphery of the mass, with no enhancement at its center, a finding that was considered highly suggestive of a paraganglioma (Figure 3). Fluorine-18 fluorodeoxyglucose positron emission tomography was also performed, demonstrating a highly metabolic mass (Figure 4).

The case was discussed with the heart team and other departments, such as endocrinology and oncology, concluding that the patient had a clear indication for surgery, with α- and β-blockade, high sodium intake, and adequate hydration before the procedure. However, given that there were doubts regarding the emergence of the left coronary artery and its pathway, coronary angiotomography was performed. The mass was found to surround the left main coronary artery, the proximal segment of the left anterior descending coronary artery, the circumflex coronary artery, and two septal arteries, as well as the great cardiac vein (Figures 5–7). At that time, and because of these findings, the intervention was considered to be a high-risk procedure. Isotopic radiation with ^{131}I meta-iodine benzyl guanidine (MIBG) was considered as a palliative intervention, but this approach was rejected because of the risk for hypertensive crises of unpredictable severity. Another approach that was considered was the use of octeotride, but this alternative was not accepted by the multidisciplinary group, because there was a risk for irradiation of adjacent tissue, including the coronary arteries, with an unknown benefit. The risk/benefit assessment of this therapy did not favor the patient either, and surgery was thought to be the only option. Coronary angiography was done looking for a main feeding artery that could be embolized preoperatively to reduce the tumor size and intraoperative blood loss. However, embolization could not be done, because there were many small feeding arteries coming from the left main coronary artery (Figure 8). The patient underwent mass resection, requiring a complete transverse arteriotomy of the ascending aorta, pulmonary trunk, and section of the superior vena cava. The mass was exposed using caudal traction and was found to be closely associated with the posterior wall of the ascending aorta, the pulmonary artery, and the left atrial roof, without infiltration of these structures. Involvement of the left coronary artery trunk was documented, which required ligation and revascularization of the anterior descending coronary artery and the circumflex coronary artery. The mass could be completely resected (Figure 9).

The patient progressed well and was able to be extubated and have her vasopressor support discontinued. Follow-up echocardiography showed that systolic function was moderately affected, with an ejection fraction of 35% and diffuse hypokinesia, which was more pronounced in the anterior descending coronary artery territory. Because of these findings, new coronary angiography was performed, ruling out saphenous bridge compromise (Figure 10). Further

From the Universidad del Rosario Escuela de Medicina y Ciencias de la Salud, Fundación Cardioinfantil, Instituto de Cardiología, Bogota, Colombia (L.A.); Fundación Cardioinfantil, Instituto de Cardiología, Bogota, Colombia (J.B., J.F., C.J.); Clínica Colombia, Bogota, Colombia (J.A.); and Fundación Clínica Shaio, Bogota, Colombia (A.C.).

Keywords: ■■■

Conflicts of interest: The authors reported no actual or potential conflicts of interest relative to this document.

2468-6441

https://doi.org/10.1016/j.case.2018.07.011

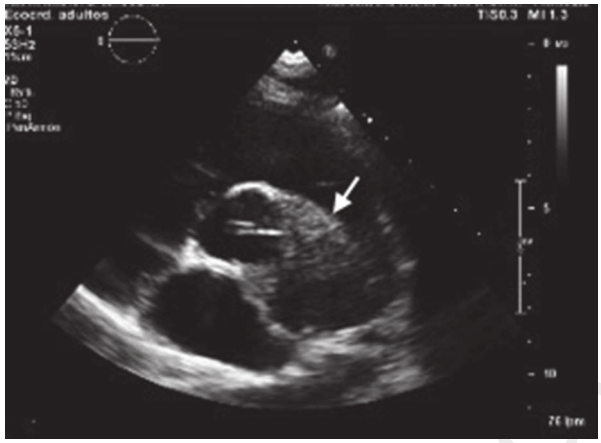

Figure 1 Transthoracic echocardiography. Mass with intermediate echogenicity in relation to the great vessels.

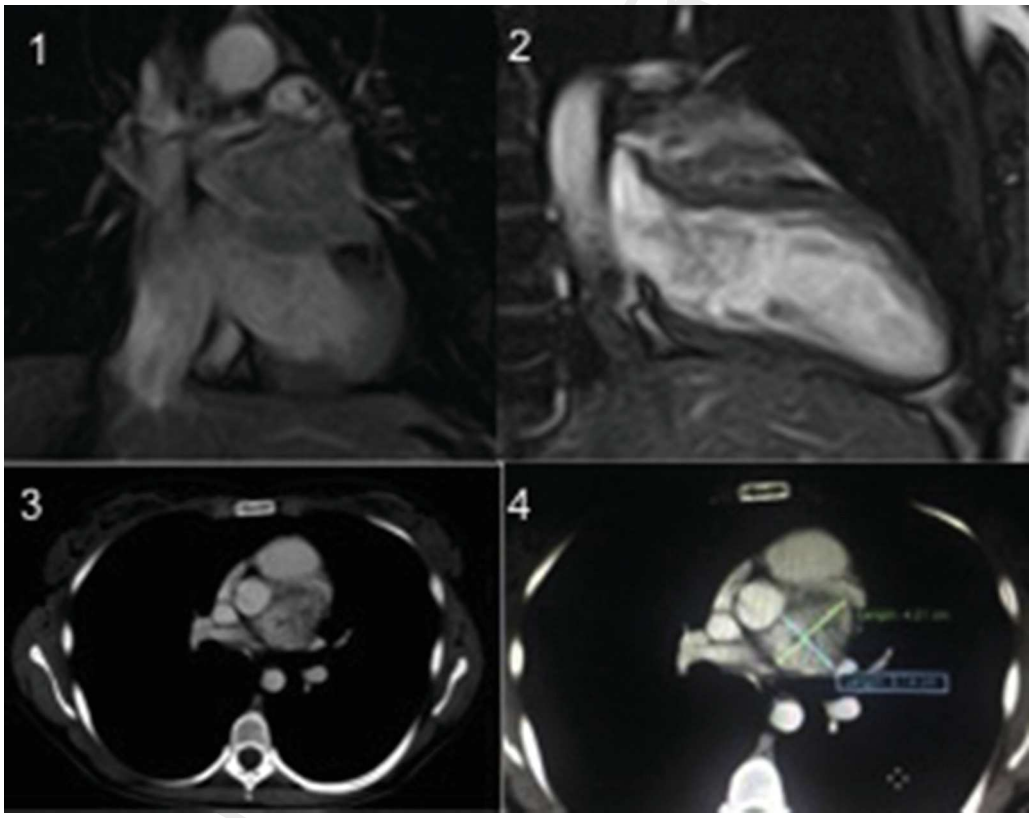

Figure 2 Cardiac magnetic resonance. **(1)** Coronal: isointense mass in relation to the left atrial roof. **(2)** Two-chamber longitudinal: isointense mass in the left atrioventricular groove. **(3,4)** Axial: mass in relation to the aortic root and the pulmonary artery.

follow-up echocardiography showed improvement in systolic function, with an ejection fraction of 55% and preserved contractility of all segments except the basal segment of the anterior septum, which continued to be akinetic. There was also moderate pericardial effusion without increased intrapericardial pressure (Figure 11, Videos 3 and 4).

The pathology report of the surgical specimen described round and oval cells in an organoid pattern with fine chromatin nuclei and degenerative focal atypia (Figure 12). These findings and the immunohistochemical studies were compatible with a paraganglioma. The genetic study showed a succinate dehydrogenase subunit B mutation. The patient progressed satisfactorily and was discharged. One month later, it was found that one of her father's cousins had a para-aortic pheochromocytoma, an incidental finding in the emergency department due to abdominal pain.

Figure 3 Cardiac magnetic resonance. Delayed enhancement. Focal deposit of gadolinium in the periphery of the mass.

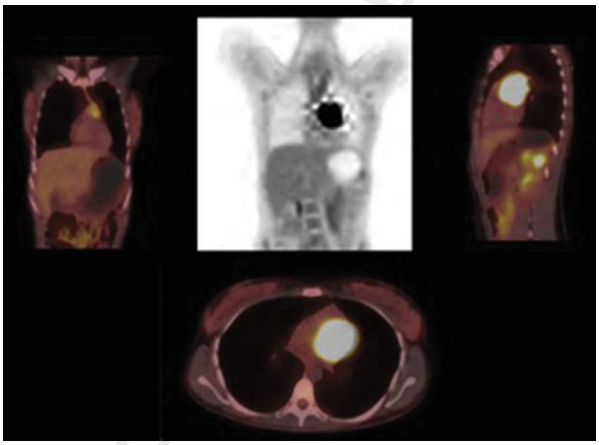

Figure 4 Positron emission tomography with 18F-fluorodeoxyglucose (10 mCi). Hypermetabolic mass in the middle mediastinum.

DISCUSSION

Paragangliomas are tumors derived from extra-adrenal chromaffin cells located in the sympathetic paravertebral ganglia of the thorax, abdomen, and pelvis.[3] In the heart, the tumor originates from the paraganglionic cells located in relation to the great arteries, the coronary arteries, or the atria. Its most common location is in the left atrium (55%), followed by the interatrial septum (16%), anterior surface of the heart (10%), and the right atrium, aortic root, or left ventricle in 5% of cases.[2] Cardiac paragangliomas can be secretory or nonsecretory tumors. Secretory tumors produce endogenous catecholamines that lead to an excessive sympathetic discharge, causing arterial hypertension, tachycardia, anxiety, tremors, and palpitations, as in the case of our patient. In the nonsecretory type, patients may present symptoms such as dyspnea and angina, related to compression of the cardiac chambers or coronary arteries.[4] It is one of the most infrequent primary cardiac tumors, with <50 cases reported in the literature.[1]

These types of tumors are usually found during the study of secondary arterial hypertension, generally in young patients. The prevalence in patients with high blood pressure varies between 0.2% and 0.6%.[5] Cardiovascular morbidity and mortality without treatment are high, and these tumors may eventually produce compression of cardiac structures and invade adjacent organs.

According to the recommendations of the American Society of Endocrinology guidelines,[6] initial biochemical tests should include measurements of metanephrines in urine and free metanephrines in plasma, in the supine position. The elevation of these metanephrines has diagnostic sensitivity of 97%.[7] Once there is clear biochemical evidence, imaging studies should begin with contrast computed tomography, because of its excellent spatial resolution, with diagnostic sensitivity of 88% to 100%.[8] These tumors may be solid or cystic, with a homogeneous or heterogeneous appearance, peripheral enhancement, areas of calcification, and sometimes central areas of low attenuation, representing central necrosis. They usually have an

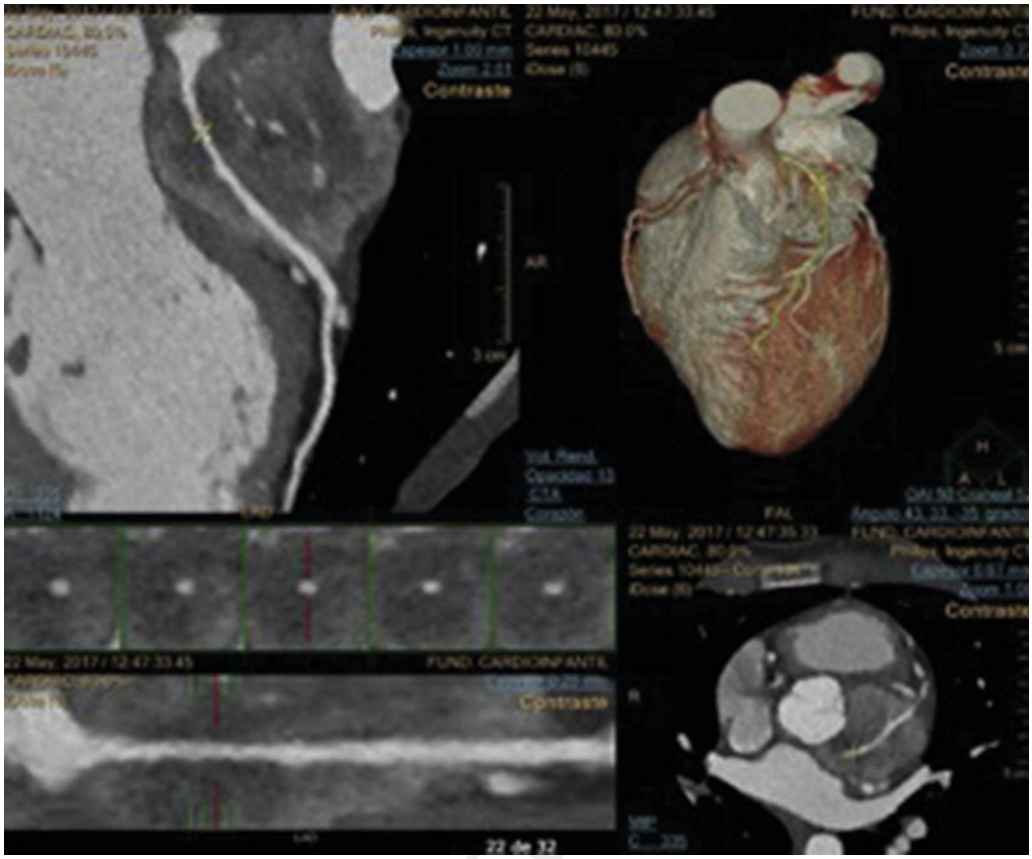

Figure 5 Coronary computed tomography. Mass surrounding the left main coronary artery and the proximal segment of the anterior descending and the circumflex coronary arteries.

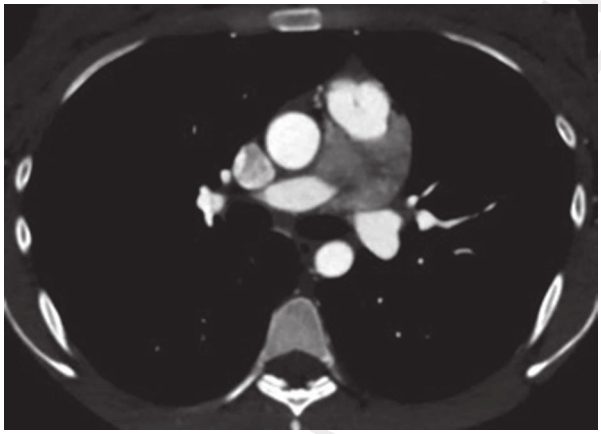

Figure 6 Coronary computed tomography. Mass surrounding the pulmonary artery.

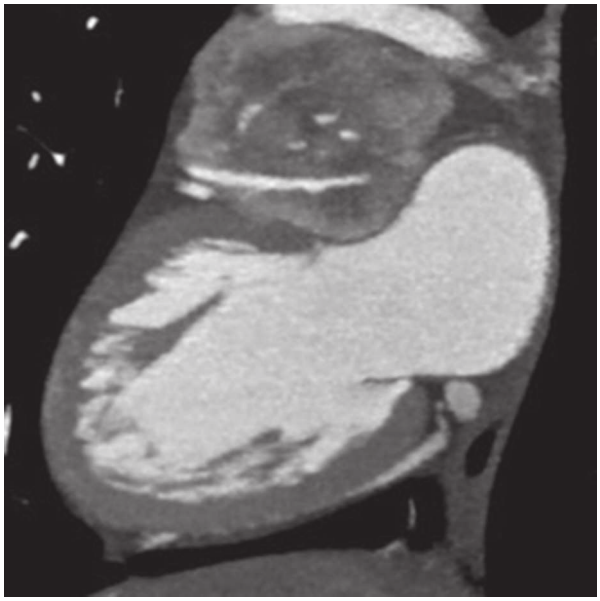

Figure 7 Coronary computed tomography. Mass located in the left atrioventricular groove.

average attenuation of 10 Hounsfield units on computed tomography without contrast. Cardiovascular magnetic resonance imaging should be reserved for patients with metastatic paragangliomas or those with contraindications to computed tomography.[1] The main advantage of this technique in this type of tumor is the possibility of tissue characterization. Paragangliomas are usually hyperintense on T2-weighted sequences and hypointense on T1-weighted sequences, although cases of paragangliomas with a hyperintense signal on T1-weighted sequences have been reported (as in the case of our patient), probably related to intratumoral hemorrhages.

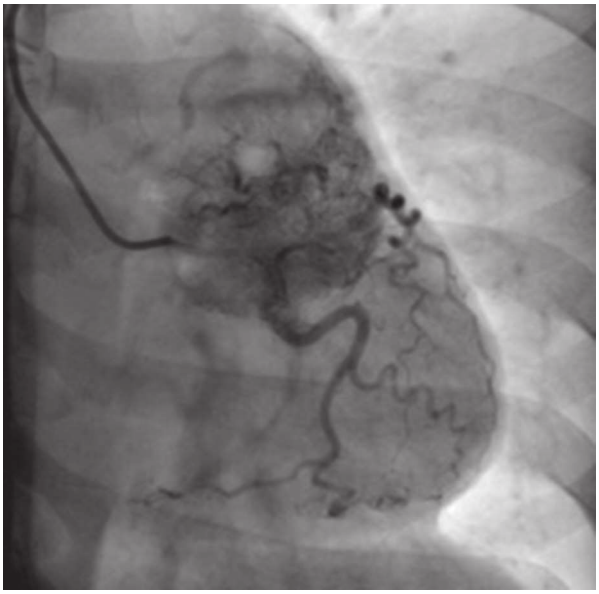

Figure 8 Coronary arteriography. Mass irrigated by multiple small vessels arising from the anterior descending coronary artery.

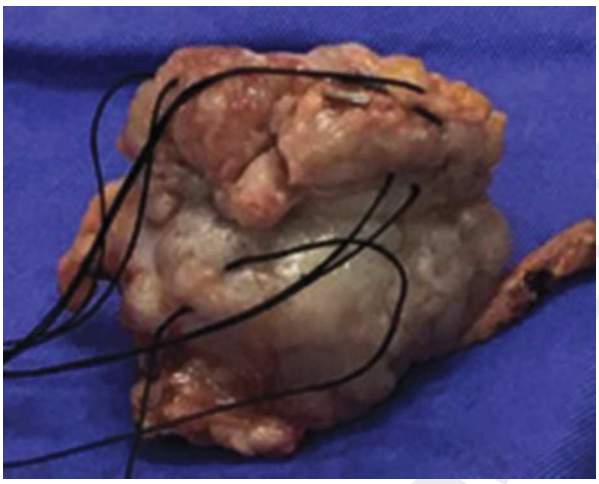

Figure 9 Surgical specimen. Resected mass.

Given that these tumors are highly vascularized masses, it is expected that they will show dynamic filling of the contrast in the perfusion sequence. These kinds of masses are characterized by peripheral LGE without central enhancement, because of tumor necrosis, as we found in this case.

The reported sensitivity of echocardiography in this type of tumor is low. However, according to different cases reported,[9] the evidence of a cardiac or pericardial mass of unclear etiology should direct attention to the heart and establish the need for other methods of diagnostic imaging, as in the case of our patient. Transesophageal echocardiography for these kinds of tumors has been used in a few cases, particularly when seeking a more detailed description of the relationship of the tumor with cardiac structures, thus becoming an important complementary tool when selecting appropriate candidates for surgery.[2,4] The use of intraoperative echocardiography has made it possible to evaluate the immediate results of the procedure

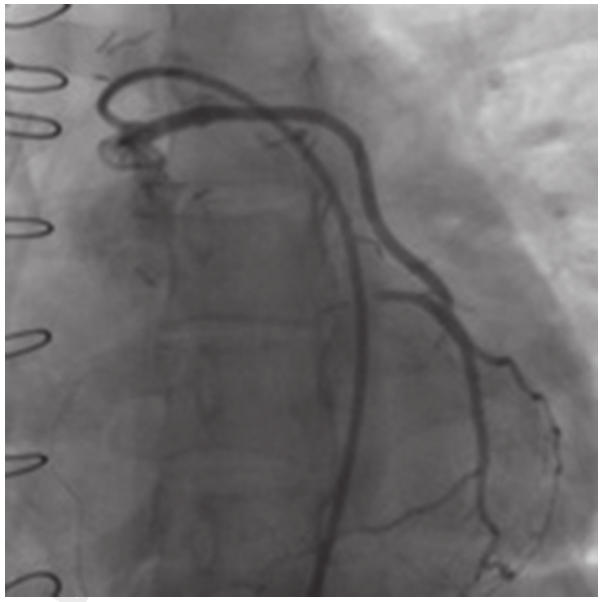

Figure 10 Coronary angiography. Saphenous bridge patent to the anterior descending artery, without lesions.

and, above all, to promptly detect possible perioperative complications.[4]

Because these tumors are hypervascular, some authors routinely perform coronary angiography, given the close anatomic relationship of the paraganglioma with the coronary circulation. Most of the vessels that nourish the tumor originate in the right coronary artery (57.9%) and in the circumflex coronary artery (20.9%).[4] Coronary angiography must definitely be considered in surgical planning.

Positron emission tomography/computed tomography is the preferred imaging modality for the detection of metastatic paragangliomas, with a sensitivity of 74% to 100% (10).

The use of ^{123}I MIBG, a guanethidine analogue that is structurally similar to norepinephrine and absorbed by adrenergic blood vessels, is recommended as a functional imaging technique. It has been used in patients with suspected metastasis detected by other imaging modalities, as well as to plan radiation therapy with ^{123}I MIBG. It is also useful in patients with large primary tumors, who are at high risk for metastasis. This diagnostic method has sensitivity of 56% to 75% and specificity of 84% to 100%.[10] It is especially indicated in patients in whom surgery is not an option. If the result is positive, treatment with MIBG should be considered.[6]

At least one third of patients with cardiac paragangliomas have germline (inherited) mutations, and 50% of these develop the disease.[11] Genetic studies should be considered in all patients diagnosed with paragangliomas and should include tests for the detection of succinate dehydrogenase mutations, and in the presence of metastasis, tests for the detection of succinate dehydrogenase subunit B mutation,[6] which was the one we found in our patient. Mutations in the gene encoding the B subunit of succinate dehydrogenase have been linked to the presence of pheochromocytoma and metastatic disease in 40% of patients. Studies suggest that all carriers of this mutation should also offer surveillance for renal cells carcinoma.[6]

If the most viable option is surgery, all patients should receive α-adrenergic blockers for at least 7 to 14 days before the procedure, seeking to prevent perioperative cardiovascular complications.

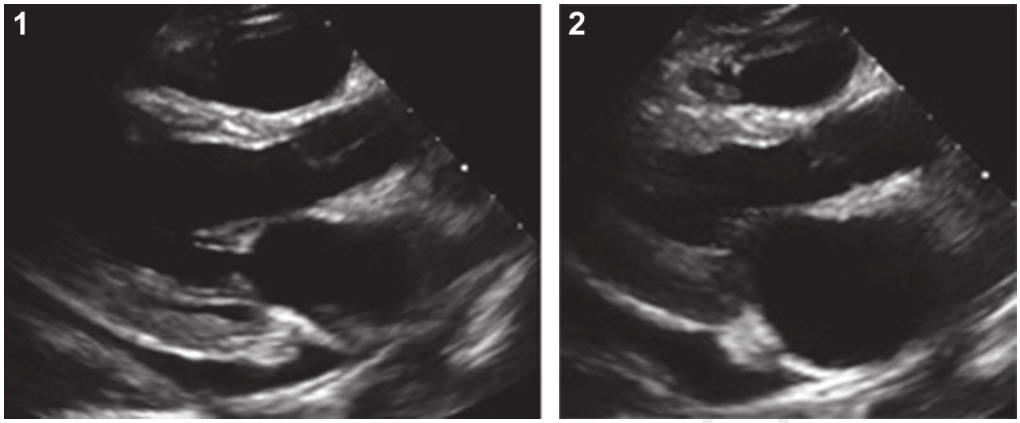

Figure 11 Transthoracic echocardiography. **(1)** Parasternal view in diastole: pericardial effusion. **(2)** Parasternal view in systole: akinesia of the basal anteroseptal segment.

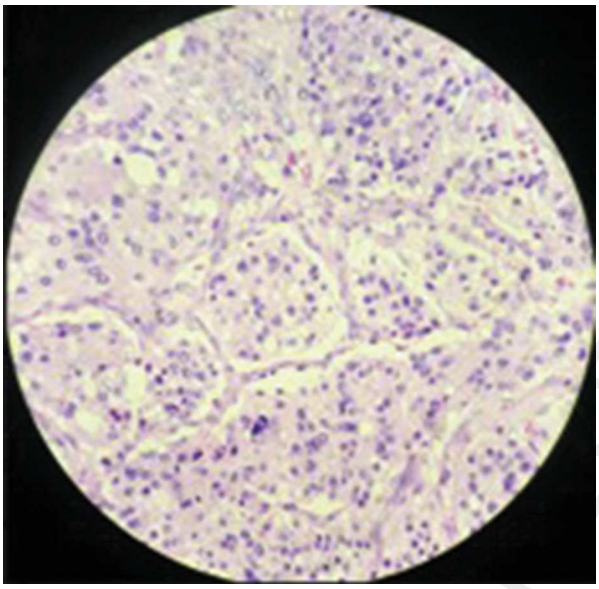

Figure 12 Round and oval cells, arranged in an organoid pattern, with degenerative focal atypia.

It is also important to increase water and sodium intake, in order to prevent hypotension after tumor resection.[6] The use of extracorporeal circulation facilitates a safe and complete resection of the tumor and also reduces the possibility of hemodynamic complications due to the release of catecholamines, which may occur when handling the mass. The complications related to the surgical resection of these cardiac tumors are due to the fact that they are usually very invasive masses.[2] Preoperative embolization of the feeding arteries may be effective in reducing intraoperative blood loss.[12] However, when this option is not possible and the mass extends to the atrioventricular groove of the left ventricle, or has direct involvement with the coronary arteries, resection with an adequate margin leads to high mortality and morbidity, resulting in fatal hemorrhage and myocardial infarction. In this group of patients, heart transplantation is the best treatment option, provided that distant metastases have been excluded.[13] Even with complete mediastinal tumor resection, the literature reports that up to 64% of patients remain hypertensive.[14]

CONCLUSION

Cardiac paragangliomas are infrequent tumors and may be an unexpected finding during the study of young patients with secondary arterial hypertension. The evidence of elevated plasma and urine metanephrines requires an exhaustive search for the tumor. Two-dimensional echocardiography can guide its diagnosis and is probably one of the first steps in managing these patients. Other cardiovascular imaging techniques, such as tomography and cardiac resonance, are required because of their high spatial resolution, which helps determine the tumor's relationship with adjacent structures, which is important when planning the surgical procedure. Furthermore, tissue characterization sequences allow an approach to etiologic diagnosis. The role of nuclear medicine is also important, not only in diagnosis, as a functional imaging technique with MIBG, but also as a therapeutic option, especially in patients with unresectable masses.

We emphasize the importance of cardiovascular multimodality imaging as an essential tool for the diagnostic and therapeutic approach to this type of tumor. Multidisciplinary medical management is also essential.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2018.07.011.

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Video 2 ■■■.

Video 3 ■■■.

Video 4 ■■■.