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CASE

A primary right atrium paraganglioma in a 15-year-old patient

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Abstract Thoracic pheochromocytomas account for less than 2% of reported cases, while primary cardiac paragangliomas are even rare. The following case illustrates a 15-year-old patient with primary right atrium paraganglioma. This patient was referred for paroxysmal hypertension and excessive perspiration. Pheochromocytoma was suspected and then confirmed by very high serum nor-metanephrine which increased more than 30-fold above the upper limit of normal. ^{131}I-metaiodobenzylguanidine (MIBG) scintigraphy showed high uptake only in the middle mediastinum, but not in the adrenal glands or elsewhere. Both contrast CT and gated MRI of the chest disclosed a 5.0 × 4.0 cm^2 mass in the right atrium. Coronary angiography demonstrated the mass with feeding vessels from the right coronary artery. When the patient's blood pressure was well controlled with doxazosin and metoprolol, surgery was then performed. A 6.0 × 4.9 × 4.0 cm^3 round solid right atrium paraganglioma weighing 41.7 g was resected. The second day after surgery, serum nor-metanephrine and urinary noradrenaline levels dropped rapidly to normal range, and the patient was free of clinical symptoms with normal BP. Postoperative cardiac function, as measured by echocardiogram, was normal. Although cardiac paraganglioma may be difficult to resect, it can be cured.

Keywords Paraganglioma · Right atrium · Heart · Pheochromocytoma

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Introduction

Pheochromocytomas are rare neoplasms of the chromaffin cells derived from the embryonic neural crest. Pheochromocytomas usually occur within the adrenal medulla, however, extra-adrenal pheochromocytomas, which are also called paragangliomas, may arise in ganglia of the sympathetic nervous system. Both the clinical and biochemical features of pheochromocytomas result mostly from the overproduction of catecholamines. Thoracic pheochromocytomas account for less than 2% of reported cases and are usually located in the posterior mediastinum when they occur in the chest. Primary cardiac paragangliomas are rare, with only about 50 cases reported in the literature. We report a case of a 15-year-old patient with a primary right atrium paraganglioma.

Clinical summary

A 15-year-old girl was found to be hypertensive during routine medical examination. A blood pressure of 209/133 mmHg was detected and she was treated with β-blocker, calcium channel blocker, angiotensin-converting-enzyme inhibitor, and angiotensin II receptor blocker with no satisfactory effect. She has had no complaints, but on further questioning, there was a history of excessive perspiration ever since childhood. Her previous medical history was otherwise negative. Her mother had a history of hypertension with the highest BP of 150/90 mmHg. On admission, her BP was 160/90 mmHg and heart rate was 86 bpm.

Urinary noradrenaline was 1451.2 μg/24 h (normal: 7.0–65.0 μg/24 h), urine dopamine 540.63 μg/24 h (normal: 75–440 μg/24 h), urine nor-metanephrine 1892.2 pg/ml (normal: <460 pg/ml), and serum nor-metanephrine 4044.6 mg/24 h (normal: 19–121 pg/ml). Thus, pheochromocytoma was highly suspected [1]. Computed tomography of both adrenals showed normal results. Thus, ^{131}I-metaiodobenzylguanidine(MIBG) scintigraphy was performed which revealed high uptake only in the middle mediastinum, but not in the adrenal glands or elsewhere (Fig. 1a). Both contrast computed tomographic scan and gated magnetic resonance imaging of the chest disclosed a 5.0 × 4.0 cm^2 mass in the right atrium (Fig. 1b). Echocardiography confirmed a heart tumor in the lateral and posterior wall of the right atrium (Fig. 1c). There was no demonstrable hemodynamic effect on intra-cardiac flow. The tumor had a well-defined capsule. Coronary angiography demonstrated the mass with feeding vessels from the right coronary artery (Fig. 1d) [2]. The clinical diagnosis of cardiac paraganglioma was made.

The patient's blood pressure was well controlled with doxazosin and metoprolol. Surgery with the aim of total resection, plus cardiac reconstructive surgery and coronary bypass, was therefore performed via a median sternotomy [3]. The mass was to the right atrium, a part of the right ventricle and right atrioventricular groove. The patient's mean arterial pressure remained stable during the operation. The aorta was crossclamped, and the heart was arrested and emptied. A 6.0 × 4.9 × 4.0 cm^3 round solid right atrium paraganglioma weighing 41.7 g was removed *en bloc* with portions of the right atrium, right ventricle, and right coronary artery. The defect in the right atrium and right ventricle was closed with a pericardial patch. The patient was weaned easily from cardiopulmonary bypass, uncomplicated. The second day after surgery, serum nor-metanephrine and urinary noradrenaline levels dropped rapidly to normal range. Histopathologic examination demonstrated a right atrium paraganglioma (Fig. 2). The patient had no antihypertensive medication at discharge. She was free of clinical symptoms with normal blood pressure. At follow-up 6 months postoperatively, the patient was normotensive, on no treatment, and urinary and plasma nor-metanephrine levels remained normal.

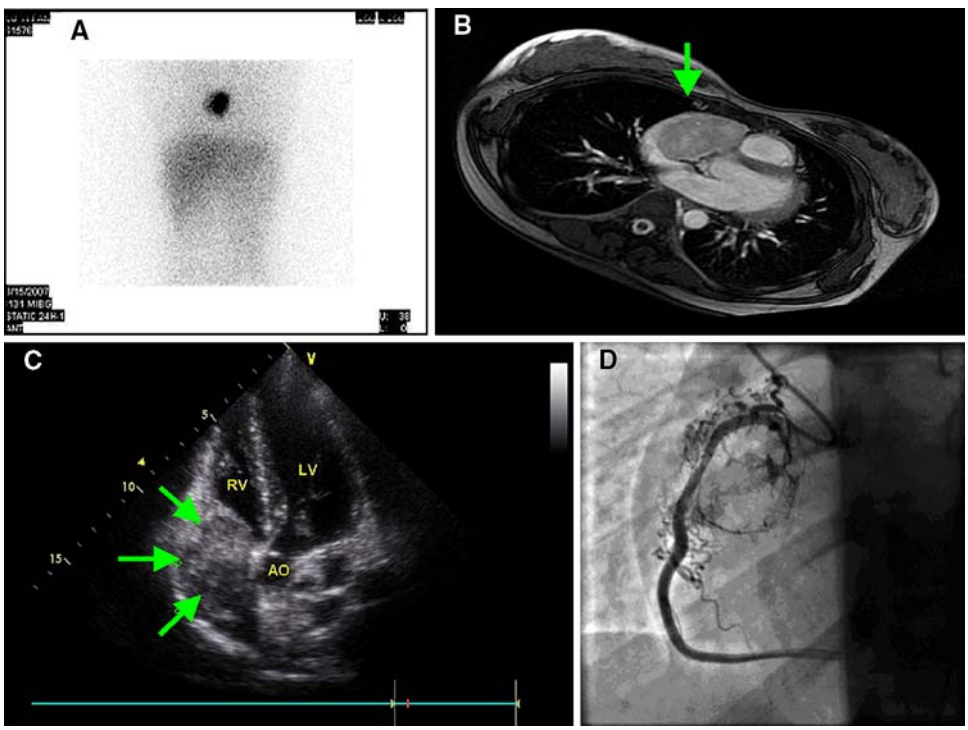

Fig. 1 (**a**) ^{131}I-metaiodobenzylguanidine (MIBG) scintillation scan illustrating an area of intense uptake in the thorax (ANT, anterior.). (**b**) Gated magnetic resonance imaging showing a large right atrial mass (arrow). The location of this mass corresponded to the positive uptake detected by ^{131}I-MIBG scintigraphy. (**c**) Echocardiogram showing a large right atrial mass (arrow). (LV left ventricle, RV right ventricle, AO aorta). (**d**) Coronary angiography showing the collateral supply feeding the tumor, arising from the right coronary artery

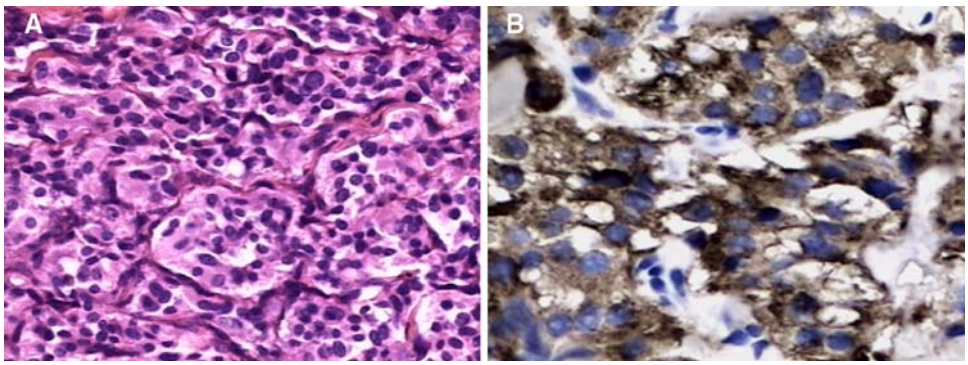

Fig. 2 (**a**) A photomicrograph showing nests of uniform bland polygonal cells with no mitotic activity, separated by vascular septa (H&E, 200×). (**b**) Tumor cells were positive for chromogranin A staining (IHC, DAB, 400×)

Discussion

Pheochromocytomas are catecholamine producing tumors arising from the cells of the sympathetic nervous system that are distinguished by their embryological derivation from primitive neural crest cells. Tumors that arise from chromaffin cells of the adrenal medulla are referred to as pheochromocytomas, and those that arise in paraganglia are termed paragangliomas. Around 90% of the pheochromocytomas in adults are found in the adrenal glands. Paragangliomas account for 10% of the tumors and are mainly in the abdomen. However, in children, paraganglioma may account for about 30–40% [4]. Less than 2% of all pheochromocytmas occur in the thorax, usually in the posterior mediasterium, and develop from ectopic islets of chromaffin cells that persist in the mediastinum instead of being replaced by lymphoid tissue after birth. Cardiac paragangliomas are rare tumors which can arise from several sites including the intra-atrial septum, left and right atrium, intra-pericardial aorta, pulmonary artery, and the left ventricle [5]. Around 60% of cardiac pheochromocytomas are located in the roof of the left atrium. The rest are located (in order of frequency) in the interauricular septum, the anterior surface of the heart, and the aortopulmonary window. Right atrium paragangliomas are extremely rare tumors. As tumors usually have a close relationship with heart valves and coronary arteries, it is difficult to resect and the prognosis is poor. Ever since Besterman et al. reported the successful resection of the cardiac paraganglioma in 1974 for the first time, there are about 50 cases reported in the literature up till now. Previous cases have shown that the diagnosis and treatment of cardiac paraganglioma is of great challenge. More than 50% of all cases had complications during or after surgery and the death rate was rather high [6].

Symptoms of paragangliomas can be divided into two categories. The first category includes symptoms due to an excess of catecholamines and are similar to their adrenal counterpart. The second category includes symptoms that are due to the specific location of the tumor and may help in localizing the tumor. Symptoms in patients with intracardiac pheochromocytomas may occasionally be precipitated by deep breathing or arm lifting for extended periods of time [7–9]. In addition, patients with intra-cardiac lesions may develop recurrent attacks of angina as the tumor competes with the myocardium for coronary blood supply [2]. In our case, the patient showed no compression symptoms of the cardiac tumor which may be explained by the early diagnosis and resection of the tumor. Hypertension appears to be uniformly present and is sustained in 80–90% of affected children at the time of diagnosis. Occasionally, children with sustained hypertension also have paroxysmal episodes. The paroxysms are occasionally precipitated by excitement or a particular physical activity, such as bending over or lifting a heavy object. Headache is the most frequent symptom in children (75%), followed by sweating in two-third of patients, and nausea and vomiting in half of patients. Affected children are often emotionally labile and have an anxious expression. Occasionally, these children are labeled hyperactive with an attention deficit disorder.

The diagnosis of cardiac paragangliomas include multiple parameters, such as urinary and plasma catecholamines, I-MIBG, CT or MRI scan, and coronary angiography, each of which is different to others and has a unique characteristic. Biochemical results could give a clue to the diagnosis of pheochromocytoma. However, for paragangliomas, to search for the exact localization of the tumor is of no ease. The advent of I-MIBG scintigraphy introduced by the University of Michigan in 1982 made it easier. This radiopharmaceutical molecular structure closely resembles that of norepinephrine and it concentrates in catecholamine storage vesicles such as within the adrenalin medulla and in pheochromocytoma [10]. Dynamic computed tomography or magnetic resonance image scanning provides optimal visualization of the anatomic extent of the tumor. At the present time, the gated MRI is the best technique for the demonstration of the detailed anatomy of cardiac pheochromocytoma and its relationship to other structures. Coronary angiography is useful in judging local

extent of disease, specifically, coronary artery involvement, and screening for atherosclerotic disease in these hypertensive patients. In our case, ^{131}I-MIBG showed high uptake in the mediastinum and angiography demonstrated that the tumor was from the right coronary artery which was confirmed by the operation.

Pheochromocytomas can occur in patients in all levels of age, including children. It accounts for 0.5–2% of cases of secondary hypertension in children. In children, pheochromocytoma is more frequently associated with other familial syndromes, such as neurofibromatosis, von Hippel-Lindau disease, or multiple endocrine neoplasia (MEN) syndromes. In childhood, pheochromocytomas are present most frequently in children aged 6–14 years (average, 11 years). Around 62% of the pheochromocytomas in girls occur during menarche between the ages of 11 and 15 years. In our case, the patient also developed severe sweating since her menarche. Most pheochromocytomas in children predominantly produce norepinephrine, unlike the normal adrenal medulla, which, in humans, contains 85% epinephrine. Rarely, tumors produce epinephrine exclusively; in some cases, the clinical picture is dominated by signs of beta-receptor stimulation, such as tachycardia and hypermetabolism. Children have a higher frequency of bilateral tumors than adults (20% vs. 5–10%) and a lower incidence of malignancy (3.5% vs. 3–14%). More than one-third of affected children have multiple tumors, most of which are recurrent. In 30–40% of children with pheochromocytomas, tumors are found in both adrenal and extra-adrenal areas, or in only extra-adrenal areas. In our case, ^{131}I-MIBG scan ruled out pheochromocytomas in both adrenals and any other location.

Whenever possible, tumor excision should be attempted, reserving transplantation for extensive masses that cannot be resected due to involvement of the atrioventricular groove, the mitral valve apparatus, the left ventricle, or the coronary arteries. However, certain cardiac paragangliomas carry a particularly poor prognosis because of technical difficulties encountered with surgical resection. Surgery with cardiopulmonary bypass allows safe resection, as it prevents malignant arrhythmias and hypertensive crises when handling the tumor and helps control hemorrhage. Reconstruction of part of the heart wall after tumor excision is often necessary, and patches of various materials can be used for this purpose, for example, autologous pericardium [11, 12]. In several previous cases, orthotopic heart transplantation was performed when total surgical resection was not possible [6]. Long-term medication after heart transplantation is a heavy burden to the patient which should always be considered before operation.

Malignant pheochromocytoma may also occur. Neither histopathologic characteristics nor clinical or biochemical markers can distinguish between benign and malignant pheochromocytoma. The distinction is made on the finding of direct local invasion or spread to sites that do not normally have chromaffin tissue. Extra-adrenal pheochromocytomas are more likely to be malignant than adrenal pheochromocytomas. So this patient should be closely followed up with biochemical analysis, ^{131}I-MIBG and CT scan.

In conclusion, right atrium paragangliomas are rare but life threatening. In children, an evaluation of pheochromocytoma should always be considered when the young patient has sweating and hypertension. ^{131}I-MIBG scan plays an important role in the diagnosis of paraganglioma. After preoperative treatment, surgical resection can be curative. Long-term follow-up is extremely necessary for children.

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