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CASE REPORT

Nonhypertensive male with multiple paragangliomas of the heart and neck: A case report

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Abstract

BACKGROUND

Paraganglioma is a rare disease that can be lethal if undiagnosed. Thus, quick recognition is very important. Cardiac paragangliomas are found in patients who have hypertension. The classic symptoms are the triad of headaches, palpitations, and profuse sweating. We describe a very rare case of multiple paragangliomas of the heart and bilateral carotid artery without hypertension and outline the management strategies for this disease.

CASE SUMMARY

A 46-year-old man presented with the chief complaint of recently recurrent chest pain with a history of hemangioma of the bilateral carotid artery that had been surgically removed. He was found to have an intracardiac mass in the right atrioventricular groove and underwent successful excision. The final pathology demonstrated that the intracardiac mass was a cardiac paraganglioma, and the patient had an increased level of normetanephrine in the blood. The pathology and immunohistochemistry results showed that the bilateral carotid masses were also paragangliomas. During the 3 mo follow-up period, the patient did not experience recurrence of chest pain.

CONCLUSION

To our knowledge, this is the first case of multiple paragangliomas of the heart and neck without hypertension. This rare disease can be lethal if left undiagnosed. Thus, quick recognition is very important. The key to the diagnosis of cardiac paraganglioma is the presence of typical symptoms, including headaches, palpitations, profuse sweating, hypertension, and chest pain. Radiology can demonstrate the intracardiac mass. It is important to determine the levels of normetanephrine in the blood. The detection of genetic mutations is also recommended. Surgical resection is necessary to treat the disease and obtain pathological evidence.

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Core Tip: Paraganglioma is a very rare disease. The clinical presentation of paraganglioma is dependent on the symptoms caused by local invasion and/or hypersecretion of catecholamines. The classic symptoms are the triad of headaches, palpitations, and profuse sweating. Surgical resection is necessary to treat the disease and obtain pathological evidence. We describe a first case of multiple paragangliomas of the heart and neck without hypertension and management with surgical resection.

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INTRODUCTION

The incidence of paraganglioma is approximately 6 cases per 1000000 person-years. This rare disease can be lethal if undiagnosed. Therefore, quick recognition is very important[1,2]. The clinical presentation of paraganglioma is dependent on the symptoms caused by local invasion and/or hypersecretion of catecholamines. Cardiac paragangliomas are found in 0.05%-0.2% of patients who have hypertension[3]. The classic symptoms are the triad of headaches, palpitations, and profuse sweating. Anxiety and panic attacks are also common. Cardiac paragangliomas can also be asymptomatic. To our knowledge, this is the first case of multiple paragangliomas of the heart and neck without hypertension. Here, we describe the case of a 46-year-old male with a history of hemangioma of the bilateral carotid artery who presented with recent recurrent chest pain and was found to have multiple paragangliomas of the heart and neck without hypertension, Table 1.

CASE PRESENTATION

Chief complaints

A 46-year-old man presented to our hospital with the chief complaint of recently recurrent chest pain.

History of present illness

The patient had no history of present illness.

History of past illness

He had a history of hemangioma of the bilateral carotid artery that had been surgically removed in 2003 and 2018.

Personal and family history

The patient had no personal or family history.

Physical examination

The patient's heart rate was 125 beats/min, and blood pressure was 134/76 mmHg. There were no other abnormal findings on physical examination.

Laboratory examinations

Electrocardiogram demonstrated sinus tachycardia (heart rate 125 beats/min) (Figure 1). Other laboratory examinations are shown in Table 2.

Table 1 Timeline

Timeline of the patient	
Initial presentation	Presented with the chief complaint of recently recurrent chest pain
Day 1	Echocardiography revealed an intracardiac mass in the right atrioventricular groove, wrapped around the proximal segment of the right coronary artery
Day 2	Coronary artery computed tomography showed that abnormal blood vessels were presented between the right atrium and right ventricle
Day 5	Coronary angiography showed that there were abundant blood vessels that were wrapped around and supplied the intracardiac mass in the right atrioventricular groove
Day 6	Positron emission tomography/computed tomography suggested that the intracardiac mass was a malignant tumor
Day 8	The level of normetanephrine in the blood was obviously increased
Day 18	Open heart surgery was performed, and the intracardiac mass was completely excised. Quick freezing pathology indicated that the intracardiac mass was a mesenchymal malignant tumor
Day 25	The final pathology results demonstrated that the intracardiac mass was a cardiac paraganglioma
Day 26	The combination of pathological and immunohistochemistry results demonstrated bilateral carotid masses, these bilateral carotid masses were also paragangliomas
Day 27	Discharged from hospital
Day 83	At the 3-mo follow-up, the patient did not have recurrent chest pain

Imaging examinations

Echocardiography revealed a 4.26 cm × 2.98 cm intracardiac mass in the right atrioventricular groove, which was wrapped around the proximal segment of the right coronary artery (Figure 2). Coronary artery computed tomography (CT) showed that abnormal blood vessels were present between the right atrium and right ventricle, indicating that there might be a fistula between the right coronary artery and right atrium or a right coronary artery malformation. Coronary angiography (CAG) demonstrated that there were abundant blood vessels from the proximal segment of the right coronary artery that were wrapped around and supplied the intracardiac mass in the right atrioventricular groove (Figure 3). Positron emission tomography/CT suggested that the intracardiac mass in the right atrioventricular groove was a malignant tumor (Figure 4).

Further diagnostic work-up

Normetanephrine blood level was 950.5 pg/mL, which was 5.8 times the upper limit of the normal range (normal range, < 163 pg/mL). The level of metanephrine and 3-methoxytryramine in the blood and vanillylmandelic acid in urine were all normal.

Interventions

Considering his symptoms, physical examination, history, and laboratory examinations, we suspected that the intracardiac mass was a paraganglioma. The patient was referred to the Department of Cardiac Surgery. Open heart surgery was performed, and a dark red intracardiac mass was found located in the right atrioventricular groove. The right coronary artery crossed over the intracardiac mass. The mass, which was 3 cm × 2.5 cm × 2 cm in size, was completely excised. When the mass was cut open, it showed a solid content dark red in color (Figure 5). Quick freezing pathology indicated that the intracardiac mass was a malignant mesenchymal tumor, and a hemangiosarcoma could not be excluded. The combination of immunohistochemistry results and final pathology results demonstrated that the intracardiac mass was a cardiac paraganglioma. Given the patient's history of surgery for bilateral carotid hemangioma in 2003 and 2018, we considered whether this hemangioma could also be a paraganglioma. On magnetic resonance imaging, an obvious mass in the left neck was observed. Immunohistochemistry demonstrated the following parameters: Synaptophysin (positive), chromogranin A (positive), Ki67 (3% positive), CD56 (positive), S100 (positive), CD34 (vascular positive), and epithelial membrane antigen (negative) (Figure 6). The combination of pathology and immunohistochemistry results demonstrated that the bilateral carotid masses were also paragangliomas.

Table 2 Laboratory data of this patient on arrival to our hospital

Laboratory examinations		
Variable	**Reference range**	**Results (this hospital on arrival)**
White cell count, × 10^9/L	3.5-9.5	13.54
Hemoglobin, g/L	130-175	114
Platelet count, × 10^9/L	125-350	196
Hematocrit, %	40-50	34.7
Urea nitrogen, mmol/L	2.9-8.2	6.5
Creatinine, μmol/L	44-115	100
Glucose, mmol/L	3.9-5.6	5.6
Sodium, mmol/L	137-147	141
Potassium, mmol/L	3.5-5.3	3.9
Chloride, mmol/L	99-110	103
Phosphorus, mmol/L	0.9-1.34	0.93
Calcium, mmol/L	2.15-2.55	2.35
Protein, g/L		
Total	65-85	68
Albumin	35-55	43
Globulin	20-40	25
Cardiac troponin, ng/mL	< 0.03	0.011
NT-proBNP, pg/mL	0-100	52.9
MM subtype of creatine kinase, U/L	24-174	186
Creatine kinase, U/L	34-174	200
FT3, pmol/L	3.1-6.8	4.5
FT4, pmol/L	12-22	15.3
TSH, μIU/mL	0.27-4.2	3.65
Prothrombin time	10-13	10.8
International normalized ratio	0.5-1.2	0.99
Partial thromboplastin time	25-31.3	27.6

FT3: Free triiodothyronine; FT4: Free thyroxine; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; TSH: Thyroid-stimulating hormone.

FINAL DIAGNOSIS

Multiple paragangliomas of the heart and neck without hypertension.

TREATMENT

None.

OUTCOME AND FOLLOW-UP

At the 3-mo follow-up, the patient did not experience recurrence of chest pain.

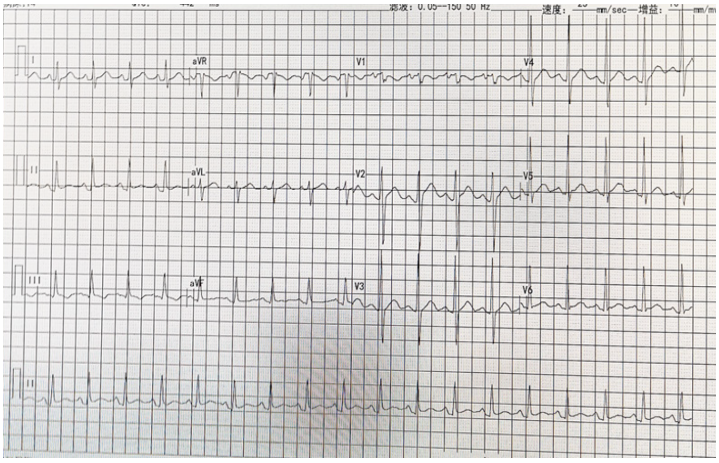

Figure 1 Electrocardiogram demonstrated sinus tachycardia. The heart rate was 125 beats/min.

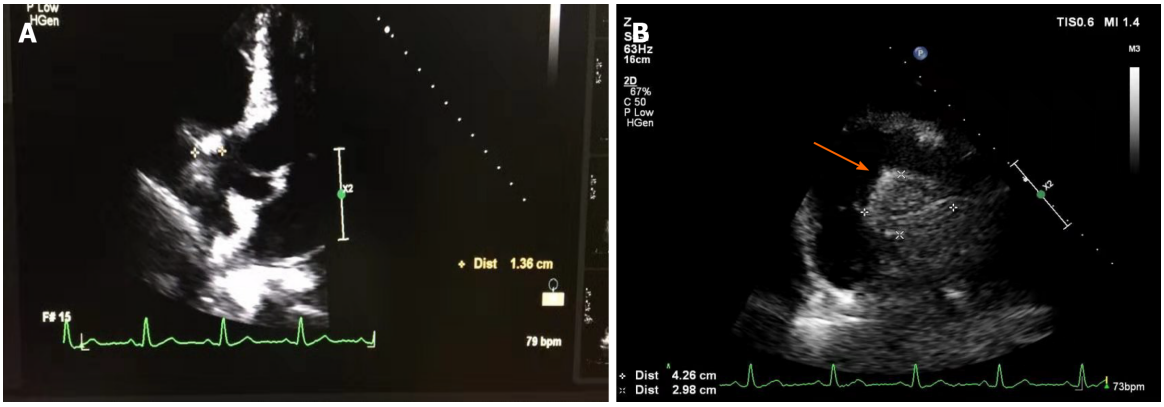

Figure 2 Echocardiography. A and B: Echocardiography revealed a 4.26 cm × 2.98 cm intracardiac mass in the right atrioventricular groove, which was wrapped around the proximal segment of the right coronary artery (arrow).

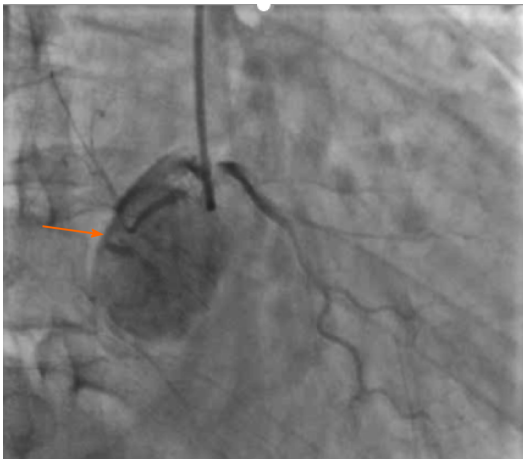

Figure 3 Coronary angiography. Coronary angiography demonstrated that there were abundant blood vessels from the proximal segment of the right coronary artery that wrapped around and supplied the intracardiac mass in the right atrioventricular groove (arrow).

DISCUSSION

The incidence of paraganglioma is approximately 6 cases per 1000000 person-years. This rare disease can be lethal if undiagnosed. Thus, quick recognition is very important[1,2]. Both pheochromocytoma and paraganglioma can secrete catecholamines, and although they cannot be differentiated based on histology, they can be

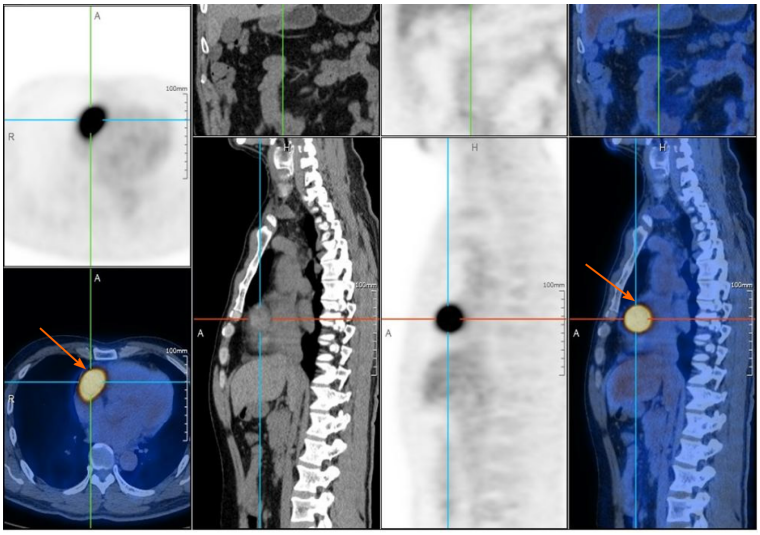

Figure 4 Positron emission tomography/computed tomography. Positron emission tomography/computed tomography demonstrated an abnormal increased glucose metabolism nodule in the right atrioventricular groove. The maximum standardized uptake value was 21.1, suggesting that the intracardiac mass in the right atrioventricular groove (arrow) was a malignant tumor.

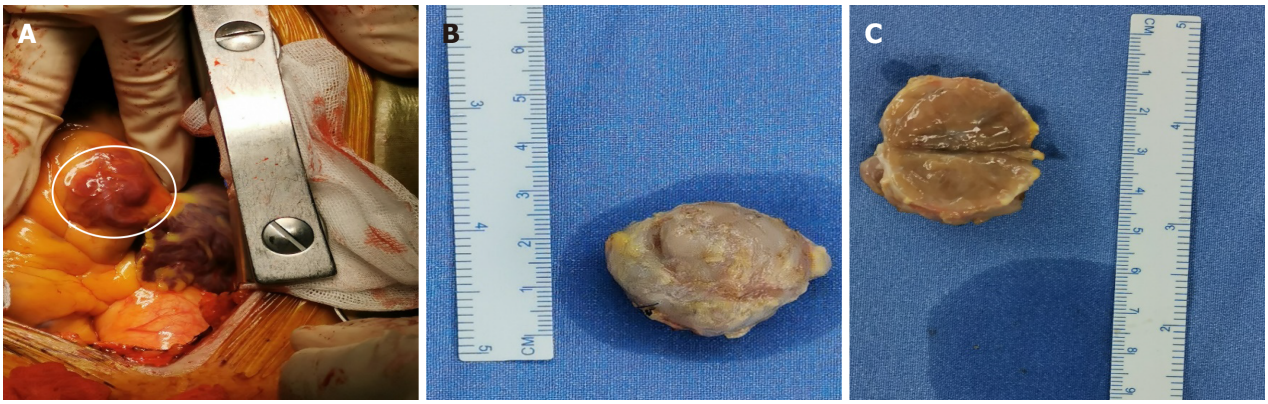

Figure 5 Intracardiac mass. A: An intracardiac mass that was dark red was located in the right atrioventricular groove, and the right coronary artery crossed over the intracardiac mass; B: The intracardiac mass 3 cm × 2.5 cm × 2 cm in size was completely excised; C: When the mass was cut open, a solid content dark red in color was observed.

differentiated on anatomical location. Pheochromocytoma is an adrenal tumor, and paraganglioma is an extra-adrenal tumor[3]. The clinical presentation of paraganglioma is dependent on the symptoms caused by local invasion and/or hypersecretion of catecholamines. Cardiac paragangliomas are found in 0.05%-0.2% of patients who have hypertension[4]. The classic symptoms are the triad of headaches, palpitations, and profuse sweating. Anxiety and panic attacks are also common. Cardiac paragangliomas can also be asymptomatic.

To our knowledge, this is the first case of multiple paragangliomas of the heart and neck without hypertension. As this patient had multiple tumors (bilateral carotid artery and cardiac paraganglioma), it was necessary to determine whether they were multiple benign tumors or metastatic malignant tumors. Paraganglioma is generally considered a benign tumor and in most instances cured by complete excision. The only sure and undeniable sign of malignant behavior is demonstration of metastases. The updated World Health Organization classification of endocrine tumors has replaced the term "malignant paraganglioma" with "metastatic paraganglioma"[5]. Metastases are located where chromaffin tissue is normally not found (*e.g.*, lymph nodes, lung, liver, and bones), and frequently, metastases are not confirmed histologically but are instead documented on nuclear imaging[6]. With regard to the biological behavior of this tumor, the right carotid artery paraganglioma did not recur for over 10 years, and previous reports have revealed that the Ki67 expression in malignant paraganglioma in the immunohistochemistry was higher than 5%[7]. The present patient's Ki67 expression in the cardiac and bilateral carotid masses was lower than 5%, which was

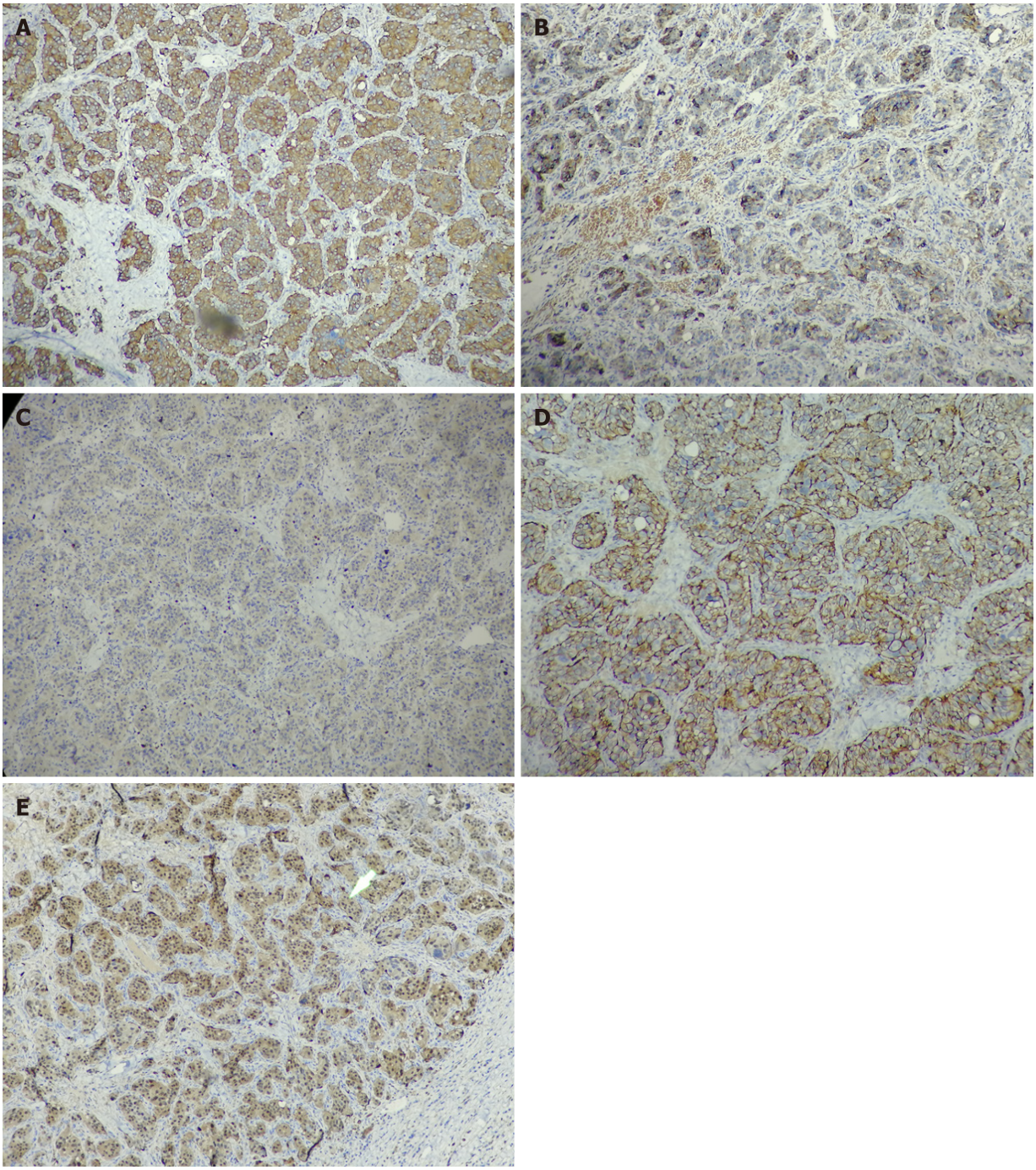

Figure 6 Immunohistochemistry. A: Synaptophysin (positive); B: Chromogranin A (positive); C: Ki67 (3% positive); D: CD56 (positive); E: S100 (positive).

determined both in our hospital and in a local hospital in Shanghai. The patient's symptoms were cured by complete excision of the paraganglioma, and we had already done the positron emission tomography/CT to exclude the distant metastases. Thus, we considered that the biological behavior of this cardiac paraganglioma was benign.

The reason for this patient's chest pain was the direct toxicity of catecholamine. A previous paper demonstrated that hypersecretion of catecholamine and its oxidation products can cause coronary vasospasm, enhanced lipid metabolism, disorders of energy metabolism, changes in cell membrane permeability, and intracellular calcium overload, inducing chest pain, cardiac dilatation, and malignant arrhythmia[8].

Based on this patient's history, physical examination, laboratory data, and radiological findings, the common causes of chest pain including acute myocardial infarction, aortic dissection, and pulmonary embolism were excluded. On the other hand, the patient's chest pain was not typical of coronary artery disease, as his pain was not related to activity, usually lasted for hours, and CAG did not reveal significant coronary artery stenosis. Therefore, coronary atherosclerotic heart disease was

excluded. Coronary artery aneurysm is common in coronary atherosclerotic heart diseases. However, CAG did not reveal coronary artery aneurysm, and the diagnosis of coronary artery aneurysm was excluded. Coronary arteriovenous fistula can also cause chest pain, but this disease is a rare congenital heart defect caused by abnormal cardiovascular development in the embryonic period. This patient did not have a history of congenital heart disease, heart auscultation revealed no murmur, and CAG did not reveal coronary arteriovenous fistula. Thus, the diagnosis of coronary arteriovenous fistula was also excluded.

With regard to treatment, surgical resection can significantly reduce the levels of catecholamines and improve hormone-related symptoms[9]. Surgical resection should be the first treatment option for cardiac paraganglioma.

CONCLUSION

We report a very rare case of multiple paragangliomas of the heart and bilateral carotid artery. This is a very rare disease and can be lethal if undiagnosed. Thus, quick recognition is very important. The key to the diagnosis of cardiac paraganglioma is the presence of typical symptoms, including headaches, palpitations, profuse sweating, hypertension, and chest pain. Radiology can demonstrate intracardiac masses. It is important to determine the levels of normetanephrine in the blood. The detection of genetic mutations is also recommended. Surgical resection is necessary to treat the disease and obtain pathological evidence.

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