CASE REPORT

Paraganglioma as a rare cause of left ventricular thrombus in the setting of preserved ejection fraction: discussing the literature

Ali Shafiq,¹ Phuc Nguyen,² Michael P Hudson,² Bobak Rabbani²

¹Henry Ford Hospital, Detroit, Michigan, USA

²Department of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA

Correspondence to
Dr Ali Shafiq,
alishafiq82@yahoo.com

SUMMARY

Paragangliomas and pheochromocytomas are catecholamine-secreting tumours which if remain undiagnosed may cause severe morbidity and mortality. In rare circumstances these tumours can cause left ventricular (LV) thrombi to form by inducing cardiomyopathy and subsequent embolic complications. After a thorough literature review, six previous cases were found that presented the formation of an LV thrombus in the setting of a pheochromocytoma or paraganglioma. A majority of these cases were associated with significant wall motion abnormalities and their cardiac ejection fraction (EF) was compromised. This is a rare case of a patient developing LV thrombi in the setting of a paraganglioma with normal cardiac EF. We present this case to compare the similarities and differences of our case with previously reported cases and emphasise the importance of suspecting these LV thrombi in patients with these neuroendocrine tumours.

BACKGROUND

Paragangliomas are very much correlated to pheochromocytomas.¹ Like pheochromocytomas, paragangliomas lead to symptoms of catecholamine excess, of which hypertension is one of the most common features.² These neuroendocrine tumours may result in hypertensive emergencies and acute myocardial ischaemia. More rarely, paragangliomas may cause embolic complications.³ About half of paragangliomas are hereditary so family history of the patient may provide an important diagnostic clue.⁴ We are writing this case report to describe such a case and raise provider awareness of this serious and reversible disorder.

CASE PRESENTATION

A 47-year-old man with no medical history presented to the emergency room with chest pain and palpitations. On physical examination he was found to have tachycardia, systolic blood pressure (BP) of 230 mm Hg and hyperdynamic pulses. CT scan of the head was unremarkable for intracranial haemorrhage. CT scan of the chest did not reveal any pulmonary embolism or aortic dissection. Incidentally a para-spinal lobulated mass measuring approximately 3.4×4.7×5.3 cm was found consistent with a possible paraganglioma (figures 1 and 2). Troponin I level was 0.15 ng/mL.

He was admitted to the coronary intensive care unit with a diagnosis of non-ST elevation myocardial infarction and hypertensive emergency. Aspirin,

Figure 1 CT scan of paraganglioma.

intravenous labetalol and intravenous nitroprusside were administered to the patient and his BP gradually improved. Plasma-free and urine-free metanephrine levels were very high at 16 121 pg/mL and 14 551 µg/24 h. Plasma renin, aldosterone and parathyroid hormone were within normal limits. A comprehensive lipid panel and liver function tests were performed which were within normal limits. Treatment was started for pheochromocytoma and the patient was given prazosin and phentolamine. A Metaiodobenzylguanidine Nuclear Study did not reveal any metastases. β-Blockers were further held and prazosin was continued in anticipation for surgical resection 1 week later.

Figure 2 CT scan of paraganglioma.

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On the next day the patient experienced sudden left-sided weakness in his upper and lower extremities. MR angiogram of the brain showed multiterritory areas of focal restricted diffusion, involving vertebral basilar as well as carotid circulations. The images were reviewed and there was no evidence of haemorrhage. An urgent transthoracic echocardiogram (TTE) revealed two large echogenic masses within the left ventricle. There was mild hypokinesis of the distal anterolateral and peripical wall (figures 3 and 4). A cardiac paraganglioma versus thrombus was suspected. The patient was started on intravenous heparin and transferred to the neurology intensive care unit for close follow-up. Carotid doppler was performed which did not reveal any significant atherosclerotic disease. Phenoxybenzamine and prazosin were continued with no adverse effects. A cardiac MRI and a TTE was subsequently performed which revealed no evidence of any intracardiac mass or thrombus. The ejection fraction (EF) was 60–65% with no wall motion abnormality noted. The rest of the patient's hospital course was uneventful. He underwent a left thoracotomy with the resection of mediastinal ganglioneuroma with no postoperative complications. Biopsy confirmed the diagnosis of the paraganglioma.

OUTCOME AND FOLLOW-UP

A left thoracotomy was performed on our patient with the resection of the mediastinal ganglioneuroma. A biopsy confirmed the diagnosis of the paraganglioma. There was complete recovery of his symptoms. His BP remained stable and he required no further antihypertensive medications.

DISCUSSION

The patient presented with intracardiac thrombi and multifocal cerebral embolisms as a complication of a paraganglioma. Functional paragangliomas have been rarely reported to cause the formation of left ventricular (LV) thrombi which consequently may lead to embolic complications. Functional paragangliomas resemble pheochromocytomas in structure and function. They are known to lead to complications including cardiogenic shock and cerebrovascular incidents.⁵ The catecholamine excess from these tumours can cause ADP-mediated platelet aggregation leading to thrombotic events. They may also lead to stress-induced cardiomyopathy.^{6–8} Cardiac systolic function is often rigorously reduced in these cases. Virchow's triad lists the conditions; blood stasis, inflammatory changes

Figure 3 Echocardiographic image of thrombus.

Figure 4 Echocardiographic image of thrombus.

and hypercoagulability that favour the formation of a thrombus in vivo. There is also some controversial proof from studies that indicate that β -blockers might be involved in increased blood stasis and thrombus formation.⁹ Our patient's BP was controlled with the use of β -blockers along with other antihypertensive medications. He was in a hypercoagulable state from the release of excessive catecholamines from the paraganglioma. He had underlying subendocardial damage as evident from elevated cardiac biomarkers causing inflammation. Although his EF was normal, there was some mild hypokinesis of the distal ventricular walls. These factors were likely involved in the aetiology of his LV thrombi formation. This is a unique occurrence of LV thrombi in the setting of a paraganglioma with no major wall motion abnormalities. There have been six other reported cases of LV thrombi associated with paraganglioma or pheochromocytomas^{8–14} (table 1). One case was about a young 18-year-old girl with a history of multiple endocrine neoplasia type 2 who was found to have medullary thyroid carcinoma as well as pheochromocytoma.⁸ Her echocardiogram was unremarkable for any abnormal LV function or wall motion abnormality; however, an LV thrombus was identified. She did not suffer from any embolic complications. No anticoagulation was used and the thrombus was surgically resected. Another report describes an incidentally found pheochromocytoma in a 43-year-old man who presented with nausea and tachypnoea.¹⁰ An LV thrombus was identified on echocardiogram which resolved with anticoagulation and had no complications. Four of the patients were middle-aged men like our patient and suffered from embolic strokes. Their presenting symptoms were different such as abdominal pain, shortness of breath and pneumonia. In all of them a diagnosis was made after measuring either serum catecholamine excess or high urinary vanillyl mandelic acid levels. No specific ECG findings were noted. However, repolarisation findings were seen. Echocardiography did show hypokinetic or akinetic changes in three of these men. The seventh case was of a 43-year-old woman admitted to the intensive care unit with acute rapidly progressive dyspnoea, tachycardia and vomiting. Her course was complicated with systemic embolisation leading to renal infarction. Her echocardiogram showed inferior wall akinesis with a normal EF of 50%. There was also no suggestion of hypertrophy or dilated cardiomyopathy.^{11–14} These cases show a pattern of presentation of LV thrombi in patients with neuroendocrine tumours. Excessive catecholamine release was common in all these cases. The presentation of LV

Table 1 8–14

	Pishdad ⁸	Heindel <i>et al</i> ¹¹	Yebra Yebra <i>et al</i> ¹²	Buchbinder <i>et al</i> ¹³	Wiyono <i>et al</i> ¹⁰	Zhou <i>et al</i> ¹⁴	Shafiq <i>et al</i>
Age (years)	18	49	59	49	43	43	47
Sex	Female	Male	Male	Male	Male	Female	Male
Family history	Medullary carcinoma thyroid	None mentioned	None mentioned	Cancer but no endocrine neoplasia	None mentioned	None mentioned	Sisters with pheochromocytomas
PMH	None	Migraine headaches and HTN	HTN	Decreased exercise tolerance	TIA	Viral myocarditis	None
Presentation	Vomiting, abdominal pain	Pneumonia	Paroxysm	Abdominal pain, dysphasia, weakness	Nausea, vomiting and tachypnoea	Dyspnoea, tachycardia and vomiting	Chest pain and palpitations
Embolic complication	No	Yes: stroke	Yes: stroke	Yes: stroke and systemic renal infarcts	Yes: TIA	Yes: systemic emboli	Yes: stroke
Electrocardiography findings							
QT interval	Not described	Not described	Prolonged	Prolonged	Not described	Not described	Not prolonged
T wave	Normal	Diffuse T-wave changes	T-wave inversion	T-wave inversion	T-wave inversion	ST segment elevation precordial leads	Diffuse T-wave changes
LV function							
Wall motion	Normal	Diffuse hypokinesis	Apical akinaesia	Mild hypokinesis	Normal	Inferior wall akinesis	Mild hypokinesis
Ejection fraction (%)	Normal 50	40–50	25	47	Normal 50	Normal 50	50–55
Recovery after tumour resection	Complete	Complete	Complete	Complete	Complete	Complete	Complete
LV thrombus							
Number	1	3	1	1	1	2	2
Structure	Creamy rubbery tissue adhering	Mobile, pedunculated	Adhering	Mobile, pedunculated	Adhering	Adhering	1 Mobile
Size (cm)	2×2×2	0.5–1.0	0.6×3.0	1.3×1.9	Large (dimensions not mentioned)	0.07–2.8	1.43–1.8
Location	Apex and interventricular septum	Apex	Apex, posterior wall	Interventricular septum	Apex	Apex	Apex
Treatment for thrombus	Surgical resection	Anticoagulation	Anticoagulation	Anticoagulation	Anticoagulation	Anticoagulation	Anticoagulation
Response to anticoagulation	Not given	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved
Underlying tumour	Pheochromocytoma	Pheochromocytoma	Pheochromocytoma	Functional paraganglioma	Pheochromocytoma	Pheochromocytoma	Functional paraganglioma
Excessive catecholamine release	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tumour							
Size (cm)	5×8	10	3.5	7.7×5.2×7.7	(Dimensions not mentioned)	4.0×3.0×3.0	3.4×4.7×5.3
Side	Right	Left	Left	Left	Left	Right	Left
Cardiac biomarkers	Normal	Elevated	Elevated	Elevated	Elevated	Elevated	Elevated

LV, left ventricular.

thrombi along with neuroendocrine tumours was more common in middle age patients and involved both sexes but favoured predominance in men. ECG changes and elevated biomarkers were present in almost all of the cases. These tumours were predominantly left sided. Majority of the patients had severe embolic complications. All the patients when treated with anticoagulation showed a resolution of the LV thrombus. Family history was significant in our patient with sisters of the patients having pheochromocytomas. Although the family history was not mentioned in most of the patients we described, when present it is a very essential piece of information for clinicians to diagnose this condition.

Learning points

- ▶ Clinicians should have an increased index of suspicion for a left ventricular thrombus and systemic embolism in a patient with suspected paraganglioma or pheochromocytoma.
- ▶ A mass identified within the ventricles of these patients is likely an intracardiac thrombus and these patients may benefit from prompt, systemic anticoagulation.
- ▶ Timely diagnosis of such cases may help reduce morbidity and mortality.

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REFERENCES

- DeLellis RA, Lloyd RV, Heitz PU, *et al.* Tumors of the adrenal gland. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C, eds. *Pathology and genetics of tumours of the endocrine organs. WHO classification of tumours*. Lyon, France, IARC press, 2004:164–8.
- Erickson D, Kudva YC, Ebersold MJ, *et al.* Benign paragangliomas: clinical presentation and treatment outcomes in 236 patients. *J Clin Endocrinol Metab* 2001;86:5210.
- DeMers G, Portouw S. Paraganglioma causing a myocardial infarction. *J Emerg Trauma Shock* 2012;5:190–2.
- Young WF Jr. Paragangliomas: clinical overview. *Ann N Y Acad Sci* 2006;1073:21–9.
- Manger WM. An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. *Ann N Y Acad Sci* 2006;1073:1–20.
- Zegdi R, Parisot C, Sleilaty G, *et al.* Pheochromocytoma-induced inverted Takotsubo cardiomyopathy: a case of patient resuscitation with extracorporeal life support. *J Thorac Cardiovasc Surg* 2008;135:434–5.
- De Souza F, Altenburg Odebrecht Curi Gismondi R, Henriques Cunha Neto S, *et al.* Tako-tsubo-like cardiomyopathy and extra-adrenal pheochromocytoma: case report and literature review. *Clin Res Cardiol* 2008;97:397–401.
- Pishdad GR. Ventricular thrombosis in Sipple's syndrome. *South Med J* 2000;93:1093–5.
- Delewi R, Zijlstra F, Piek JJ. Left ventricular thrombus formation after acute myocardial infarction. *Heart* 2012;98:1743–9.
- Wiyono SA, Vletter WB, Soliman OI, *et al.* Thrombus in a normal left ventricle: a cardiac manifestation of pheochromocytoma. *Echocardiography* 2010;27:195–7.
- Heindel SW, Maslow AD, Steriti J, *et al.* A patient with intracardiac masses and an undiagnosed pheochromocytoma. *J Cardiothorac Anesth* 2002;16:338–43.
- Yebra Yebra M, Martin Asenjo R, Arrue I, *et al.* Acute myocardial ischemia and ventricular thrombus associated with pheochromocytoma. *Rev Esp Cardiol* 2005;58:598–600.
- Buchbinder NA, Yu R, Rosenbloom BE, *et al.* Left ventricular thrombus and embolic stroke caused by a functional paraganglioma. *J Clin Hypertens (Greenwich)* 2009;11:734–7.
- Zhou W, Ding SF. Concurrent pheochromocytoma, ventricular tachycardia, left ventricular thrombus, and systemic embolization. *Intern Med* 2009;48:1015–19.

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