CASE REPORT: ADRENAL PHAEOCHROMOCYTOMA PRESENTING WITH ILEUS, RENAL VEIN THROMBOSIS AND PULMONARY EMBOLISM

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Introduction

Phaechromocytomas are catecholamine-secreting neuroendocrine tumours arising from chromaffin cells in the adrenal medulla. They may potentially present with a wide variety of symptoms – including, classically, headache, palpitations, diaphoresis, and paroxysmal or sustained hypertension[1-2]. However, making the diagnosis can still be challenging, particularly if the clinical presentation is atypical. We report one such case.

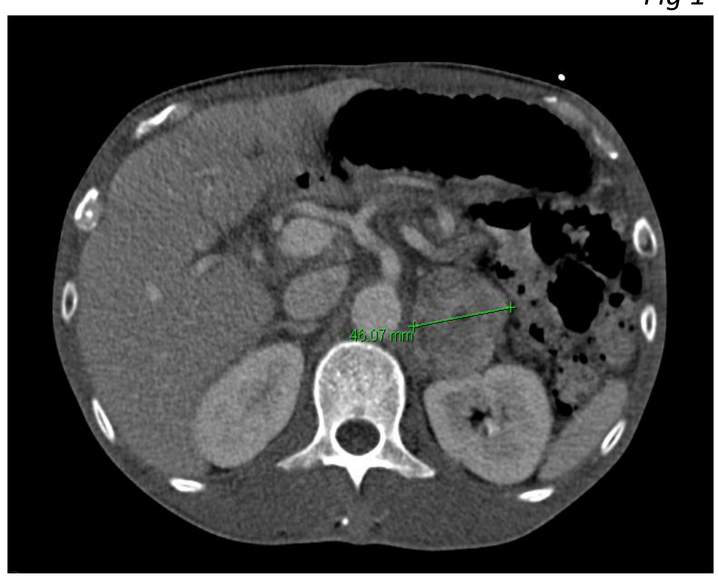
Case Presentation

A 56 year old man, previously well, presented to our Emergency Department with a 5-day history of abdominal distension, vomiting, breathlessness, and haemoptysis. He had a preceding history of hypertension, which had been diagnosed one year ago, and for which he was not on treatment.

Physical examination revealed a temperature of 38.3°C, BP 159/95mmHg, and sinus tachycardia at HR 126/min. Lung fields were clear to auscultation. The abdomen was distended but non-tender, with hyperactive bowel sounds.

An urgent CT scan of the abdomen revealed gross dilatation of a long segment of small bowel, with a transition point at the distal jejunum. Incidental note was made of a heterogeneous 4.6 x 4.5 x 4.9cm left adrenal mass, with associated left renal vein thrombosis (Fig 1). The imaged lung bases showed a suggestion of a left lower lobe segmental pulmonary embolism, the presence of which was confirmed on a subsequent CT pulmonary angiogram (Fig 2). Doppler ultrasound of both lower limbs showed no deep venous thrombosis.

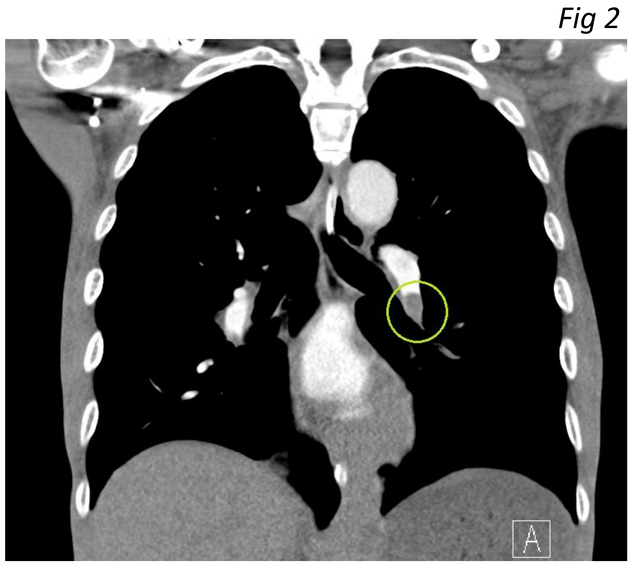
Fig 1



The patient underwent an emergent laparotomy and bowel decompression. Intra-operatively, no obstructing bowel lesion was identified. Post-operatively, blood pressure was noted to range up to 200/120mmHg, with persistent tachycardia up to 120-140/min – these improved over the course of 3-4 days with anti-hypertensive treatment (nifedipine) and hydration. Anticoagulation with SC enoxaparin was commenced for venous thromboembolism. The patient recovered well post-operatively and was discharged.

Attention was thereafter directed towards evaluation of his left adrenal mass. Adrenal biochemistry, sent 6 days post-operatively, demonstrated urinary metanephrines and normetanephrines elevated over 10 times the normal range (Table 1), supporting the diagnosis of a left adrenal phaeochromocytoma. The patient was switched to phenoxybenzamine for BP control, with atenolol added later.

Fig 2



An elective laparoscopic left adrenalectomy was scheduled. Intra-operatively, a 4.0 x 4.8 x 3.4cm left adrenal tumour, with no extra-adrenal invasion into surrounding structures, was identified and resected. Histology was consistent with phaeochromocytoma; no mitotic activity was identified within clusters of tumour cells.

Table 1

Test	Pre-op	POD 3	POD 15	6 wks post-op	Reference Range
24h urinary adrenaline (nmol/day)	4046	45.2	<10.0	<10.0	9.3 – 122
24h urinary noradrenaline (nmol/day)	6707	802	352	203	72 – 505
24h urinary metanephrine (nmol/L)	45232	960	520	298	700 – 2000
24h urinary normetanephrine (nmol/L)	34032	4521	2014	935	480 – 2424

Post-operative recovery was uneventful, and the patient was discharged stable. His urinary metanephrines and normetanephrines fell to normal by 15 days post-surgery (Table 1). A repeat CT scan of the thorax 6 weeks post-operatively showed complete resolution of the left lower lobe pulmonary embolus. Anticoagulation was discontinued, and blood pressure normalised with maintenance on low-dose bisoprolol and lisinopril. The patient has since remained well.

Discussion

Paralytic ileus and venous thromboembolism are two relatively uncommon manifestations of phaeochromocytoma. It is rarer still for both to occur simultaneously, as in our patient.

The gastrointestinal effects of phaeochromocytoma may range from mild and non-specific abdominal pain and vomiting[1] to more severe refractory constipation, ileus, and enterocolitis[3-8]. Catecholamines suppress intestinal motility via direct effects on alpha- and beta-adrenergic receptors in the gut, resulting in reduced intestinal tone and peristalsis, and contraction of intestinal sphincters[4,6]. Furthermore, catecholamine-mediated contraction of smooth muscle in the mesenteric vasculature, in combination with increased intestinal metabolic demand, result in bowel ischaemia, which in itself may contribute to dysmotility[4,6-8].

Cases of paralytic ileus associated with phaeochromocytoma have been occasionally reported since the mid-1900s[3-8], with ileus usually resolving after tumour resection and/or alpha-blockade[3-4,8]. The recognition of ileus as a complication of phaeochromocytoma is important, as there is a possibility of progression to bowel infarction and perforation if diagnosis and treatment are delayed[4,6-7].

In contrast, the haemostatic effect of catecholamine excess has been spotlighted only in more recent literature (Table 2), with several postulated pathophysiological mechanisms.

Firstly, catecholamines exert direct effects on primary and secondary haemostasis[9] – adrenergic infusions have been shown *in-vivo* to increase fVIII activity, vWF antigen, tPA activity, and platelet activation and aggregation in a dose-dependent fashion[10]. Conversely, administration of the beta-blocker propranolol was found in one study to reduce fVIII:C levels in patients with deep vein thrombosis, as compared to untreated controls[11].

A review of the cases highlighted offers possible alternative explanations for thrombotic phenomena – including direct tumour invasion into the inferior vena cava, arising from a right adrenal tumour[12-13,15,19,22]; venous stasis due to extrinsic tumour compression[14]; a prothrombotic state further contributed by malignancy[21,29] or polycythaemia (arising in one case from tumour secretion of erythropoietin[21]); and catecholamine-induced cardiomyopathy with intracardiac thrombus and thromboembolism[28-30,32,34,36-37].

Nonetheless, there are cases of thrombosis for which these "alternative" mechanisms fail to account – for example, intracardiac thrombi without evidence of cardiomyopathy[31,33,35]. This corroborates the likely independent effect of catecholamine excess on systemic hypercoagulability. Our patient, too, experienced venous thromboembolism on the background of an apparently benign, moderately-sized tumour. While no strong recommendation for prophylactic anticoagulation in phaeochromocytoma can yet be made, increased vigilance for arterial and venous thromboembolism in these patients could allow for earlier intervention and the avoidance of morbidity.

In summary, while paralytic ileus and thrombotic events are not typically associated with phaeochromocytomas, this case report underlines their importance as clinically relevant manifestations of catecholamine excess.

REFERENCES

1. Manger WM, Gifford RW. J Clin Hypertens (Greenwich). 2002 Jan-Feb;4(1):62-72.
2. Manger WM, Eisenhofer G. Curr Hypertens Rep. 2004 Dec;6(6):477-84.
3. Hughes LE, et al. Proc R Soc Med. 1962 Dec;55:998.
4. Turner CE. Am J Gastroenterol. 1983 Apr; 78(4):214-7.
5. Baba T, et al. Endocrinol Jpn. 1985 Apr;32(2):337-45.
6. Hashimoto Y, et al. Jpn J Med. 1990 May-Jun;29(3):341-6.
7. Fee HJ, et al. Ann Surg. 1977 Apr;185(4):448-50.
8. Osinga TE, et al. Neth J Med. 2013 Dec;71(10):512-7.
9. van Zaane B, et al. Semin Thromb Hemost. 2013 Jul;39(5):489-95.
10. von Kanel R, Dimsdale JE. Eur J Haematol. 2000 Dec;65(6):357-69.
11. Hoppener MR, et al. J Thromb Haemost. 2004 Aug;2(8):1316-20.
12. Dural C, et al. Minerva Chir. 2010 Aug;65(5):485-8.
13. Hartgrink HH, et al. Eur J Surg Oncol 2001 Feb;27:115-9.
14. Kota SK, et al. J Cardiovasc Dis Res. 2012 Apr;3(2):160-4.
15. Ku CF, et al. Hong Kong Med J. 2005 Feb;11(1):59-62.
16. Lucon AM, et al. Sao Paulo Med J. 2001 Mar;119(2)86-8.
17. Lucon AM, et al. BJU Int. 2004 Jul;94(1):70-3.
18. Novick AC, et al. Ann Surg. 1990 Oct;212(4):472-6.
19. Rotker J, et al. Ann Thorac Surg. 1996 Jan;61(1):222-4.
20. Shigemura K, et al. Int Urol Nephrol. 2007;39(1):103-6.
21. Shulkin BL, et al. Am J Med. 1987 Oct;83(4):773-6.
22. Waidelich R, et al. Int Urol Nephrol. 2002;34(2):241-3.
23. Osman Y, et al. Urol Int 2011;87(2):182-5.
24. Stella P, et al. Nephrol Dial Transplant. 2000 May;15(5):717-8.
25. Brauchlin AE, et al. Am J Emerg Med. 2009 Jun;27(5):630.e3-5.
26. Robert B, et al. Diagn Interv Imaging. 2012 Jul;93(7-8):625-8.
27. Stevenson S, et al. J Vasc Surg. 2005 Sep;42(3):570-2.
28. Buchbinder NA, et al. J Clin Hypertens (Greenwich). 2009 Dec;11(12):734-7.
29. Dagartzikas MI, et al. Pediatr Emerg Care. 2002 Feb;18(1):33-5.
30. Heindel SW, et al. J Cardiothorac Vasc Anesth. 2002 Jun;16(3):338-43.
31. Hou R, et al. J Med Case Rep. 2011 Jul 13;5:310.
32. Mrdovic I, et al. Tex Heart Inst J. 2008;35(4):480-2.
33. Pishdad GR. South Med J. 2000 Nov;93(11):1093-5.
34. Shafiq A, et al. BMJ Case Rep. 2013 Nov 19;2013.
35. Wiyono SA, et al. Echocardiography. 2010 Feb;27(2):195-7.
36. Yebra Yebra M, et al. 2005 May;58(5):598-600.
37. Zhou W, Ding SF. Intern Med. 2009;48(12):1015-9.
38. Kaiser S, et al. J Vasc Surg 2013 Oct;58(4):1069-72.
39. Thewjitcharoen Y, et al. Urology. 2013 Sep;82(3):e17.
40. Battimelli A, et al. Am J Emerg Med. 2014 Mar;32(3)286.e5-9.

Table 2

Case Report	Age	Gender	Tumour location / largest diameter	Arterial thromboembolism / venous
Dural[12]	17	M	Right adrenal, 10cm	IVC, right atrium
Hartgrink[13]	38	F	Right adrenal, 16cm	IVC, right atrium Left latero-basal pulmonary embolism
Kota[14]	48	M	Right adrenal, 7.6cm	IVC up to confluence of hepatic veins
Ku[15]	21	F	Right adrenal, 12cm	IVC, right atrium
Lucon[16]	43	M	Right adrenal, 6.5cm	IVC
Lucon[17]	46	M	Right adrenal, 8cm	IVC
	43	M	Right adrenal, 10.6cm	IVC
	24	F	Right adrenal, 5.5cm	IVC
Novick[18]	U	U	Adrenal, details unknown	IVC
Rotker[19]	51	M	Right adrenal, 4.3cm	IVC
	58	F	Right adrenal – resected 2 yrs prior	IVC, right atrium
Shigemura[20]	61	M	Right adrenal, 6.7cm	IVC
Shulkin[21]	31	M	Multiple abdominal phaeochromocytomas	IVC, right common femoral vein, right inferior epigastric veins
Waidelich[22]	78	F	Right adrenal, 8cm	IVC, right adrenal vein
Osman[23]	U	M	Adrenal, details unknown	Adrenal +/- renal vein
Stella[24]	38	M	Right adrenal, 4-5cm	Cerebral venous sinuses
Brauchlin[25]	51	M	Ectopic (pelvis), recurrent, 8cm	Portal vein
Robert[26]	43	M	Ectopic (organ of Zuckerkandl), 7cm	Superior mesenteric vein
Stevenson[27]	46	M	Ectopic (organ of Zuckerkandl), 9cm	Left iliofemoral vein
Buchbinder[28]	49	M	Left retroperitoneal paraganglioma, 7.7cm	Left renal vein LV thrombus (1.3x1.9cm) Stroke Multiple left renal infarcts
Dagartzikas[29]	13	M	Left adrenal, 8.5cm	LV thrombus Right middle cerebral artery Bilateral acute lower limb ischaemia
Heindel[30]	49	M	Left adrenal, 10cm	3 LV thrombi (0.5-1.0cm) Right cerebellar and cortical infarcts; right frontal lobe infarct Right foot ischaemia
Hou[31]	47	F	Left adrenal, 8cm	"Large" LV thrombus Left axillary artery
Mrdovic[32]	53	F	Left adrenal, size unknown	"Large" LV apical thrombus
Pishdad[33]	18	F	Right adrenal, 8cm	LV thrombus (2cm)
Shafiq[34]	47	M	Mediastinal paraganglioma, 5.3cm	2 LV thrombi (1.43- 1.8cm) Multiterritory (anterior / posterior circulation) cerebral infarcts
Wiyono[35]	43	M	Left adrenal, size unknown	"Large" LV thrombus
Yebra Yebra[36]	59	M	Left adrenal, 3.5cm	LV thrombus, 3x0.6cm Left-sided cerebral infarct
Zhou[37]	43	F	Right adrenal, 7cm	LV thrombi (28x17mm, 0.8x0.7mm) Multiple renal infarcts Bilateral femoral arteries; peroneal, anterior / posterior tibial arteries
Kaiser[38]	50	F	Left adrenal, 7.8cm	Right middle cerebral artery Right distal subclavian to radial artery
Thewjitcharoen[39]	47	F	Right adrenal, size unknown	Right renal artery
Battimelli[40]	63	F	Left adrenal, 7cm	Right posterior tibial artery

U = unknown

IVC = inferior vena cava; LV = left ventricle

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