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Pheochromocytoma Crisis Triggered by Extra-Corporal Membrane Oxygenation Explantation

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Context: We report a 59 year old Chinese woman in pheochromocytoma multisystem crisis and was initially stabilised with ECMO; subsequently she manifested rapid cyclical fluctuation of blood pressure precipitated by explantation of ECMO.
Case Description: Madam L presented with chest pain and giddiness. She developed cardiogenic shock refractory to double inotropes and intra-aortic balloon pump (IABP); but responded to Extra-Corporal Membrane Oxygenation (ECMO). Subsequently rapid cyclical blood pressure fluctuations from 230 mmHg to 50mmHg systolic occurred after explantation of ECMO. Biochemically urine metanephrines and normetanephrines were more than seven times above upper limit of normal. Imaging confirmed the presence of right adrenal mass likely pheochromocytoma. She was started on alpha blockade and underwent an uneventful laparotomy with removal of a 10 cm adrenal mass. Histology confirmed a large cystic pheochromocytoma with haemorrhagic components.
Conclusions: Pheochromocytoma crisis should be suspected in cases of unexplained shock or Takutsubo cardiomyopathy; early recognition and ECMO support can be life-saving. In addition, ECMO explantation can trigger rapid cyclical blood pressure fluctuations and should be closely monitored for.

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Keywords: Pheochromocytoma crisis; ECMO explantation; Takutsubo cardiomyopathy; adrenal mass.

1. INTRODUCTION

Pheochromocytoma multisystem crisis (PMC) is defined as multiple organ failure, lactic acidosis, and temperature often greater than 40℃, encephalopathy, and hypertension and/or hypotension [1]. Presentation as unexplained shock is one of the most dangerous situations for undiagnosed pheochromocytoma [2-4]. Cystic pheochromocytoma has been associated with special clinical, imaging and histological phenotype [5]. In this case we present a patient with a large cystic pheochromocytoma who presented with cardiogenic shock from Takutsubo cardiomyopathy responsive only to ECMO support, and subsequently manifested unusual rapid cyclical blood pressure fluctuations [6] likely precipitated by explantation of ECMO.

2. CASE REPORT

A 59 year old lady with no past medical history presented with intermittent retrosternal chest pain of 1 day duration. This was associated with temporal headache, giddiness and near-syncope but no diaphoresis. She also had sudden onset epigastric pain associated with retching and nausea.

She had lost weight and had occasional palpitations for the last two years. Her blood pressure was noted to be 160/90 during a health screening two months prior. Whereas her home blood pressure was between 120 and 150 mmHg systolic. She did not have significant family history for young hypertension, cancer or unexplained deaths.

Physical examination revealed a cachectic lady with no mucosal or palmar crease hyperpigmentation. She had no stigmata of neurofibromatosis. She was afebrile but hypotensive with tachycardia. Her blood pressure was 84/54 mmHg, pulse rate 110 beats per minute, and oxygen saturation was 80 to 90% despite 100% oxygen supplementation. Otherwise examination was unremarkable.

Laboratory investigations are summarised in Table 1. Her cardiac enzymes were significantly elevated with electrocardiogram showing concave ST segment elevation (STEMI) on lateral leads. Chest radiograph showed bilateral chest infiltrates suggestive of acute pulmonary oedema (APO). She was treated as cardiogenic shock from STEMI with APO and underwent coronary angiogram which was normal. Her transthoracic echocardiography showed estimated left ventricular ejection fraction of 10 to 15% with regional wall motion abnormalities suggestive of Takutsubo cardiomyopathy.

She rapidly deteriorated within 48 hours of admission; was persistently hypotensive despite double inotropes and intra-aortic balloon pump (IABP). ECMO was initiated which stabilised her blood pressure. Explantation of ECMO after 12 days occurred as she was improving; Etomidate 2 mg was given for sedation and Phenylephrine 200 mg was given intra-op because of hypotension. She developed rapid cyclical blood pressure fluctuations about every 20-30 minutes ranging from 230 to 50 systolic after the explantation (Fig. 1). A pheochromocytoma was suspected and 24-hour urinary catecholamines and metanephrines performed were noted to be markedly raised (Table 1).

An abdominal ultrasound showed a 10.1x8.6x9.4 cm solid cystic lesion with an internal calcific focus related to segment 6 of the liver. A computed tomography (CT) of the abdomen showed a 9x8.5 cm solid cystic mass in the right supra-renal region inseparable from the right liver lobe. CT was unable to distinguish whether this mass originated from the liver or the right adrenal. Magnetic resonance imaging (MRI) however, clearly demarcated the mass to be arising from the right adrenals. She underwent a ^{68}Gallium Dota-peptide scan as ^{123}-MIBG scan was not available in our institution, which demonstrated a rim enhancing lesion with central areas of cystic changes likely adrenal with moderate tracer uptake is seen in the solid component of this lesion along the margins likely a cystic pheochromocytoma (Fig. 2).

The diagnosis of pheochromocytoma was confirmed based on her clinical presentation, biochemical and imaging results. She was initiated on intravenous phentolamine infusion. Her blood pressure was maintained on 0.5-3 mg/hour of phentolamine. Fluid repletion was achieved with intravenous normal saline 2 to 3 litres per day and oral salt tablets 4.5 grams per day. The rapid cyclical blood pressure fluctuations did not recur after phentolamine was initiated. Her blood pressure remained stable while on the phentolamine infusion and was converted to oral Phenoxybenzamine 1 week prior to right adrenalectomy.

Table 1. Relevant laboratory investigations

Test	Result	Normal range
CK	**950**	44-201 U/L
CKMB	**75.5**	1.0-5.0 Ug/L
Trop T	**3821**	<30 Ng/L
24-hour urine Epinephrine	243 nmol/day	3-109 nmol/day
24-hour urine Dopamine	1074 nmol/day	424-2612 nmol/day
24-hour urine Metanephrine	**11692 nmol/day (7X)**	400-1500 nmol/day
24-hour urine Normetanephrine	**25076 nmol/day (13X)**	600-1900 nmol/day

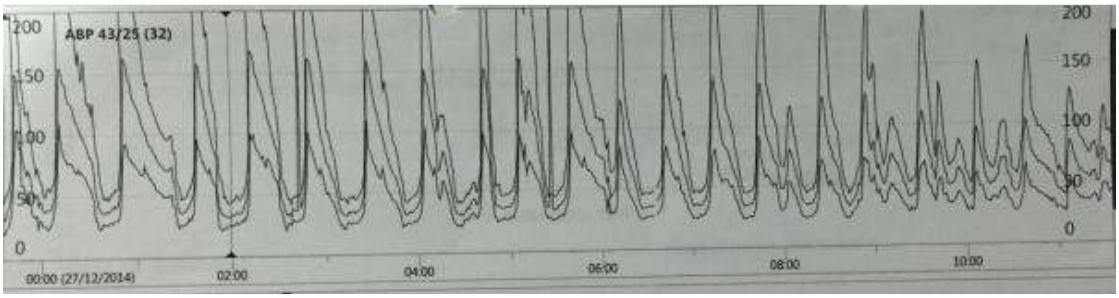

Fig. 1. Telemetric chart in intensive care unit showing blood pressure fluctuation after ECMO explantation. Highest blood pressure was 210/110; lowest blood pressure was 43/25. Fluctuations happened about every 20 minutes

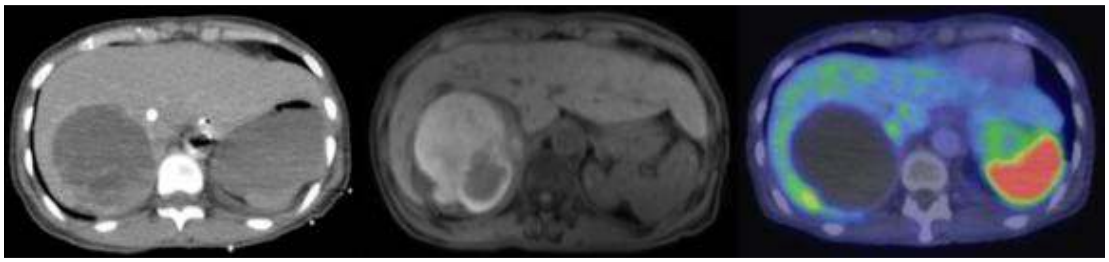

Fig. 2. CT scan vs MRI (T1) vs 68 Gallium Dota-peptide scan of the right abdominal mass demonstrating clear delineation of the adrenal from liver on MRI but not on CT, functional scan showed large cystic adrenal mass

She underwent an uneventful open right adrenalectomy which removed a 10 cm adrenal mass. Pheochromocytoma was confirmed histologically with clear resection margins. The tumour cells are immunoreactive for chromogranin and synaptophysin. Ki-67 immunolabelling reveals a proliferation fraction of <2%. Post op outpatient biochemical evaluation was normal 4 weeks after surgery.

3. DISCUSSION

Presentation of pheochromocytoma is protean and the classical triad described as headache, palpitations, sweating associated with hypertension. Pheochromocytoma should be considered in patients who present with unexplained shock, cardiac arrest or stress (Takutsubo) cardiomyopathy [7]. Conventional vasopressor therapy is ineffective in patients who have chronic exposure to catecholamines as they develop functional adrenergic desensitisation. ECMO support as a bridge to definitive pharmacological treatment and subsequent surgical resection of pheochromocytoma is increasingly reported to be strongly associated with survival [8,9]. In addition there are reports of patients undergoing

adrenalectomy with ECMO support. ECMO explantation triggering catecholamine surge resulting in rapid cyclical blood pressure fluctuations however has not been reported. The pheochromocytoma crisis in this patient was possibly precipitated by the stress of ECMO explantation.

Pharmacological treatment is usually with alpha blockers such as Phenoxybenzamine or Doxazosin. Phenoxybenzamine, which is an irreversible non-competitive antagonist with a long half-life of 24 hours, was felt to be unsuitable in the management of this patient in view of the wide cyclical blood pressure fluctuations ranging from systolic 210 mmHg to 40 mmHg. Phentolamine, a short acting intravenous alpha-blocker, has been shown to be effective in the management of pheochromocytoma peri-operatively at low doses. The dose of phentolamine used in this patient was low (maximum of 3 mg) compared to reported series where doses as high as 40 mg were required to control the blood pressure of these cases [10]. The reason for the difference is unclear, but could be related to cystic nature of the mass resulting in reduced secretion of the catecholamines and normetanephrines [5].

4. CONCLUSION

Pheochromocytoma should be suspected when patients have unexplained shock or Takutsubo cardiomyopathy; early recognition and ECMO support can be life-saving. ECMO explantation may trigger another crisis after initial stabilisation and should be closely watched out for. (Word count 977).

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kenneth A Newell, Richard A Prinz, Jack Pickleman, Susan Braithwaite, Marion Brooks, Tom H Karson, Silas Glisson. Pheochromocytoma multisystem crisis. A surgical emergency. Arch Surg. 1988;123: 956–959.
2. Bergland BE. Pheochromocytoma presenting as shock. Am J Emerg Med. 1989;7:44–48.
3. Mohamed HA, Aldakar MO, Habib N. Cardiogenic shock due to acute hemorrhagic necrosis of a pheochromocytoma: A case report and review of the literature. Can J Cardiol. 2003;19:573–576.
4. Hanna JS, Spencer PJ, Savopoulou C, Kwasnik E, Askari R. Spontaneous adrenal phaeochromocytoma rupture complicated by intraperitoneal hemorrhage and shock. World J Emerg Surg. 2011;6:27.
5. Cassio Andreoni, Rodrigo K Krebs, Paulo C Bruna, Suzan M Goldman, Claudio E Kater, Maria TS Alves, Valdemar Ortiz. Cystic phaeochromocytoma is a distinctive subgroup with special clinical, imaging and histological features that might mislead the diagnosis. BJU International. 2008;101(3): 345-350.
6. Ganguly A, Clarence Grim, Myron H Weinberger, Henry DP. Rapid cyclic fluctuations of blood pressure associated with an adrenal pheochromocytoma. Hypertension. 1984;6(2 Pt 1):281-284.
7. Fabio Galetta, Ferdinando Franzoni, Giampaolo Bernini, Fallawi Poupak, Angelo Carpi, Giuseppe Cini. Cardiovascular complications in patients with pheochromocytoma: A mini-review. Biomedicine & Pharmacotherapy. 2010;64: 505–509.
8. Whitelaw BC, Prague JK, Mustafa OG, Schulte K-M, Hopkins PA, Gilbert JA, McGregor AM, Aylwin SJB. Phaeochromcytoma crisis. Clin Endocrinol (Oxf). 2014;80:13–22.
9. Flam B, Broomé M, Frenckner B, Bränström R, Bell M. Pheochromocytoma-induced inverted takotsubo-like cardiomyopathy leading to cardiogenic shock successfully treated with extracorporeal membrane oxygenation. Journal of Intensive Care Medicine. 2014;10.

   DOI: 10.1177/0885066614552992

10. Wesley D McMillian, Bryan J Trombley, William E Charash, Rose C Christian. Phentolamine continuous infusion in a patient with pheochromocytoma. American Journal of Health-System Pharmacy. 2011;68(2):130-134.

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