



Open Adrenalectomy for a Giant Pheochromocytoma in a Patient with End Stage Renal Disease: Dilemma, Preparation, Anaesthesia and Haemodynamic Monitoring

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Abstract

The diagnosis and management of pheochromocytoma in renal failure patients requires scrupulous preparations due to the challenges its excision poses in terms of estimating and managing intravascular volume and vascular tone. This report summarizes the perioperative management of a 24-year old patient on haemodialysis who underwent open adrenalectomy for a ginormous unilateral pheochromocytoma, in order to provide reference to managing similar cases. The tumour presented as a suspicious mass during random imaging and was confirmed by clinical, CT scan and serum catecholamine by-product assay data. Large tumour size, arduous surgery and strong functional activity resulted in near haemodynamic collapse in spite of reasonable preoperative optimization. The ability of FloTrac monitoring system to reflect and assess circulatory changes and to guide fluid and vasopressor usage was also analyzed and presented.

Keywords

Pheochromocytoma; Adrenalectomy; ESRD; Vasopressor; Systemic Vascular Resistance; Cardiac Output

Introduction

Pheochromocytoma (PCC) is a rare catecholamine (CA) secreting chromaffin tissue tumour, occurring in less than 0.5% of patients with hypertension (HTN) [1]. About 30 percent of PCC occur in association with familial neuroendocrine syndromes (MEN), while majorities are sporadic. Roughly 10–40% of these tumours are found incidentally and the classic symptomatology, i.e., paroxysmal HTN, palpitation and diaphoresis is present in only 40% of the cases. These tumours may secrete epinephrine (E), norepinephrine (NE), or dopamine in either a continuous manner (leading to sustained HTN) or episodic pattern (leading to paroxysms of symptoms). Surgery, wherever feasible, is the treatment of choice for these tumours with diligent preoperative optimization involving vascular expansion and control of HTN[2]. The true incidence of PCC in patients with end stage renal disease (ESRD) is unknown and considered exceedingly uncommon. Most data on the anaesthetic management and perioperative outcomes have been reported in small case series, consequently there is obscurity in diagnosis, preparation, and intra operative monitoring. In addition to perplexity associated with ESRD patient's volume status, it remains unclear whether fluid deficit or vasoplegia causes shifting haemodynamics intraoperatively, while appropriate targets remain unclear. We report peri-operative management of a 24-yrs old gentleman known case of ESRD on maintenance haemodialysis (HD) who underwent open adrenalectomy and nephrectomy for a large PCC. We utilized FloTrac device (4th generation, version 4; Edwards Life science, Irvine, CA, USA) to titrate

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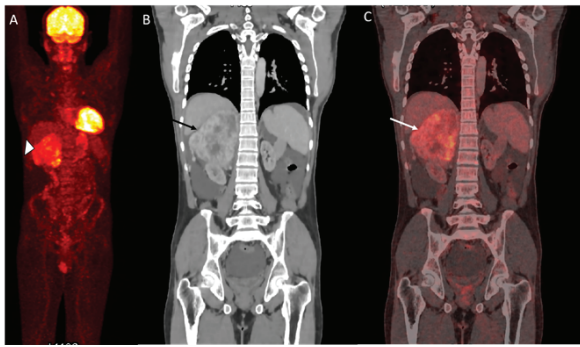


Figure 1: PET /CT image showing tumour occupying the upper pole of right kidney, pushing it down and adherent to the inferior surface of liver

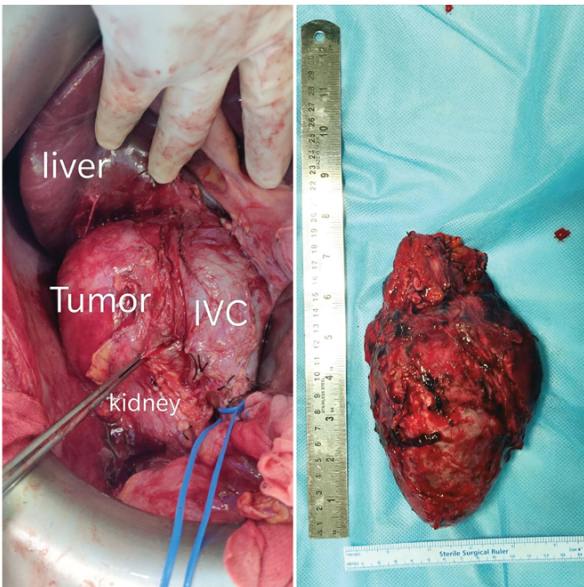


Figure 2: Image showing 17 cm tumour arising from right adrenal gland occupying the upper pole of right kidney and adherent to entire length of infrahepatic inferior vena cava (IVC). Distal to the tumour IVC is looped for vascular control.

timing and infusions of volume and vasopressors to respond to rapid changes in intra-operative haemodynamics.

Case Presentation

A 24 years old gentleman known ESRD of unknown cause, on irregular maintenance HD for 4 years was referred to surgical oncology for a suspicious right adnexal mass identified during ultrasound imaging for prospective renal transplantation evaluation. His other comorbidities were HTN, subclinical thyrotoxicosis and anaemia. His drug therapy included Injdarbepoetin 40mcg SC twice a week, tab isolazine (isosorbide dinitrate/hydralazine) 20/37.5mg half hs, tab amlodipine 5 mg bd, tab bisoprolol 2.5mg od, tab sodium bicarbonate 1gm tds and tab prazosin 2.5mg bd. His symptoms included occasional headache, palpitation, and dizziness on exertion since 17 years of age which the treating physician attributed to chronic renal failure. There was no associated family history of renal disease, HTN, thyroid cancer or any other features suggesting familial diseases. His effort tolerance was NYHA class 2 with no prior hospitalizations. On clinical examination he was pale, afebrile, pulse rate 82/min regular, blood pressure (BP) 170/90mmHg,

respiratory rate 20/min, height 174 cms and weight 66kg (post HD). Abdominal examination revealed vague fullness in right hypochondrium and shifting dullness. Abdominal CT and whole-body PET-CT scan disclosed a large intensely hyper metabolic lobulated soft tissue density lesion measuring 12X10.5X11.5 cm with central hypometabolism (necrosis) in the right supra renal region, indenting inferior vena cava (IVC) and uncinus process of pancreas; and displacing right kidney posteroinferiorly (Figure 1). This heterodense vascular mass was not visualized separately from adrenal gland with few suspicious enlarged celiac and paraaortic lymph nodes without any distant metastasis. Bilateral contracted kidneys, cardiomegaly, mild pericardial effusion, moderate intraperitoneal free fluid and normal thyroid gland were also noted. Ascitic fluid tapping and cytology was performed which ruled out malignancy. Electrocardiogram demonstrated left axis deviation with “T” wave flattening in inferior leads, and recent transthoracic echocardiography revealed concentric left ventricular (LV) hypertrophy, global hypokinesia, tricuspid regurgitation, ejection fraction of 45%, grade 2 diastolic dysfunction, dilated left and right atrium with mildly dilated ventricles. Laboratory data revealed elevated serum metanephrine levels (Table 1). Serological and imaging evaluation for MEN related endocrine tumours were negative.

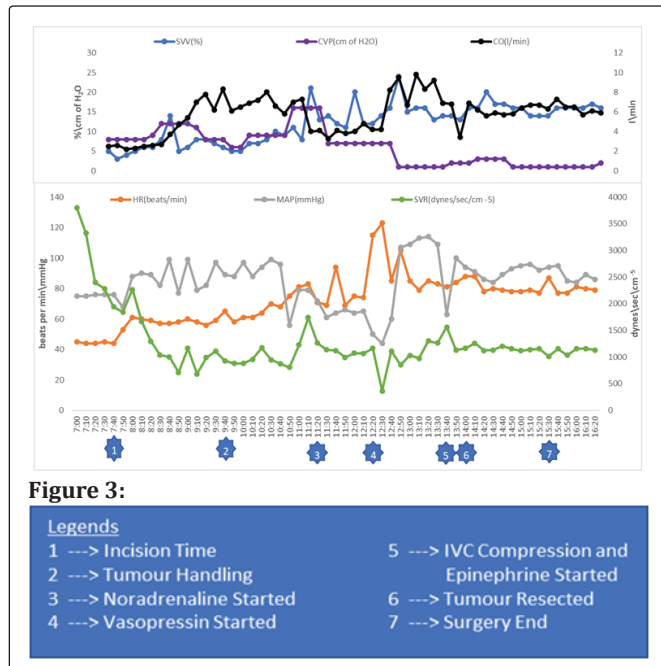
With provisional diagnosis of PCC the patient was planned for open right adrenalectomy with radical nephrectomy due to giant size of tumour. A multidisciplinary team of anaesthesiologist, nephrologist, surgeon and endocrinologist was formed to prepare a plan of optimization and treatment.

Preoperative Preparation

HD was regularized to thrice weekly schedule for a month before. Prazosin dosage was titrated upwards from 5mg/day to 15mg/day to achieve consistent BP control of <160/90mmHg as outpatient. He was admitted 3 days before surgery and daily fluid intake was restricted to 500ml/day. Day before surgery HD (heparin free) was performed to ultra-filtrate 1.5 L instead of usual 3 L. All routine anti HTN drugs were administered along with anxiolytics on the day of operation.

Investigation	Values	Units	Biological Reference
Haemoglobin	8.7	g/dl	12 to 15
S. urea	123	mg/dl	20 to 40
S. creatinine	10.2	mg/dl	0.6 to 1.2
S. sodium	135	meq/l	136 to 142
S. Potassium	5.3	meq/l	3.5 to 5.1
S. calcium	8.5	mg/dl	10-Dec
Platelets	3.18	L/cumm	10 to 12
INR	1.3		0.8 to 1.2
aPTT	31.4	seconds	25 to 32
Total leucocyte count	7680	cells/cumm	4400 to 11000
Free thyroxine T4	1.53	ng/dl	0.8 to 2.7
Free triiodothyronine T3	4.2	pg/ml	2.1 to 4.4
Thyroid stimulating hormone	0.04	mIU/ml	0.4 to 4.2
Anti-thyroid antibody (TPO)	0.41	IU/ml	<5.6
S Normetanephrine	4428	pg/ml	<196
S Metanephrine	25.2	pg/ml	<65

Table 1: Preoperative laboratory parameters



Anaesthesia, Monitoring and Surgery

Anaesthesia

In the operation theatre HD arteriovenous access in the left forearm (brachio-cephalic fistula) was duly protected. Baseline heart rate (HR) was 68/min, BP 154/92mmHg and oxygen saturation 98%. 2gm intravenous magnesium sulphate in 100ml saline bolus was administered over 30 minutes followed by 500mg/hour infusion. Epidural catheter was placed at thoracic 7-8 level and gradual incremental 6ml bolus of bupivaicaine 0.25% was administered; while right radial artery was catheterised under local anaesthesia. General anaesthesia was induced with fentanyl 3 mics/kg with titrated propofol and rocuronium. After adequate depth of anaesthesia gentle endotracheal intubation was performed with 10 % lignocaine spray on vocal cords; and right subclavian vein was cannulated. BP fluctuations were managed by intravenous nitroglycerine, esmolol and propofol boluses as indicated. After intubation, a tidal volume of 8 mL/kg of the patients' ideal body weight was set, with a respiratory rate of 10-12 bpm to maintain normocapnia.

Haemodynamic monitoring

The FloTrac device was attached to the arterial canula after surgical scrub and connected to the EV 1000 monitor (version 1.9, Edwards Life Science, Irvine, CA, USA). Information collected included HR, invasive arterial blood pressure (IBP), stroke volume variation (SVV), systemic vascular resistance (SVR), central venous pressure (CVP), anaesthetic and surgical events apart from routine monitoring. Baseline indices noted were SVR 3500dynes/sec/cm⁵, C.O 2.5 L/min, IBP 130/84mmHg, end tidal CO₂ 36mmHg, and cvp 9 cm (after ascites release). Intraoperatively we managed the intravenous fluid volume with SVV, cvp and ongoing losses obtained and assessed the fluid responsiveness clinically too. Vasopressors and vasodilators were initiated and adjusted as per SVR, systolic and diastolic bp as required. We didn't have predefined strict targets since the BP instability and swings were expected to be quite unpredictable; instead tried to attain acceptable range of haemodynamics indices.

Operation

Surgery was performed in supine position with a modified

Makkuchi incision 2.0 L ascites was drained and replaced by intravenous albumin. It was a large vascular tumour occupying and encasing predominantly the upper pole of right kidney, indenting IVC and adherent to capsule of liver and diaphragm (Figure 2). As surgeon started ligating multiple small feeder vessels, IBP remained stable but gradually SVR reduced to 876 dynes.sec.cm⁻⁵ and C.O increased to 7.5 L/min. At this stage magnesium infusion and nitroglycerine infusions were discontinued. With further fall in BP and SVR, NE infusion was initiated. One moment during tumour mobilization IVC got compressed resulting in unexpected drop in BP and CO which reverted swiftly when compression was released. Finally, ligation of major feeder veins resulted in profound persistent hypotension requiring escalating doses of NE 27mcg/min, E 2mcg/min and vasopressin 2U/hr infusions gradually along with fluid boluses (Figure 3). Surgery lasted for 7 hours with approximate blood loss of 1.5 L. Patient received 4 units of packed cells, 2 unit of plasma, 1 L of gelatin, 4.0 L of crystalloid and 200 ml of 20% albumin.

Post-Operative

Due to intense vasoplegia, metabolic acidosis and persistent hypotension patient was not extubated and ventilated overnight post-operatively (PO). Hypoglycemia and acidosis were managed by intravenous dextrose and bicarbonate infusions. Persistent low IBP resulted in thrombosis of the brachio-cephalic vascular access, in consequence we inserted internal jugular dialysis catheter as HD access. Gradually vasopressin and E infusions were weaned off first followed by NE infusion to 5mcg/min by PO 16 hrs and discontinued after PO 23 hrs. Ventilator was liberated at PO 18 hrs along with CO monitoring. On PDay-1 slow low efficiency dialysis was performed for high potassium (6.6 Meq/L) and residual acidosis with 600 ml ultrafiltrate removal only. Next day oral liquid diet and epidural analgesia were initiated and intravenous fluids discontinued by evening. Following PDay-3 drains, urinary catheter, arterial line and nasogastric tube were withdrawn and routine maintenance HD initiated. On PDay-4, low dose anti HTN (tab bisoprolol 2.5mg OD and prazosin 2.5mg bd) were commenced as BP started gradually escalating. Patient was shifted to ward on day 5 and discharged on day 8. Histopathology reported adrenal tumour (17X11X7.5 cm) weighing 400 gm, conveying features of PCC with clear cell and spindle cell variants. Immunohistochemistry exhibited strong positivity for S-100, chromogranin and synaptophysin. Outpatient follows up after 3 months demonstrated reduced serum normetanephrines (156 pg/ml) and no evidence of tumour recurrence on CT scan. He is now listed and awaiting renal transplantation.

Discussion

Although HTN is widely observed in patients with ESRD, PCC as a cause is considered uncommon. It is difficult to diagnose as symptoms such as headache, palpitations, hypertension, and fluctuations of BP are common in ESRD[3]. Biochemical confirmation or exclusion of PCC in such patients is confounded by the effects of impaired renal function on the elimination of CA and their metabolites in urine and difficulty in collecting urine sample [4]. Plasma CA resting levels more than 3- fold above normal or during hypertensive attacks (where levels can raise up-to 10 times) are suggestive of PCC. [3] Measuring plasma free metanephrines have been proposed to detect PCC in renal failure[5]. Imaging with MRI, CT and scintiscan is an efficient way to identify and lineate tumour extent and metastasis. Similar to our case, most of the adrenal masses are discovered incidentally during routine radiological work as these patients have a high incidence of renal cell carcinoma. [3] Treatment of PCC in ESRD patients follows the same principle as in patients with normal renal functions but with a therapeutic dilemma encountered during

pharmacological cardiovascular manipulation and correction of circulating blood volume[6]. Patients on HD fluctuate between the volume overloaded and dry states. Furthermore, cases with compromised cardiac function and heart failure often develop intra-dialytic hypotension which limits volume removal and leads to inter-dialytic hypervolemia. Assessment of volume status is difficult, wherefore its optimization and manipulation has very narrow margin of safety [7]. We planned the perioperative fluid and dialysis therapy in consultation with the treating nephrologist and decided to ultrafiltrate 1.5 L instead of 3 L day before to avoid hypovolemia. Gradual increase in patients' dry weight with a close watch on haemodynamics, without causing pulmonary oedema is recommended[4]. Since our patient tolerated irregular HD before without any signs of pulmonary congestion, we opined that he might tolerate volume shifts. Hence, we did not alter HD to target dry weight and instead geared up for intra-operative renal replacement if required. Clinically, the goals and end points of alpha blockade and intravascular volume may not be clearly expressed due to the extreme variable feature of PCC[2].

Currently, surgical resection remains the only curative treatment option for patients with PCC, with laparoscopic adrenalectomy being a well approved technique[3]. HTN due to PCC can be masked by excessive reduction in intravascular volume by preoperative HD. With high levels of CA further reducing the circulating blood volume, true hypotensive shock can occur from sudden vasodilation after tumour ablation and even anaesthesia induction[8]. Other than nitroprusside which can cause thiocyanate toxicity in renal failure; intraoperative HTN can be managed effectively by phentolamine, nitroglycerine, calcium channel blockers, beta blocker, dexmedetomidine and deepening anaesthesia[9]. Magnesium has to be used carefully as serum levels are higher. Epidural analgesia may blunt the surgical response but does not protect against CA release during tumour handling. Patients on HD are reported to require excessive fluid and vasopressor infusion following tumour resection due to decreases in BP, SVR, CVP, and pulmonary artery occlusion pressure[10]. Tumours with giant sizes and strong functional activity add more quandaries to the situation. Our case's hypotension too was severe enough to cause arterio-venous fistula thrombosis. With marked elevation in the serum CA, large fluid shifts, intense vasoplegia, risk of volume overload and unpredictable haemodynamics, accurate estimation of BP and CO is essential for successful anaesthetic management in these cases. The surrogate gold-standard marker, thermodilution via Swan Ganz pulmonary artery catheter (PAC) has in itself an inherent bias of 10% to 20%, catheter related risks, ambiguity in interpreting the data and is gradually being replaced by lessor invasive techniques [11,12]. Minimally invasive (pulse contour analysis, oesophageal doppler[13], trans-oesophageal echocardiography,[14] and non-invasive modalities like partial gas rebreathing monitor,[15] bio-impedence cardiography[16] have been used with appreciable results in PCC resections. Despite limitations in the use of dynamic indices and the inability to assess global ventricular function, systolic pressure variation, pulse pressure variation and SVV are currently the most precise predictors of fluid responsiveness and their use does not require any specific training or the physical presence of the clinician during measurements[17]. FloTrac measures CO using index commuted with patient's quantitative characteristics (height, weight, age) and measurements of arterial pressure wave forms without the need to calibrate prior to application. It requires 40 s to measure CO, and thereafter, updates the average value every minute for every 20 s. Kato advocated that the value of SVV variation derived from FloTrac changed in tandem with the intraoperative volume status, indicating its utility as a marker of circulatory haemodynamics even when circulating

plasma volume is diminished during PCC crisis [12]. We would have preferred to use volume view thermodilution catheter (Edward Life Sciences) to assess volume and lung water indices but dissuaded by nephrologist in fear of risk of femoral arterial thrombosis jeopardizing patient's renal transplant in future. Although the absolute CO values may not be as accurate as those derived by PAC, these devices are very useful in providing acceptable trending abilities to follow changes in CO and SV. Our initial CO values were probably falsely low due to very high SVR and later when SVR decreased it increased to near physiological range. Since there were no clinical signs of decompensated LV failure, we viewed these indices with caution rather than absolute value. Clinicians should be aware of the underlying principles and limitations of each technique to choose the best modality for each clinical scenario individually [17]. PO hypoglycemia accounts for 10–15% of patients after PCC resection due to rebound hyperinsulinemia caused by sudden CA withdrawal and should be watched for[2]. We also suggest post-operative checking of HD vascular access patency in such cases especially with critical hypotension.

Conclusion

In conclusion careful planning, inter disciplinary coordination and meticulous pre-operative preparation are the keys for successful and complication free outcome in such rare and complex cases. Our observation suggests CO, SVV and SVR monitoring with FloTrac could possibly be a promising guide to fluid and vasopressor therapy for a safe outcome. It is unlikely that there will be a standardized all-inclusive algorithm, and an individualized evidence-based approach adapted to each patient's physiological needs and responses to volume and pharmacological therapy will be more beneficial.

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References

1. Martucci VL, Pacak (2014) Pheochromocytoma and paraganglioma: diagnosis, genetics, management, and treatment. *Curr Probl Cancer*.38(1):7-41.
2. Ramachandran R, Rewari V(2017) Current perioperative management of pheochromocytomas. *Indian J Urol*. 33(1):19-25.
3. Saeki T, Suzuki K, Yamazaki H, Miyamura S, Koike H, et al. (2003) Four cases of pheochromocytoma in patients with end-stage renal disease. *Intern Med*. 42(10):1011-1015.
4. Pamporaki C, Prejbisz A, Małeck R, Pistrosch F, Peitzsch M, et al. (2021) Optimized procedures for testing plasma metanephrines in patients on hemodialysis. *Sci Rep*. 11(1):14706.
5. Eisenhofer G, Huysmans F, Pacak K, Walther MM, Sweep FC, et al. (2005) Plasma metanephrines in renal failure. *Kidney Int*. 67(2):668-677.
6. Box JC, Braithwaite MD, Duncan T, Lucas G (1997) Pheochromocytoma, chronic renal insufficiency, and hemodialysis: a combination leading to a diagnostic and therapeutic dilemma. *Am Surg*. 63(4):314-316.
7. Calixto Fernandes MH, Schrickler T, Magder S, Hatzakorzian R (2018) Perioperative fluid management in kidney transplantation: a black box. *Crit Care*. 22(1):14.

8. Nakaigawa N, Komatsu R, Kamata K, Ozaki M (2010) Anesthetic management of a patient with pheochromocytoma and end-stage renal disease. *Masui*. 59(6):734-737.
9. Connor David, Boumphrey Stephen (2016) Perioperative care of pheochromocytoma. *BJA Education*. 16(5):153-158.
10. Suzuki H, Abe M, Tahira K, Ito M, Takashima H, et al. (2013) Successful treatment of pheochromocytoma in a patient with hemodialysis: a case report and review of the literature. *Ren Fail*. 35(10):1429-1433.
11. Yeo LL, Seow SC, Loh JP, Phua J (2010) Comparison of cardiac output measurement by arterial waveform analysis and pulmonary artery catheter in mitral stenosis. *Ann Acad Med Singap*. 39(8):655-657.
12. Kato A, Tamai H, Uchida K, Ikeda T, Yamada Y (2018) Intraoperative hemodynamics monitoring in a patient with pheochromocytoma multisystem crisis: a case report. *JA Clin Rep*. 4(1):35.
13. Niederle MB, Fleischmann E, Kabon B, Niederle B (2020) The determination of real fluid requirements in laparoscopic resection of pheochromocytoma using minimally invasive hemodynamic monitoring: a prospectively designed trial. *Surg Endosc*. 34(1):368-376.
14. Zhao B, Zhou Y, Zhao Y, Zhao Y, Wu X, et al. (2018) Co-Occurrence of Pheochromocytoma-Paraganglioma and Cyanotic Congenital Heart Disease: A Case Report and Literature Review. *Front Endocrinol (Lausanne)*. 9:165.
15. Ng JM (2006) The partial CO₂ rebreathing cardiac output measurement during laparoscopic resection of bilateral pheochromocytoma. *Anesth Analg*. 103(6):1600-1601.
16. Matsuda Y, Kawate H, Shimada S, Matsuzaki C, Nagata H, et al. (2014) Perioperative sequential monitoring of hemodynamic parameters in patients with pheochromocytoma using the Non-Invasive Cardiac System (NICaS). *Endocr J*. 61(6):571-575.
17. Aref A, Zayan T, Sharma A, Halawa A (2018) Utility of central venous pressure measurement in renal transplantation: Is it evidence based? *World J Transplant*. 8(3):61-67.