



Robotic-Assisted Bilateral Cortical Sparing Adrenalectomy in a Case of Bilateral Familial Pheochromocytoma: A Case Report and Review of Literature

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Authors' contributions

This work was carried out in collaboration among all authors. Author SC was involved with the case and has drafted out the manuscript and revising it for critically intellectual content. Author AP was involved with the case and has contributed to drafting out the manuscript. Author SRP was the robotic surgeon in the case and has worked as a team to deliver the surgical outcome as designed pre-operatively. He was involved in the final editing of the manuscript. Author AB was the senior consultant onco-surgeon on referral planned the bilateral cortical sparing robotic approach. He was the primary surgeon overseeing the care of the patient, taking responsibility in execution of the surgical plan, constructing an idea for the manuscript, and providing a critical review of the article prior to submission. Author PSL was the primary endocrinologist involved in diagnosing the patient, and referring for surgical management, now doing regular follow-ups. He was involved in the final editing of the manuscript. Author BD was the cardiologist involved in the peri-operative management of hypertension. He was involved in the final editing of the manuscript. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Although bilateral pheochromocytomas are frequently encountered in familial cases, a cortical-sparing approach outweighs the need for total adrenalectomy and its continuing repercussions of lifelong steroid dependency. Hereby highlighting a case of boy with bilateral pheochromocytomas managed with bilateral cortical sparing adrenalectomy. Multi-disciplinary approach and a minimal invasive technique aided the management and delayed the need for life-long steroid supplementation.

Keywords: *Familial pheochromocytoma; bilateral pheochromocytoma; bilateral adrenalectomy; cortical sparing adrenalectomy.*

ABREVIATIONS

MIBG: Metaiodobenzylguanidine

VHL: Von Hippel Lindau

NF1: Neurofibromatosis type 1

SDHD: Succinate Dehydrogenase Complex Subunit D

SDHB: Succinate Dehydrogenase Complex Subunit B

cm: centimeter

mmHg: millimetre of mercury

1. INTRODUCTION

Pheochromocytoma is a rare neuroectodermal tumor arising from catecholamine-producing chromaffin cells of the adrenal medulla [1,2]. It is the underlying pathology in 1.7% of hypertensive children with a mean age of 11-13 years [3,4]. Paraganglioma arises from the extra-adrenal paraganglia of the autonomic nervous system [1]. We report a case of bilateral pheochromocytoma and synchronous paraganglioma associated with a germline VHL mutation in a 14-year-old boy treated successfully by robotic-assisted cortical sparing bilateral adrenalectomy and excision of the paraganglioma.

2. PRESENTATION OF CASE

A 14-year-old boy was noted to have incidental asymptomatic sustained hypertension, with a negative medical or personal history contributing to the same. His mother was diagnosed with bilateral pheochromocytomas at the age of 20 years, and she underwent bilateral total adrenalectomy, hence presently on steroid supplements.

On examination, he had no abnormal physical findings except elevated blood pressure (systolic about 160 mm of Hg and diastolic of 100 mm of Hg). With a preliminary diagnosis of secondary

hypertension, a renal artery doppler was conducted; that ruled out renal artery stenosis but showed an incidental lesion in the right supra-adrenal region. CT scan of the abdomen confirmed heterogeneously enhancing bilateral suprarenal masses and suggestive of bilateral pheochromocytoma. Another intensely enhancing lesion was detected in the presacral region at the level of S1 suggestive of extra adrenal pheochromocytoma or paraganglioma.

On biochemical evaluation, his free plasma nor-metanephrine (2220 ug/l) and, 24 hour urinary nor-metanephrine levels (5772 ug) were elevated. 131 MIBG scan confirmed the diagnosis by recording increased MIBG uptake in bilateral suprarenal masses.

With a diagnosis of pheochromocytoma in a young patient and associated family history, genetic testing was advised. Genetic panel was found to be positive for a VHL gene mutation at c.239G>T(p.Ser80Ile).

Pre-operatively he was optimized by giving prazosin 5mg (alpha blocker) 12 hourly, metoprolol 50mg (beta blocker) 12 hourly and nifedipine 10mg once a day for 20 days. His blood pressure was monitored and recorded to be a systolic of 90 mmHg and diastolic of 60 mmHg with a heart rate of 70 per minute on the day of surgery.

Robotic-assisted bilateral cortical sparing adrenalectomy and excision of presacral paraganglioma was performed. Intra-operatively careful dissection was started inferiorly to avoid vascular injury to the adrenal cortex. Bilateral adrenal veins and multiple small adrenal arteries were identified and clipped. Nearing the end of dissection, two surges of blood pressures were noted which pointed towards residual blood supply to the adrenal medulla. Re-evaluation was done, and small arteries supplying the medulla

were clipped. Bilateral adrenal medullary specimens were delivered. The diaphragmatic supply to both adrenal cortexes was maintained. Adrenal cortical tissue perfusion was confirmed

by indocyanine green fluorescence. A presacral lesion around 2 cm in size was identified right to the right internal iliac artery and delivered.

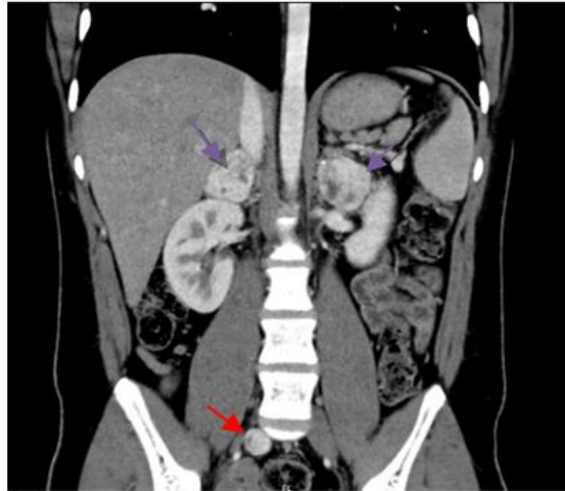


Fig. 1. In coronal plane - The left sided mass measuring – 5.3 x 3.7 x 3.7 cm and right sided mass measuring – 6 x 2.9 x 3.5 cm (yellow arrows) s/o bilateral pheochromocytomas. Another intensely enhancing lesion measuring 1.8 x 1.7 cm seen in presacral region at the level of S1 medial to right internal iliac artery s/o extra-adrenal pheochromocytoma/paraganglioma (red arrow)



Fig. 2. Right and left pheochromocytoma specimens and Sacral paraganglioma specimen



Fig. 3. Post-operative picture of the ports placed

Peri and post-operative recovery were uneventful. Blood pressures became normal from post-operative day one without any medications.

On post-operative day five, serum cortisol levels returned to normal limits (Serum cortisol: 3.09 mcg/dl at 8 am and 8.25 mcg/dl at 6 pm) confirming cortical sparing procedure. Also, CT angiogram of the abdominal aorta was done which confirmed good vascularity of both adrenal cortexes. After 1 week repeat serum and urinary metanephrine levels dropped significantly as compared to their pre-operative levels.

Histopathological examination confirmed the diagnosis and showed an encapsulated tumor composed of medullary cells arranged in nests and trabeculae with no capsular/vascular invasion and no evidence of malignancy.

Patient is in regular follow-up and is maintaining normal levels of cortisol.

3. DISCUSSION

About 80-85% of chromaffin-cell tumors are pheochromocytomas, whereas 15-20% are paragangliomas. Pheochromocytoma is characterized by a classical triad of symptoms - headache, diaphoresis, and tachycardia. The incidence of pheochromocytomas is two to eight per million annually. However, this incidence is underestimated since 50% of pheochromocytomas found on autopsy remain previously undiagnosed [5].

Etiology could be sporadic or familial. The mean age of diagnosis of pheochromocytomas is fourth to fifth decade [2]. Familial tumors are multifocal and present at a younger age as routine surveillance enables early diagnosis. About 25% of diagnosed cases have an underlying susceptible gene. Overall, SDHB, SDHD, RET, VHL, and NF1 germline mutations are often isolated. Studies have shown that pheochromocytomas in hereditary syndromes are bilateral but have a low malignant potential as compared to sporadic cases [6-8].

Medical management is the first step to gain clinical control, followed by definitive surgical management. First described by Gagner et al. in 1997, total adrenalectomy has been adopted globally for optimal disease control [9,10]. Although radical removal absolute disease control, lifelong steroid supplementation follows. It also has a potential risk of emerging

addisonian crisis (10-35%) despite proper steroid replacement [9]. A study conducted by Neumann et al on steroid dependent patients after total adrenalectomy showed that eighteen percent patients developed one adrenal crisis, six percent had two or more adrenal crisis and thirteen percent patients developed symptoms consistent with steroid overreplacement [9].

Hereditary pheochromocytomas tend to be bilateral, with a metachronous or synchronous course. So, in bilateral, familial, and recurrent disease, cortical sparing adrenalectomy is now preferred as the standard of care [11-13]. The plausibility of cortical sparing procedure is established based on a low risk of malignancy, high chances of maintaining normal cortical functions and ease of routine follow-up. The technical dilemma encountered by surgeons is to ensure complete removal of medullary tissue. Factors that make cortical sparing procedure possible are the dual venous supply of the adrenal gland with segmental arterial anatomy. One third of one gland is the minimum cortical tissue required to obviate the need for steroid supplementation [14].

Pre-operative cross-sectional imaging help in determining the feasibility of cortical sparing procedure and the quantum of residual cortex.

Cortical sparing adrenalectomy should be performed in a familial unilateral disease whenever possible. This ensures adequate cortical function in case of a contralateral disease later. In case of a bilateral disease at diagnosis, bilateral cortical sparing adrenalectomy should be performed. This enables a total adrenalectomy preserving unilateral cortical function in case of a recurrence.

Normal cortical function and no recurrences are determinants of successful cortical sparing procedure. Recent studies show a need for glucocorticoid supplementation in 43% of patients after partial adrenalectomy as compared to 100% in those undergoing total adrenalectomy [12,15]. A recurrence rate of 0-21% has been reported following partial adrenalectomy. A study by Benhammou et al had a recurrence rate of 11% with a mean follow up period of 9.25 years [13]. This necessitates regular surveillance for recurrent disease. High recurrence rates are associated with factors like younger age, larger tumor, bilateral familial disease, extrarenal and right sided tumors. [15]. Follow-up is aided with proper history, blood pressure measurement and

annual biochemical tests – plasma or urinary fractionated metanephrines. If suspicion of recurrence is raised, appropriate imaging is advised. Routine follow-ups should not include imaging to prevent radiation exposure in already vulnerable familial syndromic pathologies.

4. CONCLUSION

Pheochromocytomas require an individualized approach and a multi-disciplinary team. In familial disease, in anticipation of a recurrence and to prevent life-long steroid supplementation, cortical sparing adrenalectomy is considered an optimal procedure. The need for steroid supplementation is less than 50% in cortical sparing procedures. Lifelong surveillance weighs over the risk of late recurrence and delay in the need for steroid supplementation.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Stiru O, Dragan A, Adamache C, Dragulescu P, Stiru C, Tulin A, et al. Abdominal paraaortic paraganglioma: Management of intraoperative hemodynamic emergencies during elective resection procedures (a case presentation). *Experimental and Therapeutic Medicine*. 2021;21(5). doi:10.3892/etm.2021.9975
2. Martins R, Bugalho MJ. Paragangliomas/pheochromocytomas: Clinically oriented genetic testing. *International Journal of Endocrinology*. 2014; 2014:1–14. doi:10.1155/2014/794187
3. Bausch B, Wellner U, Bausch D, Schiavi F, Barontini M, Sanso G, et al. Long-term prognosis of patients with pediatric pheochromocytoma. *Endocrine-Related Cancer*. 2013;21(1):17–25. doi:10.1530/erc-13-0415
4. Ludwig AD, Feig DI, Brandt ML, Hicks MJ, Fitch ME, Cass DL. Recent advances in the diagnosis and treatment of pheochromocytoma in children. *The American Journal of Surgery*. 2007;194(6):792–7. doi:10.1016/j.amjsurg.2007.08.028
5. Sutton MGStJ, Sheps SG, Lie JT. Prevalence of clinically unsuspected pheochromocytoma. review of a 50-year autopsy series. *Journal of Urology*. 1982;127(2):396–7. doi:10.1016/s0022-5347(17)53807-0.
6. Eisenhofer G, Lenders JW, Siegert G, Bornstein SR, Friberg P, Milosevic D, et al. Plasma methoxytyramine: A novel biomarker of metastatic pheochromocytoma and paraganglioma in relation to established risk factors of tumour size, location and SDHB mutation status. *European Journal of Cancer*. 2012 Jul;48(11):1739-49.
7. Nölting S, Ullrich M, Pietzsch J, Ziegler CG, Eisenhofer G, Grossman A, et al. Current Management of Pheochromocytoma/Paraganglioma: A Guide for the Practicing Clinician in the Era of Precision Medicine. *Cancers (Basel)*. 2019 Oct 8;11(10):1505.
8. Cerqueira A, Seco T, Costa A, Tavares M, Cotter J. Pheochromocytoma and Paraganglioma: A Review of Diagnosis, Management and Treatment of Rare Causes of Hypertension. *Cureus*. 2020 May 5.
9. Neumann HPH, Reincke M, Bender BU, Elsner R, Janetschek G. Preserved Adrenocortical Function After Laparoscopic Bilateral Adrenal Sparing Surgery for Hereditary Pheochromocytoma¹. *The Journal of Clinical Endocrinology & Metabolism*. 1999 Aug;84(8):2608-10.
10. Gagner M, Lacroix A, Bolté E. Laparoscopic adrenalectomy in Cushing's

- syndrome and pheochromocytoma. N Engl J Med. 1992 Oct 1;327(14):1033.
11. Paul M, Boaz R, Ramakant P, Ebenazer A, Pai R, Rajaratnam S, et al. Role of cortical sparing adrenalectomy and novel variant of mutation in patient with von Hippel-Lindau disease. Indian J Endocr Metab. 2011; 15(8):402.
 12. Castinetti F, Taieb D, Henry JF, Walz M, Guerin C, Brue T, et al. Management of endocrine disease: Outcome of adrenal sparing surgery in heritable pheochromocytoma. European Journal of Endocrinology. 2016 Jan;174(1):R9-R18.
 13. Benhammou JN, Boris RS, Pacak K, Pinto PA, Linehan WM, Bratslavsky G. Functional and Oncologic Outcomes of Partial Adrenalectomy for Pheochromocytoma in Patients With von Hippel-Lindau Syndrome After at Least 5 Years of Followup. Journal of Urology. 2010 Nov;184(5):1855-9.
 14. Grubbs EG, Rich TA, Ng C, Bhosale PR, Jimenez C, Evans DB, et al. Long-Term Outcomes of Surgical Treatment for Hereditary Pheochromocytoma. Journal of the American College of Surgeons. 2013 Feb;216(2):280-9.
 15. Amar L, Servais A, Gimenez-Roqueplo A, Zinzindohoue F, Chatellier G, Plouin P. Year of Diagnosis, Features at Presentation, and Risk of Recurrence in Patients with Pheochromocytoma or Secreting Paraganglioma. The Journal of Clinical Endocrinology & Metabolism. 2005 Apr;90(4):2110-6.

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