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Case Report: Bilateral Pheochromocytoma: Clinical Characteristics and Surgical Management

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Abstract | **Case Report**

Objective*:** We would like to report the clinical presentation, surgical treatment and outcomes of this patient with bilateral pheochromocytoma. ***Introduction: Pheochromocytomas (PHEOs) are rare catecholamine-secreting neuroendocrine tumors of neural crest origin arising from chromaffin cells in the adrenal medulla with estimated incidence of 0.46 to 0.8 cases per 100,000 person-years [1]. Germline pathogenic variants associated with PHEO are now identified in 30-50% of these tumors [2]. Genetic syndromes can predispose to bilateral PHEO, such as multiple endocrine neoplasia (MEN) 2A, MEN 2B, von Hippel-Lindau (VHL), neurofibromatosis type 1 (NF1), as well as mutations in the genes of myc-associated factor X (MAX), transmembrane protein 127 (TMEM127), and mutations in the subunits of the succinate dehydrogenase complex (SDHx) [3]. When we suspect the pheochromocytoma clinically, we should look for biochemical confirmation, by dosing the plasma and urinary catecholamine (adrenaline, noradrenaline) and their metabolites (metanephrine and normetanephrine) [4]. This should be followed by tumor localisation using computed tomography (CT) imaging or magnetic resonance imaging (MRI) of the abdomen and pelvis that are the most commonly used methods and have similar sensitivities (90%-100%) and specificities (70%-80%) for tumor localisation [5]. Surgical resection followed by postoperative monitoring is the safest and the most effective therapeutic intervention for pheochromocytoma [6].

Keywords: Pheochromocytoma, VHL, MEN2, RET, NF1, SDHB, SDHC, SDHD, catecholamines, bilateral adrenalectomy, addisonian crisis, cortical sparing adrenalectomy.

CASE REPORT

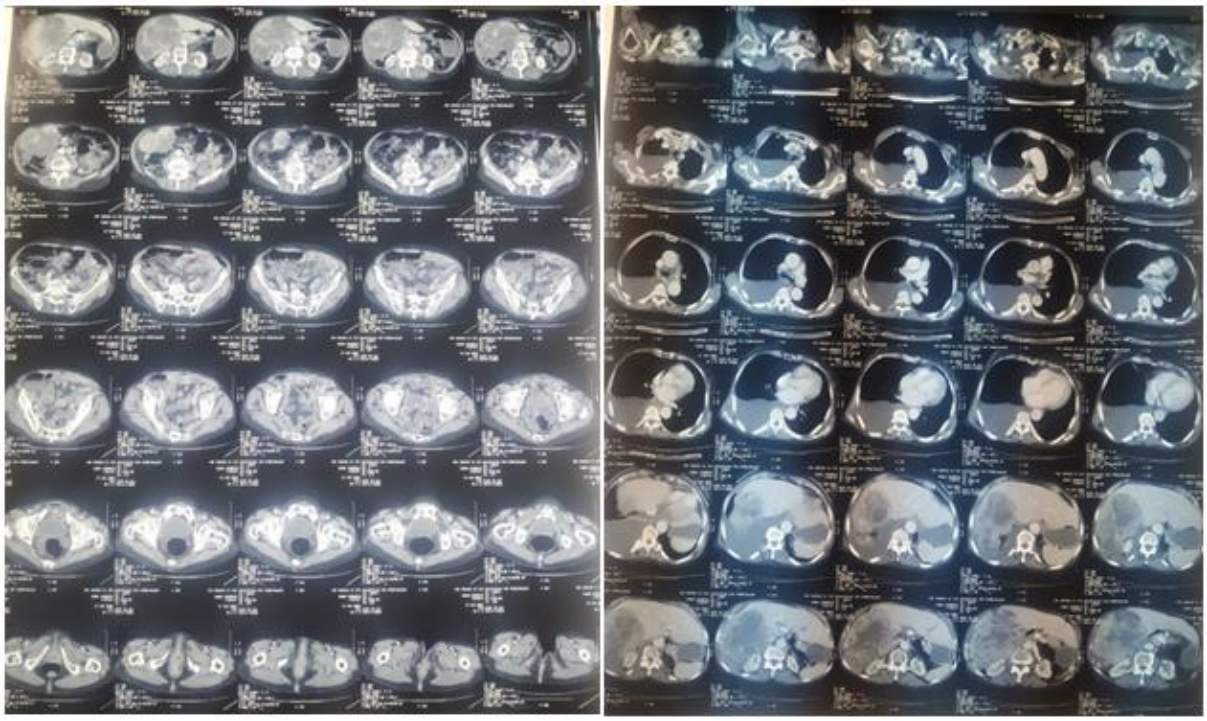
This is a 62-year-old patient admitted to our department for surgical management of a bilateral pheochromocytoma.

He was followed for hypertension for one year under treatment, for dyslipidemia, and for diabetes under insulin therapy. He had no history of surgery. As family history, he has a sister operated for pheochromocytoma who had an adrenalectomy, a daughter operated for thyroid cancer who had a total thyroidectomy with lymph node curage, cervical radiotherapy sessions and a metastatic chemotherapy, and a son who had a bilateral adrenalectomy and whose genetic study showed a heterozygous C634R mutation on exon 11 of the RET gene (high risk category) [3].

The history of his disease dates back 1 year by the discovery of a grade 3 hypertension during his hospitalization in 2017 in the endocrinology department for an acid-ketotic decompensation of an inaugural diabetes.

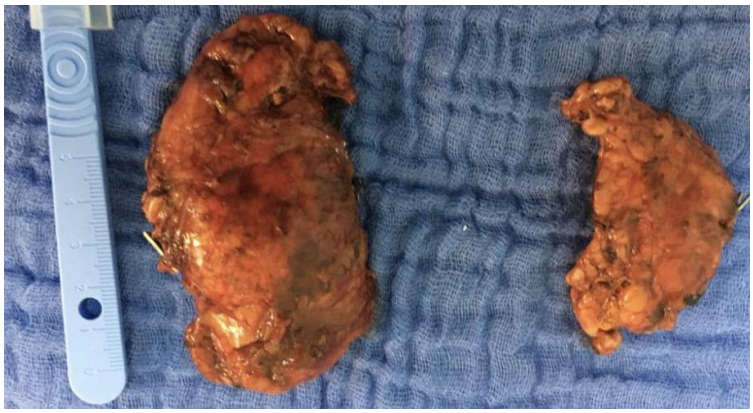
In addition to his hypertension, this patient suffered from headache, palpitations and sweating, an abdominal mass in the left flank with a feeling of heaviness.

We performed an abdominal CT scan which revealed a bilobed left adrenal mass with heterogeneous enhancement after injection measuring 32 x 20 mm and spontaneous density greater than 10 HU, with washout less than 20%, and a right adrenal mass heterogeneously enhancing after injection with a zone of necrosis measuring 20mm in diameter and with a spontaneous density greater than 10 HU and a washout greater than 20%.



He had elevated metanephrine and normetanephrine levels. We decided to operate the patient, and a bilateral adrenalectomy was performed.

The result of the anatomopathology was a PASS 1 (Pheochromocytoma of the Adrenal gland Scaled Score) score for the right adrenal gland, and a PASS 0 score for the left adrenal gland, thus rather non-aggressive tumors, likely to behave in a non-cancerous manner and that are cured by surgery alone [7].



DISCUSSION

Pheochromocytomas and extra-adrenal sympathetic paragangliomas (PGLs) are catecholamine-secreting neuroendocrine tumors arising from chromaffin cells of the adrenal medulla or extra-adrenal sympathetic ganglia [1]. Patients generally present with symptoms resulting from excessive production of the catecholamines dopamine, epinephrine or norepinephrine, although occasionally a tumor may be nonfunctioning or the patient may remain asymptomatic [8].

It's essential to perform a good examination with a particular focus on symptoms, medications, pheocromocytoma-syndrome-associated tumors [8], family history and blood pressure [9], as the likelihood of pheochromocytoma or a pheochromocytoma-associated family syndrome based on clinical assessment before any laboratory or radiological investigations [10].

CLINICAL PRESENTATION

The classic triad of clinical features consists of episodic headaches, palpitations, and diaphoresis [11]. The hallmark clinical finding is hypertension, which can be paroxysmal or sustained [12]. Hypertensive crisis can lead to cardiac arrhythmias, myocardial infarction, and even death [13].

Laboratory testing

The first step in establishing the diagnosis in a patient suspected to have a pheochromocytoma is the measurement of urinary or plasma catecholamines (dopamine, epinephrine and norepinephrine) [4] and/or metanephrines (metanephrine and normetanephrine) [14]. We can also include the measurement of vanillymandelic acid (VMA) that is another catecholamine metabolite [4].

High performance liquid chromatography (HPLC) appears to be the most sensitive and specific method for the measurement of fractionated catecholamines and metanephrines [15].

GENETIC TESTING

Overview Germline mutations associated with the development of pheochromocytoma**:**

- VHL (von Hippel–Lindau syndrome)
- RET [multiple endocrine neoplasia type 2 (MEN2)]
- NF1 (neurofibromatosis type 1)
- SDHB, SDHC, SDHD (succinate dehydrogenase subunits B, C, D) [16]

IMAGING EVALUATION

Imaging modalities for pheochromocytoma include computed tomography (CT) [5], magnetic resonance imaging (MRI) [17], metaiodobenzylguanidine (MIBG) or octreotide scintigraphy, and positron emission imaging (PET) [18]. Initial imaging is performed using either CT or MRI, depending on availability and institutional preference [19].

CT IMAGING

This is able to detect lesions >1 cm in size [5]. Pheochromocytomas typically have a homogenous appearance of soft tissue density (40–50 Hounsfield units) and uniform enhancement with IV contrast [17]. Larger tumors may have regions of cystic necrosis [20], hemorrhage or calcification, resulting in a more heterogenous appearance [21].

Indications of surgery

Bilateral adrenalectomy is the gold standart treatment of bilateral pheochcromocytoma. However, this surgical treatment remains controversial because of the need for lifelong corticosteroid therapy and the risk of Addisonian crisis associated with bilateral total adrenalectomy [22].

In our study, the patient had a bilateral adrenalectomy and an addisonian crisis postoperatively, despite a corticoid substitution therapy. We could have avoided this complication with conservative surgery, according to recent studies [23].

Recent data suggest that total bilateral adrenalectomy may be associated with mortality and major morbidity from acute adrenal insufficiency [24].

As a result, some surgeons are using a surgical strategy of subtotal or cortical-sparing adrenalectomy [25] with the intent of leaving a portion of vascularized adrenal cortex in situ in patients with hereditary or sporadic bilateral pheochromocytoma [26].

CONCLUSION

Operating patients with bilateral PHEO's can be challenging, as they have significant risk of complications related to PHEO or to bilateral adrenalectomy post-operatively, therefore, they require a regular follow-up and a good education about adrenal crisis to minimize the morbidity and mortality of this disease [27].

REFERENCES

1. Zhou, J., Ye, D., Wu, M., Zheng, F., Wu, F., Wang, Z., & Li, H. (2009). Bilateral adrenal tumor: causes and clinical features in eighteen cases. *International urology and nephrology*, *41*(3), 547-551.
2. Lerario, A. M., Moraitis, A., & Hammer, G. D. (2014). Genetics and epigenetics of adrenocortical tumors. *Molecular and cellular endocrinology*, *386*(1-2), 67-84.
3. Erlic, Z., Rybicki, L., Peczkowska, M., Golcher, H., Kann, P. H., Brauckhoff, M., ... & European-American Pheochromocytoma Study Group. (2009). Clinical predictors and algorithm for the genetic diagnosis of pheochromocytoma patients. *Clinical Cancer Research*, *15*(20), 6378-6385.
4. Crout, J.R., McKay, D., Dryer, R. Measurement of catecholamines in urine. In: Seligson D. (Ed.), Standard methods of clinical chemistry.
5. Israel, G. M., Korobkin, M., Wang, C., Hecht, E. N., & Krinsky, G. A. (2004). Comparison of unenhanced CT and chemical shift MRI in evaluating lipid-rich adrenal adenomas. *American Journal of Roentgenology*, *183*(1), 215-219.
6. Walther, M. M., Keiser, H. R., & Linehan, W. M. (1999). Pheochromocytoma: evaluation, diagnosis, and treatment. *World journal of urology*, *17*(1), 35-39.
7. Sherwin, R.P. (1959). Histopathology of pheochromocytoma. Cancer, 12:861–72.
8. Jansson, S., Tisell, L. E., Fjälling, M., Lindberg, S., Jacobsson, L., & Zachrisson, B. F. (1988). Early diagnosis of and surgical strategy for adrenal medullary disease in MEN II gene carriers. *Surgery*, *103*(1), 11-18.
9. Richard, S., Beigelman, C., Duclos, J. M., Fendler, J. P., Plauchu, H., Plouin, P. F., ... & Proye, C. (1994). Pheochromocytoma as the first manifestation of von Hippel-Lindau disease. *Surgery*, *116*(6), 1076-1081.

10. Horton, W. A., Wong, V., & Eldridge, R. (1976). Von Hippel-Lindau disease: clinical and pathological manifestations in nine families with 50 affected members. *Archives of internal medicine*, *136*(7), 769-777.
11. Walther, M. M., Keiser, H. R., & Linehan, W. M. (1999). Pheochromocytoma: evaluation, diagnosis, and treatment. *World journal of urology*, *17*(1), 35-39.
12. Barontini, M., Levin, G., & Sanso, G. (2006). Characteristics of pheochromocytoma in a 4-to 20-year-old population. *Annals of the New York Academy of Sciences*, *1073*(1), 30-37.
13. Neumann, H., Berger, D. P., Sigmund, G., Blum, U., Schmidt, D., Parmer, R. J., ... & Kirste, G. (1993). Pheochromocytomas, multiple endocrine neoplasia type 2, and von Hippel-Lindau disease. *New England Journal of Medicine*, *329*(21), 1531-1538.
14. Peuler, J. D., & Johnson, G. A. (1977). Simultaneous single isotope radioenzymatic assay of plasma norepinephrine, epinephrine and dopamine. *Life sciences*, *21*(5), 625-636.
15. Crout, J.R., McKay, D., Dryer, R. (1961). Measurement of catecholamines in urine. In: Seligson D. (Ed.), Standard methods of clinical chemistry. Academic Press, New York, 3.
16. Lerario, A. M., Moraitis, A., & Hammer, G. D. (2014). Genetics and epigenetics of adrenocortical tumors. *Molecular and cellular endocrinology*, *386*(1-2), 67-84.
17. Brandi, M. L., Gagel, R. F., Angeli, A., Bilezikian, J. P., Beck-Peccoz, P., Bordi, C., ... & Marx, S. J. (2001). Consensus: guidelines for diagnosis and therapy of MEN type 1 and type 2. *The Journal of Clinical Endocrinology & Metabolism*, *86*(12), 5658-5671.
18. Brink, I., Hoegerle, S., Klisch, J., & Bley, T. A. (2005). Imaging of pheochromocytoma and paraganglioma. *Familial cancer*, *4*(1), 61-68.
19. Caoili, E. M., Korobkin, M., Francis, I. R., Cohan, R. H., Platt, J. F., Dunnick, N. R., & Raghupathi, K. I. (2002). Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology*, *222*(3), 629-633.
20. Korobkin, M., Giordano, T. J., Brodeur, F. J., Francis, I. R., Siegelman, E. S., Quint, L. E., ... & Wang, H. H. (1996). Adrenal adenomas: relationship between histologic lipid and CT and MR findings. *Radiology*, *200*(3), 743-747.
21. Bharwani, N., Rockall, A. G., Sahdev, A., Gueorguiev, M., Drake, W., Grossman, A. B., & Reznek, R. H. (2011). Adrenocortical carcinoma: the range of appearances on CT and MRI. *American journal of roentgenology*, *196*(6), W706-W714.
22. Neumann, H. P., Tsoy, U., Bancos, I., Amodru, V., Walz, M. K., Tirosh, A., ... & Eng, C. (2019). Comparison of pheochromocytoma-specific morbidity and mortality among adults with bilateral pheochromocytomas undergoing total adrenalectomy vs cortical-sparing adrenalectomy. *JAMA network open*, *2*(8), e198898-e198898.
23. De Graaf, J. S., Dullaart, R. P. F., & Zwierstra, R. P. (1999). Complications after bilateral adrenalectomy for phaeochromocytoma in multiple endocrine neoplasia type 2-a plea to conserve adrenal function. *The European journal of surgery*, *165*(9), 843-846.
24. Neumann, H. P., Tsoy, U., Bancos, I., Amodru, V., Walz, M. K., Tirosh, A., ... & Eng, C. (2019). Comparison of pheochromocytoma-specific morbidity and mortality among adults with bilateral pheochromocytomas undergoing total adrenalectomy vs cortical-sparing adrenalectomy. *JAMA network open*, *2*(8), e198898-e198898.
25. Giordano, W. C. (1982). Preservation of adrenocortical function during surgery for bilateral pheochromocytoma. *The Journal of Urology*, *127*(1), 100-102.
26. Alesina, P. F., Hinrichs, J., Meier, B., Schmid, K. W., Neumann, H. P., & Walz, M. K. (2012). Minimally invasive cortical-sparing surgery for bilateral pheochromocytomas. *Langenbeck's archives of surgery*, *397*(2), 233-238.
27. Sood, A., Majumder, K., Kachroo, N., Sammon, J. D., Abdollah, F., Schmid, M., ... & Trinh, Q. D. (2016). Adverse event rates, timing of complications, and the impact of specialty on outcomes following adrenal surgery: an analysis of 30-day outcome data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP). *Urology*, *90*, 62-68.