2017

Pheochromocytoma with IVC Invasion: Case Report & Systematic Review of Literature

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Abstract

Background: Surgical management and outcome of pheochromocytoma with invasion of the inferior vena cava (IVC) has been scarcely reported in the literature. As surgical resection of this condition is underrepresented, we include a case report and a systematic literature review.

Results: A literature search in PubMed yielded 29 case reports between 1969 and 2014. With the inclusion of our new case report, the mean age of the patients was 43.3 years, with 33% being female (n=10) and 67% being male (n=20). 77% (n=23) of the cases were right-sided pheochromocytomas that invaded the IVC, with only one case localized in the organ of Zuckerkandl. For diagnosis, both laboratory tests and imaging modalities were used. 77% (n=23) reported using laboratory tests (serum and urine metabolites) to diagnose pheochromocytoma while 83% (n=25) reported using various imaging modalities to localize the extent of the tumor prior to surgery. On average, 2-3 different imaging types were used per case. Of the 25 cases that used imaging diagnostics, 80% (n=20) were able to detect IVC invasion prior to operation. Pre-operative treatment was reported in only 37% of the cases. Surgical approach via sternotomy, thoracophrenolaparotomy, or thoracoabdominal approaches were used to completely resect the tumor and IVC. Aggressive surgical tumor and IVC resections resulted in excellent post-operative outcomes with 0% recurrence and four deaths unrelated to the operation.

Conclusion: Pheochromocytoma with IVC involvement is curable with surgical resection. Multiple imaging modalities should be used to confirm IVC involvement and/or metastases to other organs. However, malignant characteristics of pheochromocytoma still have yet to be defined clearly and management of these cases need to be reported more consistently.

Introduction

Pheochromocytoma is a catecholamine- producing neoplasm of the adrenal gland that, if left untreated or missed, is likely fatal.[20] Pheochromocytomas are highly vascularized and can spread intravenously to adjacent adrenal veins, renal veins and, rarely, to the inferior vena cava and into the right atrium. A majority of pheochromocytomas are benign, however, 10-15% of these adrenal tumors can be malignant, with an overall 5-year survival of 40-50%. Currently, according to WHO, malignant pheochromocytoma is defined by distant metastases at sites where chromaffin is otherwise unlikely to be found.[28] Thus, tumor extension into the IVC does not necessarily indicate malignancy.[16] Invasion into the IVC may be via direct tumor invasion of the venous wall or from tumor extension via small draining veins.[17]

Although aggressive surgical resection has been indicated as the treatment of choice for these cases, surgical management of pheochromocytoma with IVC invasion is scarcely reported likely due to its low incidence.[24] Thus, surgical management of these rare cases have been variable and challenging. We give a comprehensive review of the diagnosis, localization, and surgical management of pheochromocytomas with IVC invasion in hopes to assess the most effective management strategy.

Methods

A literature search was conducted and yielded 29 cases between 1969 and 2014. Data was extracted based on the following variables: patient's age, gender, labs, size and laterality of the tumor, IVC invasion, preoperative treatment and imaging, preoperative procedures, and oncological outcomes.

Case Report

A 21 year old female presented to the ED with a 1 month history of headache, sweating and anxiety. Plasma metanephrines were elevated at 71 nmol/L. A CT abdomen/pelvis with and without contrast detected a mass of 9.8x7.7x7.6 cm from the right adrenal gland. It did not appear to invade the kidney or liver, but that could not be ruled out. Invasion of the IVC without extra vessel invasion was noted. She was referred to our Surgical Oncology clinic and deemed suitable for resection. Pre-operatively, her β-blocker was discontinued and she was treated with Doxazosin, an α1-blocker. An open right adrenalectomy via abdominal approach and en bloc adrenalectomy with IVC resection were performed. Post-operatively, the patient had no complications and was discharged on post-op Day 4. Since discharge, she has had no recurrence of headache, sweating, or hypertension and has discontinued her hypertensive medications.

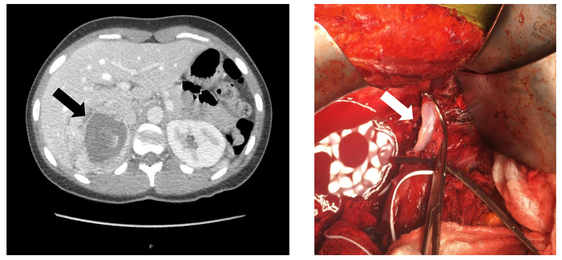

Figure 1. CT Scan of right-sided Pheochromocytoma and intra-op cavotomy.

Results

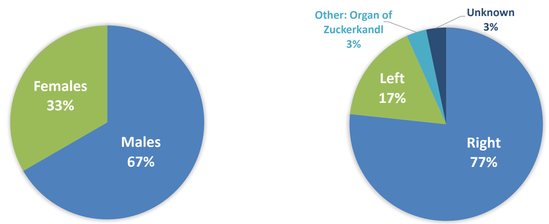

Figure 2. Male dominance and right-sided tumor laterality in cases of Pheochromocytomas with IVC invasion.

Table 1. IMAGING MODALITIES

Imaging Modality	No. of studies used	No. of IVC invasion detected
CT scan	19	6
Angiography/Vena Cavography	14	4
Ultrasound	12	6
MRI	7	4
Echocardiography	3	1
MIBG	3	0
Excretory urography	2	0
Chest X-ray	1	0

Table 2. SURGICAL MANAGEMENT

Surgical Management	n	%
History of recurrent Pheochromocytoma	7	23
Pre-operative α-blockade only	4	13
Pre-operative α and β blockade	8	27
Use of Extracorporeal circulation	6	20
IVC reconstruction	5	17

Table 3. POST-OP OUTCOMES

Outcome	n	%
Survival	26	87
Recurrence	0	0
Death	4	13

Discussion

Rarely, pheochromocytoma can extend into the IVC through direct caval wall invasion or the venous drainage system. Our systematic literature review and report of 30 cases in the past five decades revealed that there has been no consistent reporting of these cases. Only 77% of the cases reported using serum or urine metabolite tests to diagnose pheochromocytoma when these tests are considered to be the most reliable way of assessing this condition.[12] Compared to pheochromocytoma patients without IVC involvement, there is a predominant male patient population in cases with IVC involvement.[14] There was also a higher likelihood of a right-sided tumor extending into the IVC, which is expected due to the direct anatomical convergence of the right adrenal vein into the IVC compared to the left adrenal vein.

Once pheochromocytoma was diagnosed in patients with serum or urine metabolite tests, pre-operative imaging was almost universally conducted to localize the tumor. On average, 2-3 different imaging modalities were used per case to assess the extent and to confirm IVC invasion. The most common type of imaging was the CT scan, and the most effective, an ultrasound. Only 37% reported the use of α and/or β blockade even though treatment to control hypertension prior to operation is crucial. Intraoperative findings revealed variability in surgical techniques depending on the location of the tumor within the IVC. Post-operatively, patients had great outcomes with 0% recurrence. In fact, the four documented deaths were due to causes unrelated to the operation itself. For the 26 patients who survived, however, there was variability in follow-up time lengths with a mean disease-free period of 25.3 months from post-op to most recent follow-up. The discrepancy in follow-up time intervals stresses the need for more consistent monitoring. Especially since malignancy of pheochromocytomas has yet to be clearly defined, continuous monitoring of these patients should be considered to prevent the risk of metastasis in the long-term.

Conclusion

Pheochromocytoma is primarily a surgical disease that can be completely cured with resection of the tumor, but no other specific recommendations for management can be made at this time. Pre-operatively, possible invasion into the IVC should be considered when imaging, and multiple modalities should be used. There is also a need to systematically report such rare cases of IVC involvement for proper management and clarification of potentially malignant pheochromocytomas.

Limitations

The rarity of this condition and the scarcity of cases reported has made it difficult to compare the management of these cases. There is inconsistency with data reporting, and malignant pheochromocytomas lack clear features other than distant metastasis.

References

1. Castello P, Melvin EC, Robert AK, et al. Problems in the diagnosis of adrenal tumors. Radiology 1977; 125: 335–341.
2. Chen H, Sippel RS, O'Dorisio MS, et al. The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma and medullary thyroid cancer. Pancreas 2010; 39: 775–783.
3. Conception RS, Koch MO, McDougal WS, et al. Management of primary non-renal parenchymal malignancies with vena caval thrombus. J Urol 1991; 145: 243–247.
4. Davis P. Malignant pheochromocytoma with functioning metastases. Lancet 1955; 20: 52–56.
5. Dicke TE, Henry MI, and Minton JP. Intracaval extension of pheochromocytoma simulating pulmonary embolism. J Surg Onkol 1987; 34: 160–164.
6. Dossett LA, Rudzinski ER, Blevins LS, et al. Malignant pheochromocytoma of the organ of Zuckerkandl requiring aortic and vena caval reconstruction. Endocr Pract 2007; 13: 493–497.
7. Dunn CW, Snyder WH, Ring WS, et al. Pheochromocytoma with extension into the inferior vena cava: a case report. Surgery 1992; 111: 472–474.
8. Dunnick NR, Doppman JL and Geelhoed GW. Intravenous extension of endocrine tumors. AJR 1980; 135: 471–476.
9. Dural C, Bilge O, Toker A, et al. Malignant pheochromocytoma with cavo-aortal extension: transcaval removal of tumor without cardiopulmonary bypass. Minerv Chir 2010; 65: 485–488.
10. Fischer EW, Kellher JP and Pengelly AW. Invasion of the inferior vena cava in malignant pheochromocytoma. Br J Urol 1988; 62: 272–273.
11. Goldstein RE, O'Neill JA, Holcomb GW, et al. Clinical experience over 48 years with pheochromocytoma. Ann Surg 1999; 229: 755–766.
12. Grouzmann E, Drouard-Troalen L, Baudin E, et al. Diagnostic accuracy of free and total metanephrines in plasma and fractionated metanephrines in urine of patients with pheochromocytoma. *European Journal of Endocrinology*. 2010;162(5):951-960. doi:10.1530/eje-09-0996.
13. Hoffman JC, Weiner SN, Koenigsberg M, et al. Pheochromocytoma invasion of the inferior vena cava: sonographic evaluation. Radiology 1983; 149: 793–795.
14. Kassahun, Woubet T. Update On The Optimal Management Of Patients With Vascular Extension Of Pheochromocytoma. Vascular 2015; 23.3: 297-304.
15. Kikumori T, Imai T, Kaneko T, et al. Intracaval endovascular ultrasonography for large adrenal and retroperitoneal tumors. Surgery 2003; 134: 989–994.
16. Lau TN, Goddard P, Vaidaya M, et al. Involvement of the inferior vena cava by adrenal pheochromocytoma --MRI findings. Br J Radiol 1997; 70: 303–305.
17. Levine E, deVries P and Wetzel LH. MR imaging of inferior vena caval recurrence of extra-adrenal pheochromocytoma. J Comput Assist Tomogr 1987; 4: 717–718.
18. Lewi HJ, Reid R, Mucci B, et al. Malignant pheochromocytoma. Br J Urol 1985; 57: 394–398.
19. Lucon AM, Junior RF, Praxedes JN, et al. Multicentric pheochromocytoma and involvement of the inferior vena cava. Sao Paulo Med J/Rev Paul Med 2001; 119: 86–88. 29.
20. Manger W.M., and Gifford R.W.: Pheochromocytoma. J Clin Hypertens 2002; 4: pp. 62-72
21. McLigeyo SO, Oliech JS, Rana FS, et al. Renal vein and intracaval invasion by an adrenal pheochromocytoma with extension into the right atrium: a case study. Afr J Health Sci 1996; 3: 60–63.
22. Melicow MM. One hundred cases of pheochromocytoma (107 tumors) at the Columbia-Presbyterian Medical Center, 1926-1976. Cancer 1977; 40: 1987–2004.
23. Puech JL, Song MY, Rousseau H, et al. Recurrent pheochromocytoma: intrarenal and pulmonary spread. Urol Radiol 1986; 8: 49–51.
24. Rotker J, Oberpenning F, Scheld HH, et al. Pheochromocytomas with extension in to central vascular structures. Ann Thorac Surg 1996; 61: 222–224.
25. Rote AR, Flint LD and Ellis FH. Intracaval recurrence of pheochromocytoma extending into right atrium. New Engl J Med 1977; 296: 1269–1271.
26. Russinovich NAE, Recio MG, Tishler JM, et al. Intracaval extension of pheochromocytoma: ultrasonographic demonstration. JCAR 1982; 33: 53–55.
27. Scott HW Jr, Reynolds V, Green N, et al. Clinical experience with malignant pheochromocytomas. Surg Gynecol Obstet 1982; 154: 801–808.
28. Silva MB Jr, Silva HC, Sandager GP, et al. Prosthetic replacement of the inferior vena cava after resection of a pheochromocytoma. J Vasc Surg 1994; 19: 169–173. 26.
29. Singer J, Koch CA, Kassahun WT, et al. A patient with a large recurrent pheochromocytoma demonstrating the pit- falls of diagnosis. Nat Rev Endocrinol 2011; 7: 749–755.
30. Smith EJ, McPherson GAD and Lynn J. Inferior vena cava involvement by a pheochromocytoma. Br J Surg 1987; 74: 597.
31. Woods MS, Mullins JR, Shellito JL, et al. Recommendations concerning the operative approach for pheochromocytoma invading the inferior vena cava. Surgery 1994; 115: 771–775.
32. Young JD Jr, Qureshi AS, Connor TB, et al. Problem lesions in adrenal surgery. J Urol 1969; 101: 233–240.