ADRENAL PHEOCHROMOCYTOMA: A CASE REPORT

ABSTRACT

Pheochromocytoma is a rare catecholamine secreting tumour originating usually from adrenal medulla and produces signs and symptoms due excessive catecholamine secretion from tumour. A young male patient of 36 yrs age presented with hypertension since 2 yrs, palpitation, profuse sweating, weight loss. Clinical suspicion of Pheochromocytoma was confirmed by CT scan and USG abdomen followed by catecholamines levels in plasma and urine. After preoperative preparation laparascopic removal of Pheochromocytoma was done. Postoperative recovery was uneventful and BP regains to normal range from 1st postoperative day. Pheochromocytoma is a rare cause of hypertension. If the diagnosis of Pheochromocytoma is overlooked, the consequences could be disastrous, even fatal; however, if a pheochromocytoma is identified, it is potentially curable, as being one of the cause of surgically correctable hypertension.

Keywords: pheochromocytoma, catecholamines, Computed Tomography

INTRODUCTION

Pheochromocytoma is a rare but life-threatening condition that has varied clinical presentations particularly hypertension, headache, palpitation, and sweating[1]. Patients with suggestive clinical features are frequently tested for Pheochromocytoma. The medical interest in this tumor has increased with the improved availability of diagnostic laboratory tools particularly plasma or urinary fractionated metanephrines (metanephrine and normetanephrine), and other neuroendocrine markers particularly chromogranin A[2,3]. The wide universal availability of different imaging facilities, both anatomical and functional, has also improved the detection of Pheochromocytoma[4].

The growing awareness for implementing different protocols and guidelines that consider Pheochromocytoma in the work-up and differential diagnosis has improved diagnosis of the disorder Accurate diagnosis is important because if the tumor is detected early laparoscopic or surgical treatment is usually curative before other changes or complications take place[5,6].

Catecholamine-producing tumors are neuroendocrine tumors that affect the chromaffin cells of adrenal medulla and postganglionic fibers of the sympathetic nervous system. These tumors are characterized by the synthesis, storage, release, and secretion of catecholamines and their metabolites[7,8]. They include pheochromocytomas in the adrenal medulla and paragangliomas in the extra-adrenal sympathetic ganglions usually below the diaphragm in the retroperitoneum or organ of Zuckerkandl and various sites including the head, neck, thorax, and abdomen.

However, although the majority of these tumors are benign and adrenal, investigation workup should consider their tendency for being multiple, malignant, and familial with genetic pathogenesis[9].

Epinephrine (and its metabolite metanephrine) is the catecholamine that is produced exclusively by the adrenal medulla and adrenal Pheochromocytoma[10]. On the other hand, norepinephrine (and its metabolite normetanephrine) is the catecholamine produced by the adrenal medulla and adrenal Pheochromocytoma as well as by the extra-adrenal Pheochromocytoma and paraganglioma, which can also produce dopamine and its metabolite methoxytyramine. However, this is rare.

Pheochromocytomas can affect individuals of all ages. They are common in people aged between 40 and 50 years, and relatively more common among females[11]. Adrenal pheochromocytomas constitute nearly 85% of cases of pheochromocytomas, with 15% being extra-adrenal paragangliomas that affect the sympathetic ganglions anywhere from the base of the brain to the urinary bladder. Laboratory diagnosis is usually achieved by measuring the catecholamines, or more importantly their metabolites in plasma or urine[12]. Although different markers, including catecholamines and vanillylmandelic acid, are utilized as diagnostic tests, total and fractionated metanephrines in plasma or urine provide the best valid laboratory test for excluding or confirming Pheochromocytoma. In addition, chromogranin A is another reliable marker for neuroendocrine tumors, including Pheochromocytoma and is increasingly used in the diagnostic workup and follow-up of patients with these tumors[13]. Following diagnosis, removal of the adrenal gland or the tumor is done by open surgery or by the laparoscopic technique, which is considered the 'gold standard' treatment choice since 1992[14].

CASE REPORT

A 36 yrs male patient from Amravati having complaints of uncontrolled hypertension since 2 yrs, Headache, Generalised weakness, Profuse sweating suddenly, Palpitation, and Weight loss sudden 10 kg in one month, Feeling heaviness in chest, having such complaints, CT Abdomen and pelvis (contrast) was done at Amravati and was reported as Well defined moderately enhancing hypodense rounded lesion in right adrenal region with central areas of necrosis, findings are suggestive of right adrenal Pheochromocytoma in given clinical scenario. And also USG Abdomen and KUB with Doppler renal vessels was done and reported as evidence of hpoechoic mass lesion superior and medial to upper pole of right kidney measuring 4.58 x 4.36 cm. in size, suggestive of right adrenal tumor. With above mentioned complaints and investigations patient was referred to our hospital for further management. On admission patient's general condition was moderate, Afebrile, Blood pressure 150/100 mm og hg, pulse 86/min, Respiratory Rate 20/min, Respiratory system- chest clear, Cardiac system-

unremarkable, CNS examination- conscious, oriented, P/A- soft and non tender. With above history and investigations pheochromocytoma profile was advised which revealed the following parameters:

1) Plasma Epinephrine - 33 pg/ml (less than 100 pg/ml). 2) Plasma Norepinephrine - 3326.6 pg/ml (less than 600)

3) Plasma Metanephrine – 30.4 pg/ml (less than 65). 4) Plasma Normetanephrine – 533 pg/ml (less than 196)

5) 24 hrs. urine Epinephrine – 15.4 (less than 20). 6) 24 hrs. urine Norepinephrine – 955.4 (less than 90)

7) 24 hrs. Metanephrine/Creatinine ratio – 182.94 (33-109). 8) 24 hrs. Normetanephrine/Creatinine ratio - More than 8823 (86-236)

9) 24 hrs. Urine VMA – 47.6 (less than 8.0). 10) 24 hrs. VMA ratio to Creatinine – 41.18 (less than 8.0)

All the investigations were pointing towards right adrenal Pheochromocytoma. Patient was discharged with proper medication to control blood pressure and advised for surgery after 10 days.

Patient was admitted for surgery and after discussion with relatives and their consent and proper fitness from anaesthetist, patient underwent laparoscopic excision of right adrenal tumor, procedure was uneventful, specimen sent for histopathology. Patient was discharged on seventh postoperative day. In pathology department received tumor mass of size 5 cm. in diameter, cutsection brownish in colour, haemorrhagic, necrotic areas seen. Microscopically sections show trabeculae,nests,separated by fibrovascular septae and comprising of cells having finely granular cytoplasm with round to oval nuclei and prominent nucleoli. Tumor is rich in vascular net work. Necrotic material seen. So reported as suggestive of Pheochromocytoma and Immunohistochemistry advised. Blocks sent to SRL Mumbai for IHC. They confirmed it as right adrenal Pheochromocytoma. Which was chromoganin, synaptophysin -positive, S-100 protein was positive in sustentacular cells, ki-67- positive 2 %, CD56- focal positive. Pan cytokeratin and vimentin – Negative. After two years of followup patient is not having any complaints.

DISCUSSION

Pheochromocytoma is a rare neoplasm, which are derived from cells of the chromaffin tissue and mostly situated within adrenal medulla. Only approximately 15% Pheochromocytoma develops from extra-adrenal chromaffin tissue which lies in the paraganglion chromaffin tissue of the sympathetic nervous system extending from base of skull to the urinary bladder[15]. Common locations of extra-adrenal Pheochromocytomas include the organ of Zuckerkandl (close to origin of the inferior mesenteric artery), urinary bladder wall, heart, mediastinum and carotid and glomus jugulare bodies[16].

Pheochromocytomas occur in people of all races, although they are diagnosed less frequently in blacks and equal frequency in male and female. Pheochromocytomas may occur in persons of any age. The peak incidence, however, is between the third andthe fifth decades of life. Approximately 10% occur in children[17]. The majority of cases are sporadic, with only 16% having a history of associated endocrine disorder such as Multiple Endocrine Neoplasia type II (MEN IIA and IIB), Neurofibromatosis 1 (NF 1) and von Hippel-Lindau disease (VHL). Approximately 10% of pheochromocytomas are malignant. Direct invasion of surrounding tissue or the presence of metastases determines malignancy. Unfortunately, no reliable clinical, biochemical or histological features distinguish a malignant from a benign pheochromocytoma[18].

The clinical manifestations of a pheochromocytoma results from excessive catecholamine secretion by tumour. Catecholamines typically secreted, either intermittently or continuously, includes norepinephrine and epinephrine; rarely dopamine is secreted. The biological effects of catecholamines are well known[19]. Catecholamine secretion in Pheochromocytoma is not regulated in the same manner as in healthy adrenal tissue. Relative catecholamine levels also differ in Pheochromocytoma[20]. Most pheochromocytomas secretes norepinephrine predominantly, where as secretions from normal adrenal medulla are composed of 85% epinephrine[21]. The classic history of a patient with Pheochromocytoma includes spells (Paroxysms) characterized by headaches, palpitations and diaphoresis in association with severe hypertension. The spells may vary in occurrence from monthly to several times per day and the duration may vary from seconds to hours. Paroxysms may be precipitated by physical training, induction of general anaesthesia and numerous drugs and agents (contrast media, tricyclic antidepressive drugs, metoclopramide and opiates). Typically, they worsen with time, occurring more frequently and becoming more severe as the tumour grows[22].

The first step in the diagnosis of a pheochromocytoma is the biochemical confirmation of catecholamine excess. Plasma metanephrine testing has the highest sensitivity (96%) for detecting a pheochromocytoma, but it has a lower specificity. In comparison, a 24 hour urinary collection for catecholamines and metanephrines has a sensitivity of 87.5% and a specificity of 99.7%. The biochemical diagnosis is followed by the localization of the Pheochromocytoma and/ or metastases. Magnetic Resonance Imaging (MRI) is preferred over Computed Tomography (CT) scanning because contrast media used for CT scans can provoke paroxysms. Surgical resection of the tumour is the treatment of choice and usually results in the cure of

hypertension. Careful preoperative preparation requires with combined alpha and beta-blockade to control blood pressure and to prevent intraoperative hypertensive crisis[23].

Surgical management has progressed through the years. Prior to introduction of laparoscopic adrenalectomy, thoracoabdominal approach was utilized at some centers, more commonly the midline abdominal and flank approaches have been used. Since the first laparoscopic adrenalectomy for Pheochromocytoma was done in 1992, it has been performed in numerous centers with excellent success over past decade.[24-25] Laparoscopic adrenalectomy is comparable to open approach, and should be considered preferentially in patients with tumour less than 6 cm. For larger or extra-adrenal tumour an open approach is favoured. Biochemical cure should be confirmed by assay of 24 hour urinary catecholamine 2-3 weeks after surgery and the lifelong urinary catecholamine measurement should be performed to identify recurrent or metachronous Pheochromocytoma.[26-27]

CONCLUSION

Pheochromocytoma is one of the few causes of hypertension that can be treated surgically. Although it is the causative factor of hypertension in about 0.1% to 0.6% of the hypertensive population, detection is mandatory, not only for the potential cure of the hypertension but also to avoid the potentially lethal effects of the unrecognized tumor.

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REFERENCES

1. Manger WM, Gifford RW. Pheochromocytoma. J Clin Hypertens (Greenwich) 2002. Jan-Feb;4(1):62-72.
2. Lenders JW, Eisenhofer G, Mannelli M, Pacak K. Phaeochromocytoma. Lancet 2005. Aug;366(9486):665-675.
3. Jr, B. F. P. ., & Federico R. Tewes. (2021). What attorneys should understand about Medicare set-aside allocations: How Medicare Set-Aside Allocation Is Going to Be Used to Accelerate Settlement Claims in Catastrophic Personal Injury Cases. *Clinical Medicine and Medical Research*, *2*(1), 61-64. https://doi.org/10.52845/CMMR /2021v1i1a1

4. Lenders JW, Pacak K, Walther MM, Linehan WM, Mannelli M, Friberg P, et al. . Biochemical diagnosis of Pheochromocytoma: which test is best? JAMA 2002. Mar;287(11):1427-1434.
5. Grossrubatscher E, Dalino P, Vignati F, Gambacorta M, Pugliese R, Boniardi M, et al. . The role of chromogranin A in the management of patients with phaeochromocytoma. Clin Endocrinol (Oxf) 2006. Sep;65(3):287-293.
6. Havekes B, King K, Lai EW, Romijn JA, Corssmit EP, Pacak K. New imaging approaches to phaeochromocytomas and paragangliomas. Clin Endocrinol (Oxf) 2010. Feb;72(2):137-145.
7. Pacak K, Eisenhofer G, Ahlman H, Bornstein SR, Gimenez-Roqueplo AP, Grossman AB, et al. International Symposium on Pheochromocytoma . Pheochromocytoma: recommendations for clinical practice from the First International Symposium. October 2005. Nat Clin Pract Endocrinol Metab 2007. Feb;3(2):92-102.
8. Daniel, V. ., & Daniel, K. (2020). Diabetic neuropathy: new perspectives on early diagnosis and treatments. *Journal of Current Diabetes Reports*, *1*(1), 12–14. https://doi.org/10.52845/JCDR/2020v1i1a3
9. Rana HQ, Rainville IR, Vaidya A. Genetic testing in the clinical care of patients with Pheochromocytoma and paraganglioma. Curr Opin Endocrinol Diabetes Obes 2014. Jun;21(3):166-176.
10. Unger N, Deutschbein T, Walz MK, Mann K, Petersenn S. The value of immunoassays for metanephrines in the biochemical diagnosis of pheochromocytomas. Horm Metab Res 2009. Sep;41(9):676-679.
11. Gumbs AA, Gagner M. Laparoscopic adrenalectomy. Best Pract Res Clin Endocrinol Metab 2006. Sep;20(3):483-499.
12. Assalia A, Gagner M. Laparoscopic adrenalectomy. Br J Surg 2004. Oct;91(10):1259-1274.
13. Yong L, Sheng-guo D, Zhen D, Xin M, Xin-yan S. Diagnosis and treatment of Pheochromocytoma in urinary bladder. J Zhejiang Univ Sci B. 2007;8(6):435-438.
14. Daniel, V., & Daniel, K. (2020). Perception of Nurses' Work in Psychiatric Clinic. *Clinical Medicine Insights*, *1*(1), 27-33. https://doi.org/10.52845/CMI/20 20v1i1a5
15. Bentrem DJ, Pappas SG, Ahuja Y, Murayama KM, Angelos P. Contemporary surgical management of Pheocromocytoma. The American journal of surgery 2002;184:621-625.
16. Bravo EL, Gifford RW jr. Pheochromocytoma. Endocrinol Metab Clin North Am. 1993;22(2):329-341.
17. Sheps SG, Jiang NS, klee GG, van Heerden JA. Recent developments in the diagnosis and treatment of Pheochromocytoma. Mayo Clin Proc. 1990;65(1):88-95.
18. Gifford RW, Kvale WF, Maher FT. clinical features, diagnosis and treatment of Pheochromocytoma. A review of 76 cases. Mayo Clin Proc. 1964;39:281-302.
19. Daniel, V., & Daniel, K. (2020). Exercises training program: It's Effect on Muscle strength and Activity of daily living among elderly people. *Nursing and Midwifery*, *1*(01), 19-23. https://doi.org/10.52845/NM/2020v1i1a5

20. Kudva YC, Sawka AM, Young WF jr. Clinical review 164: The laboratory diagnosis of adrenal Pheochromocytoma: Mayo Clinic experience. J Clin Endocrinol Metab. 2003;88(10):4533-9.
21. De jong WH, Eisenhofer G, Post WJ, Muskiet FA, de Vries EG, Kema IP. Dietary influences on plasma and urinary metanephrines: Implications for diagnosis of catecholamine producing tumour. J Clin Endocrinol Metab. 2009;94(8):2841-2849.
22. Wong C, Yu R. Preoperative preparation for pheochromocytoma resection: Physician survey and clinical practice. Exp clin Endocrinol Diabetes 2010;118(7):400-404.
23. Goldstein RE, O'Nell JA, Holcomb GW, Morgan WM, Neblett WW, Oates JA, et al. Clinical experience over 48 years with Pheochromocytoma. Ann surg. 1999;229:755-66.
24. Gagner M, Breton G, Pharand D, Pomp A. Is laparoscopic adrenalectomy indicated for Pheochromocytoma? Surgery 1996;120:1076-9.
25. Winfield HN, Hamilton BD, Bravo EL, Novick AC. Laparoscopic adrenalectomy: the preferred choice? A comparison to open adrenalectomy. J urol. 1998;160:325-9.
26. Shen WT, Sturgeon C, Clark OH, Duh QY, Kebebew E. Should pheochromocytoma size influence surgical approach? A comparison of 90 malignant and 60 benign pheochromocytomas. Surgery 2004;136:1129-37
27. Shen WT, Grogan R, Vriens M, Clark OH, Duh QY. One hundred two patients with Pheochromocytoma treated at single institution since the introduction of laparoscopic adrenalectomy. Arch surg. 2010;145(9):893-897.