International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 5(5): September-October 2015

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Review Article……!!!

Received: 01-09-2015; Revised: 15-09-2015; Accepted: 16-09-2015

A CASE STUDY ON PHEOCHROMOCYTOMA PRESENTING WITH NEUROLOGICAL MANIFESTATIONS

*Jiguru Prasant, Sruthi Marneedi, Vikram. M, Gayathri Vyshalini. K.

Department Doctor of Pharmacy, Krishna Institute of Medical Sciences.

Keywords:

Pheochromocytoma, Neuroendocrine, Adrenal, Renal

For Correspondence:

Jiguru Prasant

Department Doctor of Pharmacy,

Krishna Institute of Medical Sciences

E-mail:

Prashant7792@gmail.com

ABSTRACT

Pheochromocytomas are rare neuroendocrine tumors. Although predominantly occurring in the adrenal glands, these tumors can present anywhere along the sympathetic chain. Indeed, classical teaching states that 10% of pheochromocytomas are extra-adrenal and 10% are malignant. We report a case of a 61-year-old female who underwent presumptive cytoreductive nephrectomy and adrenalectomy for renal carcinoma but was instead found to have malignant pheochromocytoma. Proper identification, surgical extirpation, and follow-up are imperative for treatment. We review the classic and current literature regarding management of this uncommon tumor.

INTRODUCTION Pheochromocytomas are rare but treacherous catecholamine-producing tumors, which if missed or not properly treated, will almost invariably prove fatal . Prompt diagnosis is, therefore, essential for effective treatment, usually by surgical resection. The manifestations are diverse and the tumor can mimic a variety of conditions, often resulting in erroneous and delayed diagnosis . Therefore, not surprisingly pheochromocytoma earned the title "great mimic" . The incidence of pheochromocytoma in autopsy studies is about 0.05–0.1% . Autopsy studies have also shown that up to 50% of pheochromocytomas are unrecognized Recent advances in biochemical diagnosis (the measurement of plasma free metanephrines), tumor localization (the use of positron emission tomography), surgical approaches (the use of laparoscopic adrenal-sparing surgery), and improved understanding of the pathophysiology and genetics of pheochromocytoma (the role of succinate dehydrogenase gene family or hypoxia and apoptosis pathways) are leading to earlier diagnosis and changes in management strategies and therapeutic options . Pheochromocytomas are most frequent in individuals between 40 and 50 years, with very slight predilection in females. The tumors occur in all races, but have been predominantly reported in caucasians . Pheochromocytomas typically derive in about 85% of cases from adrenal medullary chromaffin tissue and in about 15% of cases from extra-adrenal chromaffin tissue . Those arising from extra-adrenal tissue are commonly known as paragangliomas. The 2004 WHO classification of endocrine tumors defines pheochromocytoma as a tumor arising from catecholamine-producing chromaffin cells in the adrenal medulla – an intra-adrenal paraganglioma. Paragangliomas are divided into two groups: those that arise from parasympathetic-associated tissues (most commonly along cranial and vagus nerves; e.g. glomus or carotid body tumors) and those that arise from sympathetic-associated chromaffin tissue (often designated extra-adrenal pheochromocytomas). Extra-adrenal pheochromocytomas arise mainly from chromaffin tissue of sympathetic ganglia in the abdomen (in about 75%) . Extra-adrenal pheochromocytomas in the abdomen most commonly arise from a collection chromaffin tissue around the origin of the inferior mesenteric artery (the organ of Zuckerkandl) or aortic bifurcation . Both adrenal and extra-adrenal paragangliomas display similar histopathological characteristics. Less frequent sites of pheochromocytoma include kidney, urethra, prostate, spermatic cord, genital tract, and liver. Most pheochromocytomas arise sporadically, but based on recent reports up to 24% are familial . Up to 25% of patients with pheochromocytoma present with adrenal incidentaloma, whereas approximately 5% are diagnosed at surgery . In contrast to sporadic pheochromocytomas that are usually unifocal

and unilateral, familial pheochromocytomas are often multifocal and bilateral . Although metastases may be rare for adrenal (about 10%) and familial (less than 5%; except succinate dehydrogenase subunit B SDHB pheochromocytomas the prevalence is up to 36% for extra-adrenal abdominal pheochromocytomas . Finally, up to 14% of intra-adrenal pheochromocytomas show local recurrence . One study also showed that patients with mainly adrenal pheochromocytoma have an increased risk for developing other cancers (e.g. liver and biliary tract cancers, malignant melanoma, cervix carcinoma, and central nervous tumors). According to different reviews and statistics, pheochromocytomas account for approximately 0.05–0.6% of patients with any degree of sustained hypertension . However, this probably accounts for only 50% of persons harboring the tumor, when it is considered that about half the patients with pheochromocytoma have only paroxysmal hypertension or are normotensive. Also, despite the low incidence of pheochromocytoma among patients with sustained hypertension, it must also be considered that the current prevalence of sustained hypertension in the adult population of Western countries is up to 30% . Thus, the prevalence of pheochromocytoma can be estimated to lie between 1:4500 and 1:1700, with an annual incidence of detection three to eight cases per 1 million per year in the general population.

CASE REPORT:

A 51 year-old Caucasian female with a past medical history of hypertension, coronary artery disease and cerebrovascular accident presented to the emergency room with acute onset dysarthria and right-sided hemiparesis. The patient reported that she noticed these symptoms when she woke that morning, but had resolved by the time she reached the emergency room, an hour later. She denied experiencing palpitations, headache, chest pain or shortness of breath.

On review of systems, it was revealed she had intermittent nausea and vomiting for a year with increasing frequency over the past two days. She denied blood or bile in the emesis. She also admitted to a 50-pound weight loss over the past year. Both esophagogastroduodenoscopy bilaterally and colonoscopy were normal within the past year.

Her medical history was significant for coronary artery disease complicated by two myocardial infarctions the previous year. She had also suffered from two past cerebrovascular accidents – the second of which was complicated by hemorrhage and seizure. Despite several anti-hypertensive medications, the patient's blood pressure remained uncontrolled.

On admission, the patient was afebrile, had an elevated blood pressure of 167/108, pulse of 95 beats/minute, respiratory rate of 18 breathes/minute, and pulse oximetry of 97% on room

air. Generally, the patient appeared comfortable. Cardiovascular exam was benign and pulmonary exam revealed decreased breath sounds. Abdominal exam was also benign with no masses appreciated. Neurological exam was significant for slight dysarthria, right homonymous hemianopsia, and right-sided facial droop. Upper and lower extremity strength testing was significant for weakness at 4/5 strength on the left side. Comparatively, the patient's strength was 5/5 in the upper and lower extremities on the right side. Additionally, she was hyper-reflexive on the right side compared to the left. Sensation was intact throughout. These neurological deficits were consistent with her baseline deficits from past strokes.

CT of the head was significant for an old left middle cerebral artery stroke, but there was no evidence of an acute process. A CT of the abdomen was performed in the emergency room, which revealed an incidental finding of a 6.7 x 5.4 cm right sided adrenal mass (Figure 1). The laboratory work-up revealed elevated catecholamines: plasma norepinephrine of 41.6, plasma metanephrine of 27.2, fractionated urine norepinephrine of 9390 and fractionated urine metanephrine of 8231. Diagnoses of transient ischemic attack and pheochromocytoma were made. Her blood pressure medications were changed to the alpha-blocker, phenoxybenzamine. A beta-blocker was later added for additional blood pressure control. The mass was surgically removed four weeks later.

DISCUSSION:

A pheochromocytoma is a tumor that results in excess secretion of the catecholamines epinephrine and norepinephrine. It arises from chromaffin cells of the medulla of the adrenal gland, but it can also be located in extra-adrenal, retroperitoneal, pelvic or thoracic sites. Diagnosis relies on measurement of plasma levels of free metanephrines. This test has a high sensitivity (99%) and specificity (89%)[1]. Between episodes of catecholamine release, catecholamine levels may be normal, which is why the recommended test measures metabolites, rather than the catecholamines themselves. The sensitivity and specificity of other tests such as urinary catecholamines are high, but still less sensitive and less specific than measuring plasma free metanephrines[1]. Although pheochromocytomas are rare, autopsy studies suggest a higher prevalence. The National Cancer Registry in Sweden has reported that pheochromocytomas are discovered in two patients per million people each year[2]. Interestingly, in autopsy studies, the prevalence of adrenal masses may be as high as 8%[3], and of these, 4.2% are diagnosed as pheochromocytomas[1].

Due to its variable clinical presentation, pheochromocytomas have been called "the masquerader". Retrospective studies show that of people with pheochromocytomas at time of autopsy, 61% had a history of hypertension and 91% had a history of "typical" symptoms, generally considered to be headaches, palpitations and sweating, but atypical symptoms have also been described. These atypical symptoms include: abdominal pain, nausea, vomiting, and dyspnea. Causes of death in people diagnosed with pheochromocytoma incidentally at time of autopsy include: myocardial infarction, cerebrovascular accident, arrhythmias, shock, renal failure and dissecting aortic aneurysm[2]. The catecholamines released by pheochromocytomas can lead toheart failure, pulmonary edema, arrhythmias, and intracranial hemorrhage. A pheochromocytoma presenting with cerebro- vascular injury is rare and the incidence is unknown. There are two proposed mechanisms for neurological injury resulting from a pheochromocytoma: hypertension and vasospasm. During excess catecholamine release, high blood pressure may overwhelm cerebrovascular autoregulation leading to hypertensive encephalopathy. The second proposedmechanism suggests that catecholamine excess or sympathomi- metics cause spasm of the cerebral arteries. These vascular spasms can cause infarction or transient impairment of circulation[4,5]. Management of cerebrovascular injury involves inhibiting the effects of the released catecholamines, epinephrine and norepi- nephrine. When these hormones are released, epinephrine

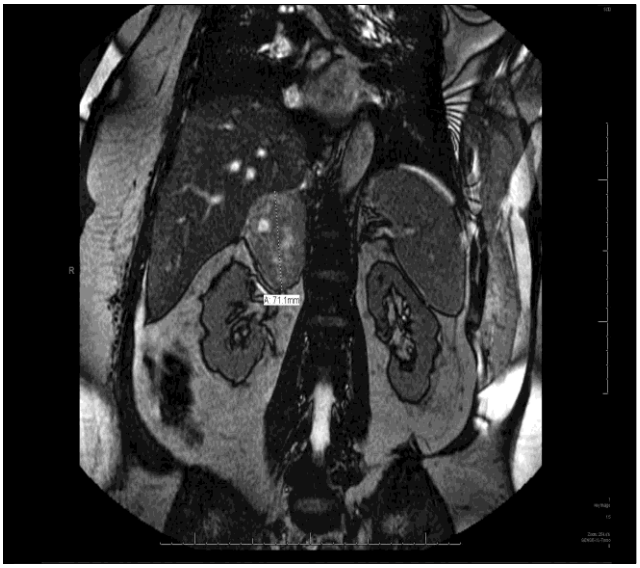

Figure 1. CT scan of the abdomen showing 6.7 x 5.4cm

Adrenal mass acts on alpha and beta adrenergic receptors while norepi-nephrine acts on the same receptors, except adrenergicreceptors. The cumulative effect is potent peripheral

vasocon-striction by alpha receptor agonism and increased heart rate by agonism[6]. Thus, management of hypertension due to a secondary cause like pheochromocytoma is very specific. Pre-operative medical management includes initial alpha antagonism followed by beta antagonism. Of importance, an alpha blocker such as Phenoxybenzamine is recommended approximately 2 days before starting beta-blockade agents[7] The rationale is that beta-blockade alone would result in blocking of beta receptors that cause peripheral vasodilation, leaving alpha mediated peripheral vasoconstriciton unopposed. Additionally, Metyrosine, a competitive inhibitor of the enzyme needed for catecholamine synthesis, has been proposed for pheochromo- cytoma management but is rarely clinically utilized at this time[6]. Definitive treatment of a pheochromocytoma is surgical removal, which is curative in up to 90% of cases[1]. Prior to surgery, the patient's clinical status is optimized with blood pressure control and volume repletion to avoid the consequences of the stress response from anesthesia and the surgery itself, which could involve a massive release of catecholamines.

ACKNOWLEDGEMENT

I would like to acknowledge the people who mean world to me, my parents, & my sister. I extend my respect to my parents and all elders to me in the family. I don't imagine a life without their love and blessings. Thank you mom, dad, for showing faith in me and giving me liberty to choose what I desired. I consider myself the luckiest in the world to have such a supportive family, standing behind me with their love and support.

REFERENCES

1. Waguespack SG, Rich T, Grubbs E, Ying AK, Perrier ND, Ayala-Ramirez M, et al. A current review of the etiology, diagnosis, and treatment of pediatric pheochromocytoma and paraganglioma. ***J Clin Endocrinol Metab***. 2010 May. 95(5):2023-37.
2. Sheps SG, Jiang NS, Klee GG, van Heerden JA. Recent developments in the diagnosis and treatment of pheochromocytoma. ***Mayo Clin Proc***. 1990 Jan. 65(1):88-95.
3. Yeterian EH, Pandya DN. Corticothalamic connections of the superior temporal sulcus in rhesus monkeys.***Exp Brain Res***. 1991. 83(2):268-84.
4. Elenkova A, Matrozova J, Zacharieva S, Kirilov G, Kalinov K. Adiponectin - A possible factor in the pathogenesis of carbohydrate metabolism disturbances in patients with pheochromocytoma. ***Cytokine***. 2010 Jun. 50(3):306-10.
5. Därr R, Lenders JWM, Hofbauer LC, Naumann B, Bornstein SR, Eisenhofer G. Pheochromocytoma: Update on Disease Management. Ther Adv in Endo and Metab. 2012;3(1):11-26.
6. Prejbisz A, Lenders JW, Eisenhofer G, Januszewicz A. Cardiovascular manifestations of phaeochromocytoma. ***J Hypertens***. 2011 Nov. 29(11):2049-60.
7. Thompson LD. Pheochromocytoma of the Adrenal gland Scaled Score (PASS) to separate benign from malignant neoplasms: a clinicopathologic and immunophenotypic study of 100 cases. ***Am J Surg Pathol***. 2002 May. 26(5):551-66.