Archives of Clinical & Experimental Surgery

Case Report
Arch Clin Exp Surg 2016;5:48-51
doi:10.5455/aces.20140907061533

Metastatic pheochromocytoma in an 18-year-old

Ali Cadili[1], Vanessa Falk[1], Lucas Diebel[2], Chris de Gara[2]

ABSTRACT

Pheochromocytoma most commonly presents with a combination of headache, sweating, and hypertension. This case report reviews the case of a young male patient presenting with hypertensive crisis following administration of general anesthetics and who was subsequently diagnosed with malignant pheochromocytoma. Up to date, no reliable predictive factors for malignant pheochromocytoma have been established. This case emphasizes the need for a systematic approach to the hypertensive crisis and advantages of nuclear imaging to differentiate benign from malignant disease through detection of local invasion and distant metastases.

Key words: *Pheochromocytoma, metastasis, paraganglioma*

Introduction

Pheochromocytomas are tumors composed of chromaffin cells that produce and secrete both norepinephrine and epinephrine. These tumors are most commonly found in the adrenal glands and are present bilaterally in approximately 10% of cases. Pheochromocytomas of extra-adrenal sites are known as paragangliomas and can be found in the neck, thorax, abdomen, and pelvis. The triad of hypertension (HTN), sweating, and headache is a common clinical presentation of pheochromocytoma. Other symptoms can include palpitations, anxiety, tremor, nausea, abdominal pain, dyspnea, and weakness. However, approximately 21% of pheochromocytoma cases are asymptomatic [1].

The "rule of ten" associated with pheochromocytoma is as follows: 10% of tumors are extra-adrenal, 10% bilateral, 10% malignant with metastases at time of diagnosis, 10% in children, 10% familial, 10% found incidentally on CT scans, 10% have multiple sites of origin, 10% of patients present with a normal blood pressure (BP), and 10% recur after surgical resection. The incidence of pheochromocytoma ranges from less than 0.5% among patients suffering from persistent HTN to 4% in patients with adrenal incidentalomas [2,3].

While 10% of pheochromocytomas may present with metastases at the time of diagnosis, metastatic disease can present as long as 20 years after the time of the initial diagnosis [4]. Common sites where malignant pheochromocytomas will metastasize to are the liver, bone, and lungs.

Author affiliations : *[1]Department of Surgery, University of Saskatchewan, Saskatoon, Saskatchewan, Canada [2]Department of Surgery, University of Alberta, Edmonton, Alberta, Canada*
Correspondence : *Ali Cadili, University of Saskatchewan, Saskatoon, Saskatchewan, Canada. e-mail: alicadili1@gmail.com*
Received / Accepted : *May 25, 2014 / September 07, 2014*

Case Report

An 18-year-old male high school student presented to the Emergency Department (ED) in January 2009 with a complaint of chest pain and had a BP measuring at 178/100 mmHg. Physical exam was otherwise unremarkable. An echocardiogram, 24-h Holter monitor, and exercise stress test were also performed at that time, but all came back normal. He was diagnosed with peritonitis, and his BP was managed initially with the beta-blocker Metoprolol, but was later switched to the angiotensin II receptor blocker Valsartan once daily.

Several months later, in November of 2009, this patient returned to the ED after entering a hypertensive crisis with a BP of 180/100 mmHg after receiving general anesthetic for wisdom tooth removal. On taking a history, the patient denied other symptoms of pheochromocytoma, including headaches, visual disturbances, and diaphoresis.

Laboratory Investigations

24-h urine samples were taken on December 9, 2009 and January 26, 2010. The first sample revealed elevated levels of total metanephrines of 33.3 μmol/24 h, total met/creatinine ratio of 3.5 μmol/mmol, total normetanephrine of 31.0 μmol/24 h, and total 3-methoxytyramine of 1.9 μmol/24 h. Repeat testing in January showed a further increase in levels: Total metanephrines of 43.9 μmol/24 h, total normetanephrine of 40.3 μmol/24 h, and total 3-methoxytyramine of 2.9 μmol/24 h.

Magnetic resonance imaging (MRI) of the abdomen revealed a large heterogeneous left suprarenal mass measuring 8.6 cm × 7.8 cm × 8 cm, as well as a smaller mass in the left paraspinal region behind the renal artery at the inferior pole of the left kidney measuring 2.7 cm × 4.1 cm × 4.4 cm. Following contrast administration, both lesions showed irregular peripheral enhancement with central hypoenhancement, consistent with necrosis. These characteristics were consistent with a left pheochromocytoma and left paraspinal paraganglioma.

A 123I-metaiodobenzylguanidine (MIBG) scan (Figure 1) was consistent with a left pheochromocytoma and paraganglioma seen on MRI; furthermore, a 7 mm pulmonary nodule in the medial segment of the right middle lobe was noted.

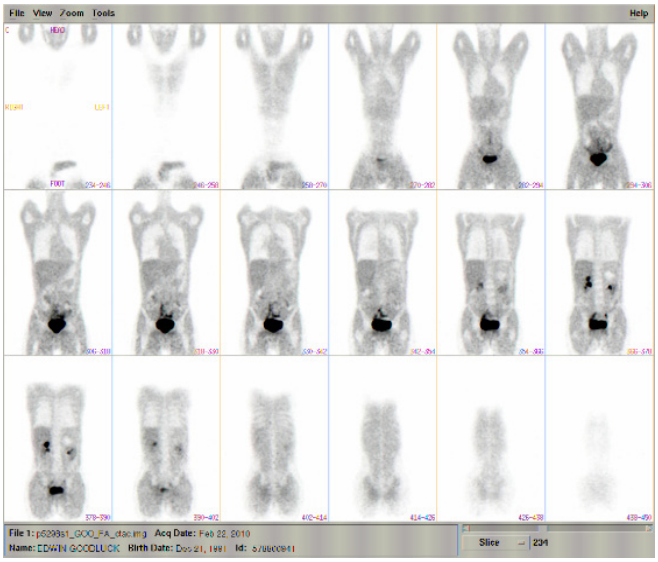

Figure 1. Abdominal 123I-metaiodobenzylguanidine scan from a patient with a left pheochromocytoma and paraganglioma.

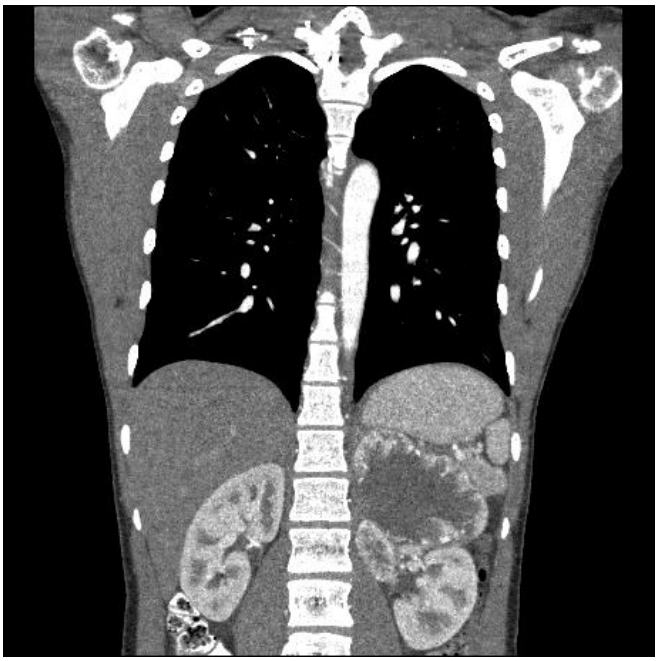

Figure 2. Chest positron emission tomography/computerized tomography scan from a patient with a pheochromocytoma.

Positron emission tomography/computerized tomography (PET/CT) scan of the chest [Figure 2] confirmed metabolic activity of the pulmonary nodule in the anteromedial middle lobe of the right lung and a diagnosis of malignant consistent with a left pheochromocytoma and paraganglioma seen on MRI; furthermore, a 7 mm pulmonary nodule in the medial segment of the right middle lobe was noted.

PET/CT scan of the chest (Figure 2) confirmed metabolic activity of the pheochromocytoma was made.

The patient's BP was well-controlled with phenoxybenzamine and bisoprolol prior to surgical resection of

the left adrenal gland and left paraganglioma and video-assisted thoracoscopic (VAT) wedge resection of the right lung middle lobe. Intra-operative findings included a well-encapsulated left adrenal mass that did not invade kidney, spleen, pancreas, stomach, or diaphragm. The paraganglioma was similarly excised within its intact capsule.

Following surgery, the patient returned to normotensive and antihypertensive medications were discontinued. He was discharged home on postoperative day 8.

Discussion

Epinephrine/norepinephrine-secreting tumors are composed of chromaffin cells from the embryonic neural crest. Although they may occur anywhere throughout the sympathetic nervous system, over 90% originate from the adrenal glands and are referred to as pheochromocytomas. Ten percent of tumors are extra-adrenal and referred to as paragangliomas [5]. Patients most commonly present with persistent HTN, headaches, and sweating.

If the diagnosis of pheochromocytoma is suspected, biochemical testing should be the first step in investigations. Suggested tests include the detection of the levels of plasma metanephrines and also 24-hour urine catecholamines and metanephrines [6]. Urinary measurement of catecholamines and metanephrines has been shown to be both 98% sensitive and specific for the diagnosis of pheochromocytoma [7,8]. Plasma metanephrine levels show high sensitivity of 99%, but lower specificity of 85-89% when compared to urinary tests [8-10]. In the above case, both plasma metanephrines and 24-h urine catecholamines were measured on two occasions. Both tests showed elevated levels of catecholamines and metanephrines, warranting further investigation with CT scanning.

Once biochemical testing has confirmed the diagnosis of pheochromocytoma, imaging such as a CT scan and/or MRI are employed for localization and work-up of possible metastatic lesions. Both CT and MRI have a sensitivity of 98-100% for adrenal pheochromocytomas, but MRI is more sensitive for paragangliomas [11,12]. Further, confirmatory studies include 131I-MIBG or 123I-MIBG scintigraphy, 123I-MIBG being better at detection of metastatic lesions [13]. MRI of the abdomen in the patient described above showed a large heterogeneous left suprarenal mass (8.6 cm × 7.8 cm × 8 cm) and a smaller mass in the left paraspinal region behind the renal artery at the inferior pole of the left kidney (2.7 cm × 4.1 cm × 4.4 cm). With a contrast, both lesions showed irregular peripheral enhancement with central hypoenhancement, consistent with necrosis. This was consistent with a left pheochromocytoma and left paraspinal paraganglioma. 123I-MIBG scintigraphy confirmed the left pheochromocytoma and paraganglioma seen on MRI; furthermore, a 7 mm pulmonary nodule in the medial segment of the right middle lobe was detected. Metabolic activity of the right pulmonary nodule was confirmed with PET/CT scan, and the diagnosis of malignant pheochromocytoma was made.

Surgery remains the only possible cure of pheochromocytoma. Preoperatively, these patients have to be stabilized. This is pharmacologically achieved with alpha-adrenergic antagonists, calcium channel blockers, or beta-blockers [6]. In the above case, preoperative BP was successfully controlled with a phenoxybenzamine and bisoprolol. The patient underwent open surgery for left adrenalectomy, VAT wedge resection of the right lung middle lobe, lymph node sampling, and removal of paraspinal paraganglioma. Intraoperative findings included a well-encapsulated left adrenal mass that did not invade kidney, spleen, pancreas, stomach, or diaphragm. Lymph nodes were negative for metastatic involvement. Postoperatively, the patient did well.

Ten percent of pheochromocytomas are malignant, presenting with or later on developing metastases of chromaffin tissue to bone, liver, or lungs. No predictive factors have been identified to assess benign versus malignant status of pheochromocytomas. Local invasion and distant metastases are the only indicators of malignancy [14].

While larger size and greater tumor weight have been suggested as possible risk factors for an increased likelihood of malignant disease, they are not predictive of malignancy [14]. In the above case of malignant pheochromocytoma, adrenal tumor size did indeed exceed the average of 7.82 cm (range 6.0-13.0 cm) [15].

Catecholamine level has been linked to tumor size, meaning that levels of catecholamines are approximately proportionate to the size of the pheochromo-

cytoma. The presented total hormone level exceeds the average highest hormone ratio for its tumor size of 27.4 described in a previous study [16]. Although this does support the theory that larger tumors present with higher hormone levels, further research is needed to correlate hormone levels to the malignancy potential of pheochromocytoma.

This case report validates the systematic approach to the diagnosis and treatment of patients with malignant pheochromocytoma and the need for further research to identify reliable predictors of malignancy.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Mannelli M, Ianni L, Cilotti A, Conti A. Pheochromocytoma in Italy: A multicentric retrospective study. Eur J Endocrinol 1999;141:619-24.
2. Stein PP, Black HR. A simplified diagnostic approach to pheochromocytoma. A review of the literature and report of one institution's experience. Medicine (Baltimore) 1991;70:46-66.
3. Mantero F, Terzolo M, Arnaldi G, Osella G, Masini AM, Alì A, et al. A survey on adrenal incidentaloma in Italy. Study Group on Adrenal Tumors of the Italian Society of Endocrinology. J Clin Endocrinol Metab 2000;85:637-44.
4. Plouin PF, Chatellier G, Fofol I, Corvol P. Tumor recurrence and hypertension persistence after successful pheochromocytoma operation. Hypertension 1997;29:1133-9.
5. Birrenbach T, Stanga Z, Cottagnoud P, Stucki A. Unexpected metastatic pheochromocytoma - An unusual presentation. Eur J Intern Med 2008;19:60-2.
6. Adler JT, Meyer-Rochow GY, Chen H, Benn DE, Robinson BG, Sippel RS, et al. Pheochromocytoma: Current approaches and future directions. Oncologist 2008;13:779-93.
7. Kudva YC, Sawka AM, Young WF Jr. Clinical review 164: The laboratory diagnosis of adrenal pheochromocytoma: The Mayo Clinic experience. J Clin Endocrinol Metab 2003;88:4533-9.
8. Sawka AM, Jaeschke R, Singh RJ, Young WF Jr. A comparison of biochemical tests for pheochromocytoma: Measurement of fractionated plasma metanephrines compared with the combination of 24-hour urinary metanephrines and catecholamines. J Clin Endocrinol Metab 2003;88:553-8.
9. Lenders JW, Pacak K, Walther MM, Linehan WM, Mannelli M, Friberg P, et al. Biochemical diagnosis of pheochromocytoma: Which test is best? JAMA 2002;287:1427-34.
10. Sawka AM, Prebtani AP, Thabane L, Gafni A, Levine M, Young WF Jr. A systematic review of the literature examining the diagnostic efficacy of measurement of fractionated plasma free metanephrines in the biochemical diagnosis of pheochromocytoma. BMC Endocr Disord 2004;4:2.
11. Goldstein RE, O'Neill JA Jr, Holcomb GW 3rd, Morgan WM 3rd, Neblett WW 3rd, Oates JA, et al. Clinical experience over 48 years with pheochromocytoma. Ann Surg 1999;229:755-64.
12. Maurea S, Cuocolo A, Reynolds JC, Neumann RD, Salvatore M. Diagnostic imaging in patients with paragangliomas. Computed tomography, magnetic resonance and MIBG scintigraphy comparison. Q J Nucl Med 1996;40:365-71.
13. Van Der Horst-Schrivers AN, Jager PL, Boezen HM, Schouten JP, Kema IP, Links TP. Iodine-123 metaiodobenzylguanidine scintigraphy in localising phaeochromocytomas – Experience and meta-analysis. Anticancer Res 2006;26:1599-604.
14. Lombardi CP, Raffaelli M, De Crea C, Traini E, D'Amore AM, Bellantone R. Pheochromocytoma: Role of preoperative diagnosis in the assessment of malignancy risk and in the choice of surgical approach. Suppl Tumori 2005;4:S211.
15. Ippolito G, Palazzo FF, Sebag F, Thakur A, Cherenko M, Henry JF. Safety of laparoscopic adrenalectomy in patients with large pheochromocytomas: A single institution review. World J Surg 2008;32:840-4.
16. Guerrero MA, Schreinemakers JM, Vriens MR, Suh I, Hwang J, Shen WT, et al. Clinical spectrum of pheochromocytoma. J Am Coll Surg 2009;209:727-32.