Bilateral Pheochromocytoma Masquerading as Acute Severe Congestive Heart Failure in a Juvenile Male Subject: A Case Report and Review of Literature

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ABSTRACT

Introduction: Pheochromocytomas are rare neuroendocrine tumours of the adrenal medulla that do not always present with classical triad of headache, palpitations and diaphoresis along with paroxysmal or sustained hypertension. Herein we present a case of young boy with pheochromocytoma who presented initially with congestive cardiac failure with no other significant manifestation.

Case report: A 17 -year-old boy was admitted in our emergency with 2 months history of unevaluated headache and one day history of breathlessness along with syncopal attacks. His initial clinical evaluation was suggestive of congestive cardiac failure (CCF) with hypotension. After initial stabilization he was shifted to intensive care unit (ICU) where his echocardiography revealed dilated cardiomyopathy with severe mitral regurgitation. Because of young age of presentation and no past significant medical history neuroendocrine cause for cardiac illness was suspected. Further investigations revealed grossly elevated levels of normetanephrines in 24-hour urine collection. Imaging studies including ultrasonography followed by computed tomography of abdomen and I^{123} MIBG confirmed presence of bilateral pheochromocytoma. An open bilateral adrenalectomy was performed successfully after initial stabilisation. Patient was discharged after one-month postoperative care. Patient is presently in our follow up on low dose steroids, mineralocorticoids along with betablocker and has shown marked improvement in biochemical and clinical parameters.

Conclusion: Pheochromocytoma though a rare catecholamine-producing tumour but if not timely intervened can lead to life-threatening consequences. Our case report highlights the importance of high clinical suspicion of pheochromocytoma even in young adolescent patients who present first time with acute severe CCF with dilated cardiomyopathy.

Keywords: Pheochromocytoma, Catecholamine Induced Cardiomyopathy, Heart Failure, Cardiogenic Shock.

INTRODUCTION

Pheochromocytoma is a rare, insidious adrenal medullary neuroendocrine tumour that secretes high levels of catecholamines. The cardiovascular manifestations of pheochromocytoma generally include paroxysmal or sustained hypertension, left ventricular hypertrophy, conduction disturbances associated with variable electrocardiographic (ECG) changes. Although rare, myocardial involvement other than sustained or paroxysmal hypertension can include angina pectoris, acute heart failure, dilated cardiomyopathy, myocardial infarction and arrhythmias. The acute onset of severe CCF secondary to catecholamine induced dilated cardiomyopathy from a pheochromocytoma is a rare entity, especially when few or none of the other classic signs or symptoms are present.

We present a case that illustrates an adolescent male with no significant past medical history, presenting with acute CCF with hypotension. He was found to have dilated cardiomyopathy with an ejection fraction (EF) of 30%, severe global hypokinesia and was later diagnosed with bilateral pheochromocytoma. The prognosis of a patient with catecholamine induced cardiomyopathy associated with pheochromocytoma depends on early identification and timely medical and surgical treatment. Thus, awareness of the variable clinical manifestations of this insidious tumour is key for optimal patient management.

CASE REPORT

A 17 years male of normal built, student of class tenth presented to our emergency department with complains of sudden onset breathlessness and syncopal attacks for last one day (Figure1). Historically he had no major complaints except a short history of headache for last two months though no specific medical consultation was sought. On admission, his pulse rate was 110/min, blood pressure was 90/60 in right upper limb with no postural drop, respirations 20/min with pulse oximetry 90% at room air, congested neck veins and mild pedal oedema. Systemic examination was suggestive of tachycardia, S3 gallop with no audible heart murmurs. Basal crackles were auscultated in bilateral lung fields. Examination of abdomen was unremarkable except mild hepatomegaly. Rest of the examination including optic fundi was normal. Neither he had significant family history nor any specific features could be elicited suggestive of syndromic

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association. Baseline laboratory tests revealed leucocytosis with mildly deranged liver function and renal function test. His ECG done in emergency room was not suggestive of any major abnormality except sinus tachycardia. The chest X ray revealed cardiomegaly (cardiothoracic ratio>0.6), bilateral obscured costophrenic angles and diffuse interstitial infiltrates (Figure2). Thus, a provisional diagnosis of CCF with cardiogenic shock was made. After initial stabilisation with inotropes and diuretics, patient was shifted to intensive care unit for further management and evaluation. To rule out any underlying cardiac illness cardiology consultation was sought and echocardiogram was performed that revealed enlarged left atrium (LA) of 48mm (normal,19-40mm), reduced interventricular septum thickness at end diastole(IVSED) of 1mm (normal, 6-11mm), ejection fraction of 30% with no regional wall motion abnormalities(RWMA) with final impression of dilated cardiomyopathy and severe mitral regurgitation (MR). (Figure3).

His ultrasonography (USG) was grossly normal with a suspicious solitary lesion of 6cm in left suprarenal region. Corroborating above radiological findings with clinical presentation of a young boy presenting first time with dilated cardiomyopathy and CCF we made a provisional diagnosis of pheochromocytoma.

Hormonal work up including serum cortisol and DHEAS (dehydroepiandrosterone) along with 24-hour urinary fractionated catecholamines were done. The results revealed normal serum cortisol and DHEAS levels but his urinary normetanephrine were markedly elevated (5572ug/day; normal, 50-650ug/day) with normal metanephrines favouring our provisional diagnosis. To localize lesion contrast enhanced computed tomography was done which revealed left adrenal lesion (6.4*4.9cm) of 20 HU on noncontrast images and peripheral rim enhancement with central nonenhancing areas on postcontrast images. Right adrenal gland was normal. (Figure 4) As the presentation of pheochromocytoma was unusual in our case thus to confirm the localisation I^{123}metaiodobenzylguanidine (MIBG) scan was done. Interestingly I^{123} scan (MIBG) revealed concentrating lesions in bilateral suprarenal regions (left 3.6 cm*2.6 cm and right of 1.4*2.2cm) thus suggestive of bilateral pheochromocytoma. (Figure5) Thus

Figure-1: Clinical photograph of the subject

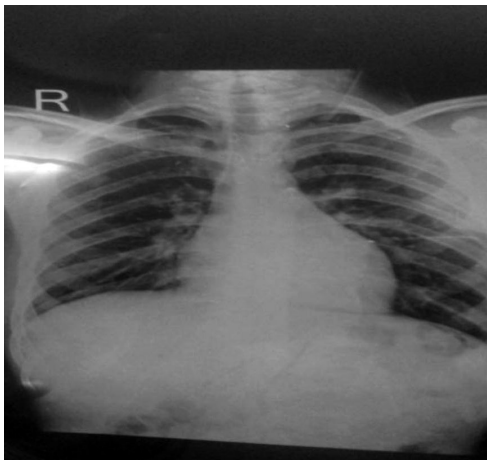

Figure-2: Preoperative chest X ray showing cardiomegaly and diffuse interstial infiltrates)

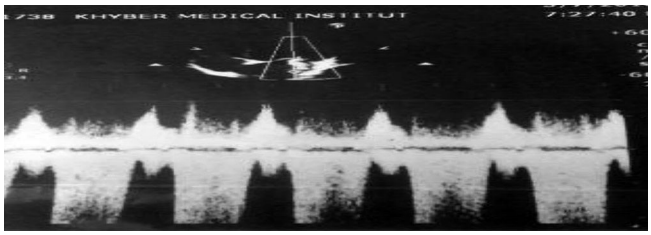

Figure-3: Preoperative images of doppler echocardiography

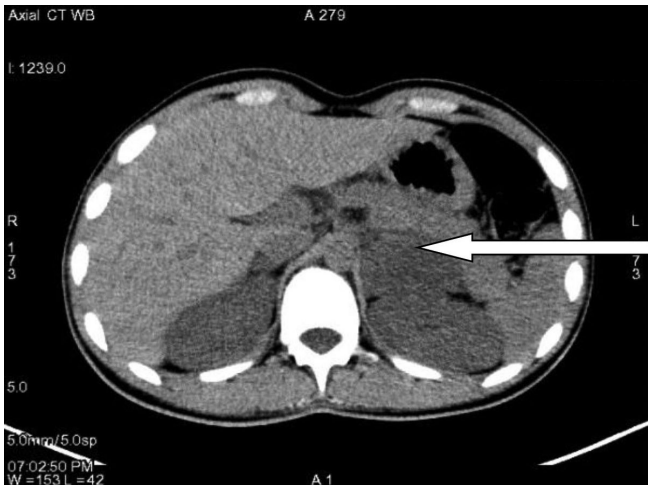

Figure-4: Preoperative CECT. Arrow indicates left adrenal lesion (6.4*4.9 cm) of 20 HU on noncontrast images

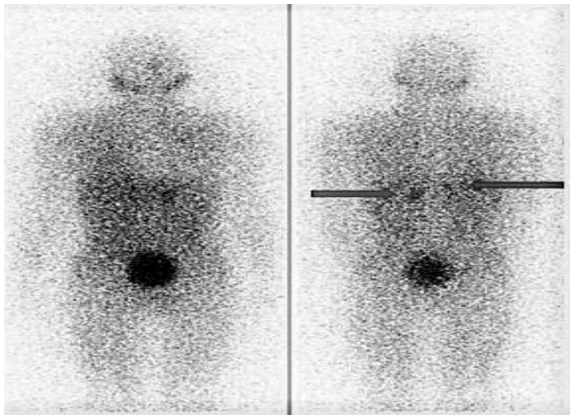

Figure-5: I123 scan (MIBG) concentrating lesions in bilateral suprarenal regions (left 3.6 cm*2.6 cm and right of 1.4*2.2cm)

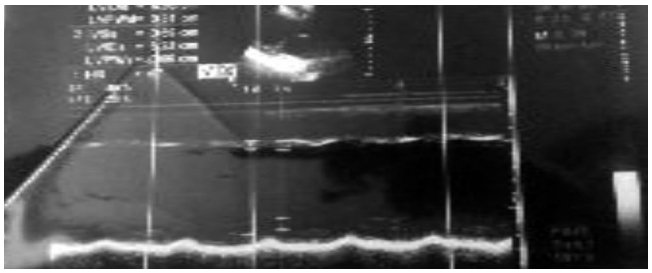

Figure-6: Postoperative images of doppler echocardiography

after confirmation of bilateral adrenal pheochromocytoma cardiology and general surgery consultation was sought and recommendations were made to proceed with bilateral adrenalectomy after preoperative preparation with low dose alpha blocker (prazosin 1mg/day) introduced ten days prior to surgery along with diuretics and intravenous (iv) fluids. Beta blockers (tab metoprolol 12.5 mg OD) were added 3 days after initiation of alpha blocker. After this preoperative optimization patient underwent bilateral open adrenalectomy. Left side 5*4 cm mass was excised and right side 2*3 cm mass was identified and excised. Postoperatively patient was managed with iv steroids which were gradually tapered and was shifted to ward in hemodynamically stable condition. However, on postoperative day 5 patient again developed sudden onset breathlessness, periorbital and pedal oedema with hypotension. Thus, with a suspicion of heart failure and cardiogenic shock patient was again shifted to ICU, cardiology consultation was sought and was managed with intravenous diuretics, dobutamine infusion and stress doses of hydrocortisone. He responded to treatment and his dobutamine infusion was gradually stopped. He was then started on oral wysolone, fludrocortisone along with tab ramipril, metoprolol and furosemide. Histomorphology and immunoprofile confirmed bilateral adrenal neoplasm to be a pheochromocytoma with no capsular or vascular invasion. After discharge patient has been in our regular follow up with overall improvement in his symptoms. His postoperative urinary fractioned catecholamines done one month after surgery were (normetanephrine level of 422ug/day (normal, 50-650ug/day) along with normal metanephrine. His postoperative echocardiography done 8 months after surgery revealed LA 24mm(19-40mm), IVSED 6mm (6-11), ejection fraction of 40% with no RWMA (Figure 6)

DISCUSSION

Pheochromocytomas are rare but treacherous neuroectodermal catecholamine secreting tumours which if missed or inadequately treated can prove fatal to patient. They occur with equal frequency in both sexes and can present from third to fifth decade. They are commonly found in the adrenal medulla (80-85%) with paragangliomas (15-20%) mainly found within the abdominal cavity, rarely in the thorax and neck. Although approximately 10% of all pheochromocytomas are inherited, overall, their prevalence varies from 0.3% to 1.9%.[2] The most prominent manifestation of pheochromocytoma is hypertension, which is paroxysmal in 45% of patients, persistent in 50%, and absent in 5%-13%.[2] Pheochromocytomas are found in 0.1% to 0.2% of hypertensive patients. In children pheochromocytoma accounts for 1% cases of hypertension with higher prevalence in boys than girls and with sustained hypertension as a most common presenting symptom in approximately 70-80% patients.

The classic triad of headache, palpitations, and diaphoresis along with paroxysmal hypertension is not always present especially in childhood. Thus, recognition requires a high index of suspicion as it may present with atypical features like pulmonary oedema, severe sepsis, myocarditis, acute myocardial infarction, arrhythmias or as in this case, cardiogenic shock with dilated cardiomyopathy. Cardiac presentations are the most unusual and unpredictable.[3,4]

One of the largest case series on pheochromocytoma with atypical cardiac manifestations were published by Marie Batisse-Lignier et al in 2015. A total of 142 cases were reported from 1961 to 2012 out of which 49 were labelled as Takotsubo cardiomyopathy and 96 were labelled as catecholamines induced cardiomyopathy. Cardiogenic shock was initial presentation in 51% cases.[5] Jae-Hyeong Park revealed in his study that the prevalence of catecholamine cardiomyopathy associated with pheochromocytoma is around 10% (3/29).[6] All three patients in his study with dilated cardiomyopathy improved with conventional treatment within three days. In 2011 Run yu showed that overall, 12% (9 out of 76) patients with pheochromocytoma presented with cardiac complications at their centre from 1995-2011 with heart failure, myocardial infarction, and arrhythmia dominating clinical profile. All these patients were of age group 40-50 and only one patient was found to have dilated cardiomyopathy.[7] They concluded that patients with large tumours and high levels of biochemical markers were more likely to develop cardiac injury. Another study by Goldstein et al reported frequency of cardiac complications in pheochromocytoma patients around 9%.[8] Although there have been many sporadic case reports and few case series about pheochromocytoma presenting as heart failure very few have been reported in pediatric population. Pheochromocytoma is thus often not considered in the initial differential diagnosis of cardiac disease in children as in our patient.

The pathogenesis of catecholamine-induced cardiomyopathy is multifactorial. Catecholamines and its oxidative by-products can cause a direct toxic effect on the myocardium mediated through calcium influx besides exerting a receptor-mediated effect on the myocardium.[9,10] They have been implicated in causing both obstructive as well as dilated cardiomyopathy.[11,12] Calcium-mediated myocyte injury remains one of the major risk factors for cardiomyopathy; however, other factors should be taken into consideration like catecholamines induced vasoconstriction and coronary vasospasm, resulting in myocardial ischemia and subsequent cardiomyopathy.[13] Clinical presentation and pathological findings of catecholamine induced cardiomyopathy are similar to stress induced cardiomyopathy (Takotsubo cardiomyopathy) which is self-limiting condition mainly seen

in postmenopausal women best treated with noradrenergic inotropes.

In our case patient's clinical presentation, age, and ultrasound findings prompted a 24-hour urine collection. Urinary catecholamines (metanephrine and normetanephrine) are highly sensitive and specific for diagnosing pheochromocytomas, as in our case and thus suspicion of pheochromocytoma was confirmed when we got high levels of urinary normetanephrines. Preoperative localization of pheochromocytomas can be carried out by a variety of radiologic studies, such as CT, magnetic resonant imaging (MRI), and radiolabelled iodine ^{123} MIBG but in patients with young age of presentation, size >10 cm or suspicion of genetic cause it is advisable to perform I^{123} MIBG.

Other causes of reversible cardiomyopathy should be kept in mind when patient presents with sole manifestations of cardiac illness including iron overload, sarcoidosis, thyrotoxicosis, renal failure, hypocalcaemia, hypophosphatemia, alcoholism and certain medications. The diagnosis of pheochromocytoma should always be considered when there is an unexplained source of a cardiomyopathy.

It has been shown that the cardiomyopathy is potentially reversible after surgical removal of pheochromocytoma, but patients who present with acute heart failure have the possibility of experiencing a poor prognosis secondary to extensive focal myocardial damage.[14,15,16] However there are reports of complete reversibility of the myocardial dysfunction with surgical treatment[17] as early as 8 days after intervention.[18] With increasing worldwide expertise, laparoscopic adrenalectomy is now regarded as the gold standard treatment. Although tumour resection results in early alleviation of symptoms in patient of pheochromocytoma but immediate postoperative period is also critical as patient may develop complications. Most commonly described complication is sudden onset hypotension which has to be managed with adequate iv fluids. Our patient on postoperative day 5 developed cardiac failure and hypotension requiring inotropes support. However, after recovery from this acute episode patient had significant improvement of symptoms related to his cardiac complications. His postoperative echocardiography done 6 months after surgery was suggestive of gradual improvement in ejection fraction (EF40%, IVSED 6mm). His repeat 24-hour urine normetanephrines also decreased (422ug/day) done one month after surgery compared to preoperative values.

CONCLUSION

Thus, finally we conclude that though pheochromocytoma is a rare catecholamine-producing tumour but it may lead to life-threatening consequences if not timely intervened. A multidisciplinary approach involving anaesthetist, endocrinologist and surgical expertise is the gold standard in maximizing patient care. Young age of presentation and reversibility of life-threatening cardiac complications with early intervention is the main highlight of our case. Aggressive preoperative optimization with alpha-adrenergic blockade, volume resuscitation, and possibly betablockade, along with surgical removal of a pheochromocytoma, has the potential to reverse catecholamine-induced cardiomyopathy and thus significantly decrease associated morbidity and mortality. Although it is rarely reported in the literature as a cause of acute severe CCF, pheochromocytomas, should be included in the differential diagnosis when no other obvious cause can be elicited.

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Consent for publication: Written and informed consent was obtained from patient. The study was approved and conducted according to the guidelines of the Institute's ethics committee.

Contributors: Dr Mohd Ashraf Ganie initially examined the patient and Dr Mona further investigated and managed the patient under guidance of Dr Ashraf. Dr Mona wrote this case article.

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REFERENCES

1. Alpert JS. The AHA Clinical Cardiac Consult. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:192–193.
2. J. Larry Jameson, Leslie J De Groot. 7th edition. Vol 2. 110:1903
3. Bravo EL, Gifford RW Jr. Pheochromocytoma. Endocrinol Metab Clin North Am. 1993; 22:329-341.
4. Werbel SS, Ober KP. Pheochromocytoma Update on diagnosis, localization, and management. Med Clin North Am. 1995; 79:131-153.
5. Marie Batisse-Lignier, Bruno Pereira, Pascal Motreff. Acute and Chronic Pheochromocytoma-Induced Cardiomyopathies: Different Prognoses? Medicine. 2015; 94:76-85
6. Jae-Hyeong Park. Prevalence and Patterns of Left Ventricular Dysfunction in Patients with Pheochromocytoma. J Cardiovasc Ultrasound 2011;19:76-82
7. Run Yu, Nicholas N Nissen, Serguei I Bannykh. Cardiac manifestations of Pheochromocytoma. Endocr Pract. 2012; 18:483-492
8. Goldstein RE, O'Neill JA Jr, Holcomb GW III, et al. Clinical experience over 48 years with pheochromocytoma. Ann Surg. 1999; 229:755-764.
9. Redfield MM, Kay GN, Jenkins LS, MianulliM, Jensen DN, Ellebogen KA. Tachycardia-related cardiomyopathy: a common cause of ventricular dysfunction in patients with atrial fibrillation referred for atrioventricular ablation. Mayo Clin Proc. 2000; 75:790-795
10. Schifferdecker B, Kodali D, Hausner E, Aragam J. Adrenergic shock—an overlooked clinical entity. Cardiol Rev. 2005; 13:69-72.

11. Jacob JL, da Silveira LC, de Freitas CG, Cêntola CA, Nicolau JC, Lorga AM. Pheochromocytoma with echocardiographic features of obstructive hypertrophic cardiomyopathy: a case report. Angiology. 1994; 45:985-989.
12. Dagartzikas MI, Sprague K, Carter G, Tobias JD. Cerebrovascular event, dilated cardiomyopathy and pheochromocytoma. PediatrEmerg Care. 2002; 18:33-35
13. Rona G. Catecholamine cardiotoxicity. J Mol Cell Cardiol. 1985; 17:291-306.
14. Sardesai SH, Mourant AJ, Sivathandon Y, Farrow R, Gibbons DO. Pheochromocytoma and catecholamine induced cardiomyopathy presenting as heart failure. BrHeart J. 1990; 63:234-237.
15. Gatzoulis KA, Tolis G, Theopistou A, Gialafos JH, Toutouzas PK. Cardiomyopahty due to a pheochromocytoma.A reversible entity. ActaCardiol. 1998; 53:227-229.
16. Wood R, Commerford PJ, Rose AG, Tooke A. Reversible catecholamine-induced cardiomyopathy. Am Heart J. 1991; 121:610-613.
17. Sadowski D, Cujec B, McMeekin JD, Wilson TW. Reversibility of catecholamine-induced cardiomyopathy in a woman with pheochromocytoma. CMAJ 1989; 141:923-4.
18. Salathe M, Weiss P, Ritz R. Rapid reversal of heart failure in a patient with pheochromocytoma and catecholamine-induced cardiomyopathy who was treated with captopril. Br Heart J 1992; 68:527-8.

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