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Case Report

Pheochromocytoma related intracerebral hemorrhage, hypertrophic obstructive cardiomyopathy and diabetes mellitus

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ABSTRACT

Pheochromocytomas are rare catecholamine secreting neuroendocrine tumors that can cause intracerebral hemorrhage sometimes and can very rarely cause cardiomyopathy simulating hypertrophic obstructive cardiomyopathy. We report a case of combination of these rare clinical complications occurring in a patient with pheochromocytoma. This case illustrates importance of early recognition of classic symptoms of catecholamine excess in young patients with hypertension.

Keywords: Pheochromocytomas, Intracerebral hemorrhage, Hypertrophic obstructive cardiomyopathy

INTRODUCTION

Pheochromocytomas are rare catecholamine secreting neuroendocrine tumors with an estimated annual incidence of 1-4 per million and prevalence among hypertensive patients of 0.1-0.6%.[1] The classical manifestations of these tumors are paroxysms of hypertension, headache, palpitations, sweating and pallor. Pheochromocytomas arise from adrenal medulla and secrete both epinephrine and nor-epinephrine whereas paragangliomas are extra adrenal pheochromocytomas which arise from sympathetic paraganglia and usually secrete nor epinephrine or are non-secretory.[1]

Intracerebral hemorrhage in the young is usually caused by arteriovenous malformations, cavernous angiomas or hypertension, followed by cerebral venous sinus thrombosis, eclampsia and sympathomimetics drugs.[1] There are very few case reports of catecholamine secreting tumors presenting with intracerebral hemorrhage, two of them as autopsy cases; few reports of pheochromocytoma induced ischemic stroke also exist.[3] There is an established association of pheochromocytoma with left ventricular hypertrophy, dilated cardiomyopathy and myocarditis due to catecholamine surge but there exist only a small number of reports of pheochromocytoma simulating hypertrophic obstructive cardiomyopathy.[1]

We present a case of pheochromocytoma with intracerebral hemorrhage and cardiomyopathy with right ventricular outflow tract obstruction and diabetes mellitus in the same patient.

CASE REPORT

A 35-year-old male presented with intermittent severe headache of 3 months duration. He had been diagnosed hypertensive for 4 years and was started on tablet telmisartan and hydrochlorothiazide (80 and 12.5 mg) daily and tablet nifedipine 20 mg three times daily before presenting to our institution. On clinical examination he had a pulse rate of 104/min regular with all peripheral pulses normal and well felt. His blood pressure was 140/100 mm of Hg. There was harsh midsystolic murmur of grade 2/6 along left lower sternal border. Fundus

examination revealed grade I hypertensive retinopathy. Rest of the examination was within normal limits.

Electrocardiogram showed sinus tachycardia. Magnetic resonance imaging (MRI) scan of brain showed presence of late subacute bleed in left parietal region and areas of chronic microhemorrhages were noted in bilateral fronto-parieto-temporal region, left thalamus and lentiform nucleus.

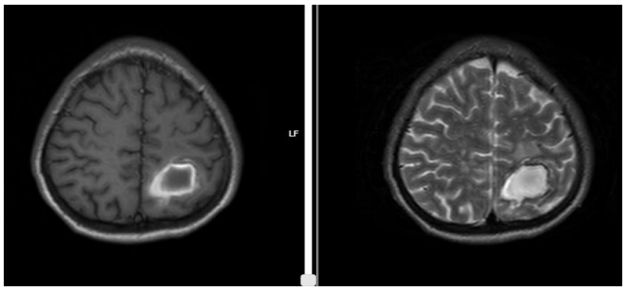

Figure 1: Late subacute bleed noted in left parietal region showing hyperintense signal on T2, hypointense on T1 with peripheral hyperintense rim.

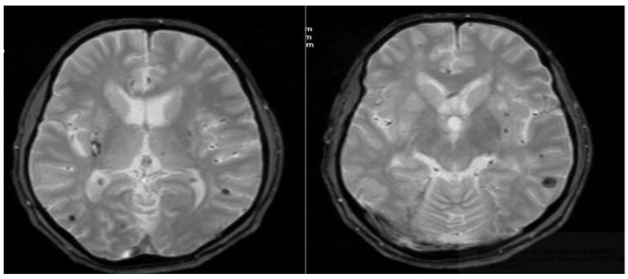

Figure 2: Chronic microhemorrhages noted in bilateral fronto-parieto-temporal region, left thalamus and lentiform nucleus.

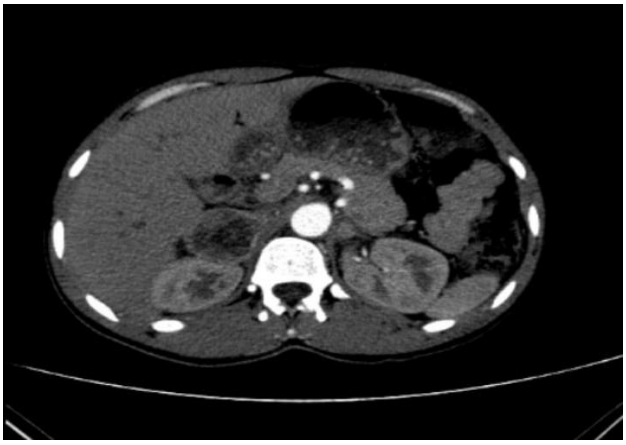

Figure 3: Well defined heterogeneously hypodense lesion in right anterior perirenal space.

2D-echocardiogram revealed generalized hypertrophy, but more in interventricular septum. Interventricular septal thickness was 21 mm and posterior wall thickness was 21 mm. There was right ventricular outflow tract obstruction with right ventricular outflow gradient of 40 mm Hg. These findings were confirmed on cardiac MRI.

Cardiac MRI revealed circumferential asymmetric left ventricular hypertrophy. There was no systolic anterior motion or left ventricular outflow tract obstruction. There was mild right ventricular outflow tract obstruction of around 42 mm.

Recent ultrasonography abdomen outside was reported as normal, however a repeat ultrasonography (USG) revealed hypoechoic lesion in right adrenal region (4×3.5×3 cm) suggestive of adrenal mass which was confirmed by contrast enhanced computed tomography (CT) scan of abdomen.

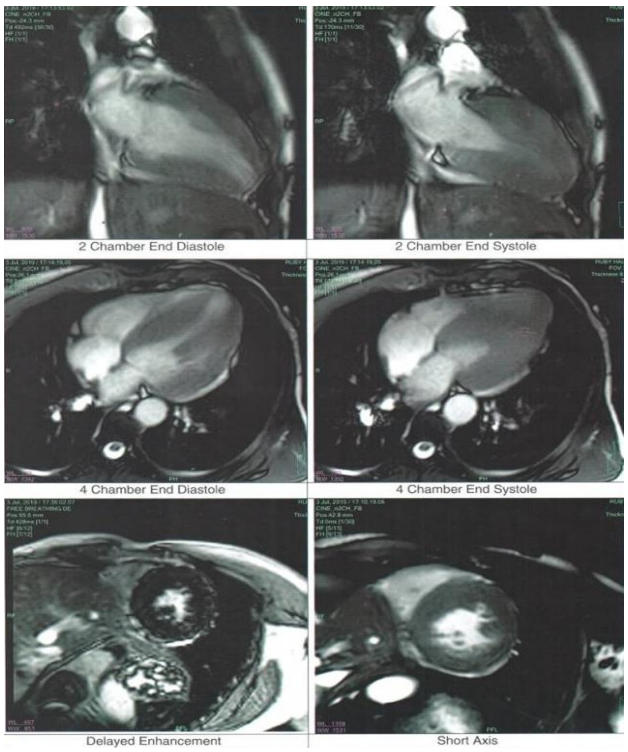

Figure 4: Circumferential asymmetric left ventricular hypertrophy with mild RVOT obstruction.

His Hba1c was 10.8%. Cerebral angiogram did not demonstrate a vascular anomaly. Further investigations revealed plasma normetanephrine value 1677 pg/ml (reference value <196 pg/ml); urine normetanephrine 5764 ug/24 hours (reference value <600 ug/24 hours) and urine metanephrine 4.48 ug/24 hours (reference value <350 ug/24 hours). Serum calcium, parathormone and calcitonin levels were within normal limits.

DOTATTATE scan revealed well defined mass in right adrenal gland with weak octreotide receptor expression/peripheral zone of metabolic activity.

Thus, he was diagnosed to have pheochromocytoma with hypertrophic asymmetrical cardiomyopathy, with

intracerebral hemorrhage, diabetes mellitus and hypertension. There were no clinical features or family history suggestive of neurofibromatosis, MEN 2A and 2B. No skin or ocular manifestations of Von Hippel-Lindau disease were found. He was initiated on tablet prazosin and later beta blocker therapy was added.

After a period of three months laparoscopic right adrenalectomy was performed under general anasthesia with removal of right adrenal gland tumor during which intraoperative blood pressure had risen to 200 mmHg. IV nitroprusside was used for intraoperative blood pressure control. Biopsy confirmed the mass to be a right adrenal pheochromocytoma.

During postoperative period and after discontinuation of antihypertensives and antidiabetic medications patient was normotensive and had normal blood sugar levels. Three months after right adrenalectomy he remained normotensive.

DISCUSSION

Pheochromocytomas are neuroendocrine tumors of adrenal medulla which arise from chromaffin cells. The classical clinical trial of paroxysmal headache, profuse sweating and palpitations is commonly a presenting feature associated with labile hypertension. But the manifestations may vary from an asymptomatic state to a life-threatening emergency and thus known as the "disease with thousand faces".[3] Pheochromocytoma can cause central nervous system (CNS) symptoms mostly by uncontrolled hypertension causing intracerebral hemorrhage, symptoms associated with metastasis in MEN 2, CNS tumors in NF 1 and with hemangioblastoma in VHL.[1] One of the rarest cause could be multiple cranial aneurysms. Stroke concurrent with pheochromocytoma has been described in the literature. Pheochromocytoma represents a very rare cause of intracerebral hemorrhage in young adults and very few cases have been reported. The mechanisms that lead to sudden increase in catecholamine release are varied and not fully understood. There are some precipitants like insufficient or compromised blood supply, direct or indirect physical stimulus to tumor, general anasthesia and certain drugs. Excess catecholamines lead to vasospasm and resultant ischemic stroke. Steroids are described in some case reports as precipitants of pheochromocytoma crisis. A patient of hemorrhagic stroke as presenting feature of pheochromocytoma during 35th gestational week is reported. Amongst a series of patients having intracerebral hemorrhage, 6 patients had pheochromocytomas, 3 had paragangliomas and one had both pheochromocytoma and paraganglioma.[3] The likely explanation of intracerebral hemorrhage in our patient is long standing uncontrolled hypertension because of significant overproduction and intermittent release of inappropriately high levels of catecholamines.

Hypertension is the most common presentation of pheochromocytoma which can be sustained or paroxysmal. Blood pressure is normal in less than 20 % patients.[5] Cerebrovascular autoregulation may get overwhelmed by excess catecholamine released leading to hypertensive encephalopathy. Beta blockers and glucocorticoids should not be used when treating a young hypertensive patient with stroke until pheochromocytoma has been ruled out as this may precipitate a pheochromocytoma multisystem crisis.

Catecholamine induced cardiomyopathy in the setting of pheochromocytomas is an unusual clinical entity. Earlier studies have reported left ventricular dysfunction in around 10% of subjects with pheochromocytoma. Catecholamine induced vasoconstriction, direct toxic effects of byproducts of catecholamine degradation and direct receptor mediated mechanisms are thought to contribute to cardiomyopathy in subjects of pheochromocytoma. There is an established association with pheochromocytoma and left ventricular hypertrophy, dilated cardiomyopathy and myocarditis due to catecholamine surge but there exist only a small number of reports of pheochromocytoma simulating hypertrophic cardiomyopathy.[2]

Patients with pheochromocytoma are known to have various cardiac compensation, including arrhythmias, heart failure, myocardial infarction, QT prolongation and cardiomyopathy. Different types of cardiomyopathies have been described and it has been proposed that chronic or acute catecholamine intoxication may lead to structural myocardial alterations.[2] Literature review confirms stress cardiomyopathy and more chronic catecholaminergic cardiomyopathies. Catecholaminergic cardiomyopathy group is a more heterogeneous group which includes mainly dilated or non-obstructive hypertrophic cardiomyopathies.

In fact, the diagnosis of pheochromocytoma should invariably lead to cardiac imaging (echocardiogram or MRI) in order to detect a potential silent cardiomyopathy, to improve perioperative management and to shorten the delay in introducing heart failure specific drugs. Catecholamine induced cardiomyopathy is usually defined as reversible left ventricular dysfunction without evidence of obstructive coronary artery disease. Histopathological features described are contraction band necrosis, fibrosis, neutrophil infiltration and a somewhat similar picture as seen in patients of cocaine abuse.[5] Treatment of pheochromocytoma associated cardiomyopathy is usually curative surgery, resection of catecholamine producing tumor which may lead to partial recovery of cardiomyopathy.

30% of pheochromocytoma patients have different forms of catecholamine induced cardiomyopathies but hypertrophic cardiomyopathy is the rarest and hypertrophic cardiomyopathy with right ventricular

outflow tract obstruction is again rare and challenging to manage.

CONCLUSION

In conclusion, this patient and review of similar rare cases, illustrates the importance of early recognition of characteristic symptoms of catecholamine excess in young patients of hypertension.

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