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Case Report

Pheochromocytoma presenting as intra-cerebral hemorrhage in a young male

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ABSTRACT

A male in his late teens presented with sudden onset left-sided hemiparesis and right-sided facial weakness. The patient had a history of persistent pulsatile headache for 1 year with the blurring of vision. He also had a history of diaphoresis and palpitations. The patient was diagnosed as a case of hypertension 1 year back. On examination, Right-sided upper motor neuron type facial palsy was present, and power was 0/5 in the left upper and lower limbs; BP was 220/120 mm Hg and was controlled using prazosin and nifedipine. A non-contrast computed-tomography scan (NCCT) of the brain revealed an intracerebral hemorrhage in the right ganglio-capsular region. Abdominal CT scan findings revealed a right suprarenal mass. 24-hour urinary normetanephrine was elevated, suggesting a diagnosis of pheochromocytoma. The surgical resection of the mass was delayed as the patient had developed Dengue shock syndrome, and he died of multiple organ dysfunction syndrome.

Keywords: Pheochromocytoma, Intra-cerebral hemorrhage, Adolescent health

INTRODUCTION

Pheochromocytomas are catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla. Although pheochromocytomas may occur at any age, they are most common in the fourth to fifth decade and are equally common in males and females.[1] The symptoms of pheochromocytomas are caused by tumoral hyper-secretion of one or combinations of the following catecholamines: norepinephrine, epinephrine, and dopamine; increased central sympathetic activity may also contribute.[2] Our case is an adolescent who presents with intra-cerebral hemorrhage, which is quite an unusual presentation at such a young age. Genetic screening for mutations should be done in patients with early presentation of pheochromocytoma. Early detection and management of the disease helps to reduce the morbidity and mortality in such patients.

CASE REPORT

A male in his late teens presented with sudden onset left-sided hemiparesis and right-sided facial weakness. The patient had a history of persistent headache for one year, localized to the bilateral frontotemporal region, and was pulsatile in nature. Headache was associated with blurring of vision and was relieved on vasograin (caffeine, ergotamine, paracetamol, and prochlorperazine). There was no diurnal variation of headache, photophobia, or aura. He had a history of diffuse diaphoresis, especially in summer, but to a lesser degree in winter. There was a history of palpitations on less than normal physical activity. There was no history of tremors. There was no significant family history.

The patient was diagnosed as a case of hypertension 1 year back, and antihypertensives were initiated in view of an elevated recording of BP but without evaluation of the

cause. The patient took medication for 1.5 months but was non-compliant after that. The patient was also diagnosed as a case of type 1 diabetes mellitus one year back. He had a history of polydypsia, polyuria, and weight loss. He was initiated on inj. huminsulin (30/70).

At the time of admission, right-sided facial drooping was present, and right-sided Frontalis was intact, suggesting upper motor neuron type facial palsy. Power in left upper and lower limbs was 0/5. His supine BP 180/100 mmHg with serial recording of 220/120 mmHg with heart rate of 100 beats/min. Inj. Labetalol administered to patient, but serial recordings of BP after 15 and 30 min persistently elevated. The BP then controlled using nitroglycerine, but BP would rise to >200/100 mmHg on its discontinuation. Use of Prazosin along with nifedipine resulted in his BP getting controlled to the levels of 170/90 mmHg with serial recordings on days 3 and 4 below 150/90 mmHg.

Investigations

A non-contrast computed-tomography scan (NCCT) of the brain revealed an intracerebral hemorrhage in the right gangliocapsular region. CT Angiography of the brain was done to rule out an aneurysmal bleed and revealed no significant abnormality.

Table 1: Laboratory investigations.

Parameters	Value
Electrolytes	
S. sodium (mmol/l)	129.4
S. potassium (mmol/l)	4.61
S. ionic calcium (mmol/l)	4.36
Hemogram	
Hemoglobin (g/dl)	14.69
Total leucocyte count (cells/mm^3)	11090
Neutrophils (%)	70
Lymphocytes (%)	26
Eosinophils (%)	2
Monocyte (%)	2
Platelet count (Lac cells/mm^3)	2.80
Mean platelet volume (fL)	13.94
Total RBCs (Million cells/uL)	6.17
Mean corpuscular volume (fL)	84.94
Mean corpuscular haemoglobin (pg)	23.81
Mean corpuscular Hb concentration (g/dl)	28.03
Red cell distribution width (%)	15.85
Hematocrit (%)	52.41
Plateletcrit (%)	0.3752
Platelet distribution width (%)	21.09
Renal function test	
S. Urea (mg/dl)	60.5
Liver function test	
S. bilirubin, total (mg/dl)	0.64
S. bilirubin, direct (mg/dl)	0.38
SGOT (IU/L)	17.6
SGPT (IU/L)	13.8
S. alkaline phosphatase (IU/L)	293.4
Blood sugar	
Random plasma glucose (mg/dl)	308.9
HbA1C (%)	13.5
Hormone and immunological assay	
Fasting insulin (uIU/ml)	20.2
C-peptide (ng/ml)	1.03
S. T3 (ng/dl)	0.40
S. T4 (ug/dl)	6.57
S. Thyroid stimulating hormone (uIU/ml)	0.54
S. Calcitonin (pg/ml)	65.75
S. parathyroid hormone (pg/ml)	33.9
Urine normetanephrine (ug/24 Hrs)	3750.62
Urine metanephrine (ug/24 Hrs)	247.80

Treatment and outcome

Patient was planned for surgical resection of tumor. The surgical resection of the adrenal mass was delayed as the patient had developed a fever. On investigating the cause of the fever, the patient came out to be Dengue positive. Patient's hemodynamic parameters started worsening, and the patient developed Dengue shock syndrome. The patient died of Multiple organ dysfunction syndrome.

Differential diagnosis

A history of persistent headache with sweating and history of unevaluated hypertension raised suspicion of secondary hypertension due to hyperthyroidism or pheochromocytoma. Paradoxical episodes of hypertension with beta-blockade with persistent hypertension and headache made us suspect a rare diagnosis of pheochromocytoma.

Investigations for possible secondary causes of hypertension conducted. Abdominal USG findings suggestive of enlarged right adrenal gland with internal anechoic areas and were a big pointer in guiding further investigations. Abdominal CT scan findings suggestive of well-defined heterogeneously enhancing lesion with an internal non-enhancing necrotic area in right suprarenal fossa. Thyroid function test was normal.

Routine laboratory investigations were suggestive of erythrocytosis. Chest radiography was normal. ECG revealed left ventricular hypertrophy. Serum calcitonin raised (65.75 pg/ml; reference value 0.1 to 10.9 pg/ml), and serum calcium and PTH levels were normal. 24-hour Urinary Metanephrine was 247.8 (Reference value <350 ug/24 hours), and 24-hour urinary normetanephrine was 3750.6 (Reference value <600 ug/24 hours) which suggested diagnosis of pheochromocytoma.

DISCUSSION

Pheochromocytomas are catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla. They are rare neoplasms, probably occurring in less than 0.2 percent of patients with hypertension.[3,4]

The annual incidence of pheochromocytoma is estimated to be approximately 0.8 per 100,000 person-years.[5]

Most catecholamine-secreting tumors are sporadic. However, in 40% of patient's disease occurs as a part of familial pheochromocytoma, which is more likely to be bilateral adrenal pheochromocytomas. Hereditary catecholamine-secreting tumors typically present at younger age than sporadic neoplasms.[6] Von Hippel-Lindau syndrome, multiple endocrine neoplasia type 2 (MEN2), and less commonly, neurofibromatosis type 1 (NF1) are some familial disorders associated with adrenal pheochromocytoma. Younger age, multifocal tumors, and extra-adrenal tumors are significantly associated with presence of mutation.[7] Approximately 95% of catecholamine-secreting tumors are in abdomen, 85-90% of which are intra adrenal (pheochromocytoma), and 5-10% are multiple.[8,9] Nearly 10-15% of catecholamine-secreting tumors are extra-adrenal and known as catecholamine-secreting paragangliomas.

Pheochromocytoma may have a myriad of presentations and is known as "disease with thousand faces".[10] Classic triad of symptoms in patients with pheochromocytoma consists of episodic headache, sweating-tachycardia.[11] However, our case presented with persistent headache. Other signs and symptoms include forceful palpitations, tremor, pallor, dyspnea, generalized weakness, visual blurring, papilledema, weight loss, polyuria, polydipsia, constipation, increased erythrocyte sedimentation rate, insulin resistance, hyper-glycemia, leukocytosis, panic attack-type symptoms (particularly in due to over-production of erythron-poietin.[2,12] Pheochromocytoma should suspected in patient presenting with hypertension at young age. One of fatal presentations of pheochromocytoma is intracerebral hemorrhage.

Intracerebral hemorrhage in young is usually caused by arteriovenous malformations, cavernous angiomas/ hypertension, followed by cerebral venous thrombosis, eclampsia and sympathomimetic drug. Pheochromocytomas are very rare causes of intracerebral hemorrhage.[13] On review of literature, Pekic et al summarized all cases of pheochromocytoma in the table. Post-2019, 3 cases were reported (Table 2).

Table 2: Review of post-2019 case reports.

Authors and year	Sex	Age at presentation (Years)	Duration of symptoms prior diagnosis	Neurological signs and symptoms	Preoperative or intraoperative anti-hypertensive regiment
Goel et al, 2020[14]	M	33	5 months	Headache, giddiness	IV nitroprusside (Intraoperative)
Diwan et al, 2021[15]	M	35	4 years	Headache	IV nitroprusside (Intraoperative)
Salloum et al, 2022[16]	F	12	2 weeks	Headache, vomiting, papillary edema, GTCS	Alpha and beta-adrenergic block (Preop)
Our patient	M	19	1 year	Headache, sudden onset left sided hemiparesis and right sided facial weakness.	NR

The diagnosis of pheochromocytoma is made by biochemical and imaging studies. Initial biochemical test for the diagnosis of pheochromocytoma is made by measuring levels of urinary and plasma fractionated metanephrines and catecholamines in a patient with high suspicion of pheochromocytoma. In patients with low suspicion of pheochromocytoma, 24-hour urinary fractionated catecholamines and metanephrines should be done.[17] If the results are normal, no further evaluation is required except in patients being evaluated for spells. During the spells episode, testing should be repeated.

When the biochemical confirmation of the diagnosis of pheochromocytoma is made, then radiological confirmation should be done to locate the tumor. Radiologically, computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen and pelvis is carried out to localize the tumor. Imaging characteristics of pheochromocytoma are increased attenuation on nonenhanced CT (most are >20 hounsfield units [HU]), increased mass vascularity, delay in contrast medium washout, high signal intensity on T2-weighted MRI, cystic and hemorrhagic changes, variable size and maybe bilateral.[18]

Management of patients with pheochromocytoma crisis should include hemodynamic stabilization before surgery. The only indication for emergency surgery without medical stabilization for crisis patients is shock due to hemorrhagic necrosis or rupture of a pheochromocytoma, with progressive multiorgan failure.[7] Adrenal surgery can be performed by laparoscopic or open technique via transabdominal or retroperitoneal approach. Pre-excision hypertension should be controlled with a small dose of a direct-acting alpha agonist, and intra-operative hypertension could be prevented with measures including pharmacologic preparation deep plane anesthesia, short-acting opioid administration, and facilitation of surgical exposure by using the muscle relaxants. Post-operative hypotension should be controlled with fluid resuscitation and a temporary vasopressor.[19]

CONCLUSION

Pheochromocytoma must be ruled out as the cause of Intra-cerebral hemorrhage in a young patient with hypertension. Young patients with pheochromocytoma must be screened for genetic mutations. Early diagnosis and management can reduce the morbidity associated with the potentially fatal disease of pheochromocytoma.

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