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Case Report

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Occult Pheochromocytoma and Acute Ischaemic Stroke in Young Adult: Cause or Association

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Running Title Occult Pheochromocytoma in a patient of Acute Ischaemic Stroke

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ABSTRACT

Pheochromocytoma is a rare catecholamine-secreting tumours of chromaffin tissues that cause a constellation of symptoms. It is closely associated with endocrine hypertension that can be masked, sustained or paroxysmal leading to hypertensive crisis, resulting in vascular and non-vascular complications and rarely cerebral ischaemia and stroke.
A healthy 22 year old male reported with acute Right upper limb(RUL) monoplegia and Motor aphasia for five days with raised blood pressure levels. hypertonia was present, deep tendon reflexes were exaggerated in RUL and Right Plantar was extensor. General and systemic findings were nonsignificant . Routine investigations showed thrombocytosis and M.R.I. Brain was suggestive of acute infarction of Left Parieto-Temporal region. Renal doppler, Carotid Intima Media Thickness, Cerebral Angiogram, 2D-E.C.H.O. and Fundoscopy were normal. AntinuclearAntibody was negative. Contrast CT of abdomen revealed right adrenal mass suggestive of isolated Pheochromocytoma. Vanyl-Mandelic Acid was positive. Patient was stabilised and managed conservatively for 4 weeks followed by adrenalectomy and appropriate medical therapy. Patient is on regular followup and does not seem to require any antihypertensives or any other intervention.
Pheochromocytoma is a notorious tumor and a great masquerader specially in young adults. A keen eye, routine checkups and evaluation is the key to detecting and preventing its associated morbidity and mortality.

Introduction

Pheochromocytomas, also famously known as the 'great mimic', is a rare intra-adrenal tumor. It develops in the chromaffin cells of the adrenal medulla, with an annual incidence of 1-4 per million [1]. This condition causes an unregulated and excessive production of the hormones epinephrine and norepinephrine. The symptoms are highly variable and range from maintained or paroxysmal hypertension, headaches, palpitations, and sweating, to less common symptoms such as fatigue, nausea, weight loss, constipation, flushing, and fever [2]. The classic triad of ephidrosis (diaphoresis), palpitations, and headache has a reported sensitivity of 89% and specificity of 67% for pheochromocytoma. In the presence of hypertension, these figures rise to 91% and 94%, respectively.

Cerebral ischemia and stroke symptoms can also occur in patients who have pheochromocytoma, but

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these are rare. However, excessive catecholamines can directly cause cerebrovascular events [3].

Since most of their clinical signs and symptoms are derived from the actions of catecholamines secreted from the adrenal glands, adrenal pheochromocytoma induces more severe clinical signs than those observed in extra-adrenal pheochromocytoma.

Stroke in young adults is indeed reported as being uncommon, comprising 10%–15% of all stroke patients. It's even rarer for it to occur in individuals less than 25 with no predisposing conditions. To our knowledge, a case of an otherwise asymptomatic underlying and undetected pheochromocytoma presenting as an acute stroke in a healthy young adult has not been reported much.

Case Report

A 22-year-old male presented with acute onset weakness of the Right Upper Limb (RUL) and difficulty in speech over the past five days. There was no history of loss of consciousness, abnormal body movements, paresthesia, facial deviation, or difficulty in swallowing.

The patient did not report dyspnea on exertion, chest pain, palpitations, leg swelling, headache, or excessive sweating. There was no history of diabetes, hypertension, smoking, alcohol, substance abuse, or long-term medications.

On admission, the patient's B.P. was 184/110 mmHg of Hg, and all pulses were palpable with a normal rhythm.

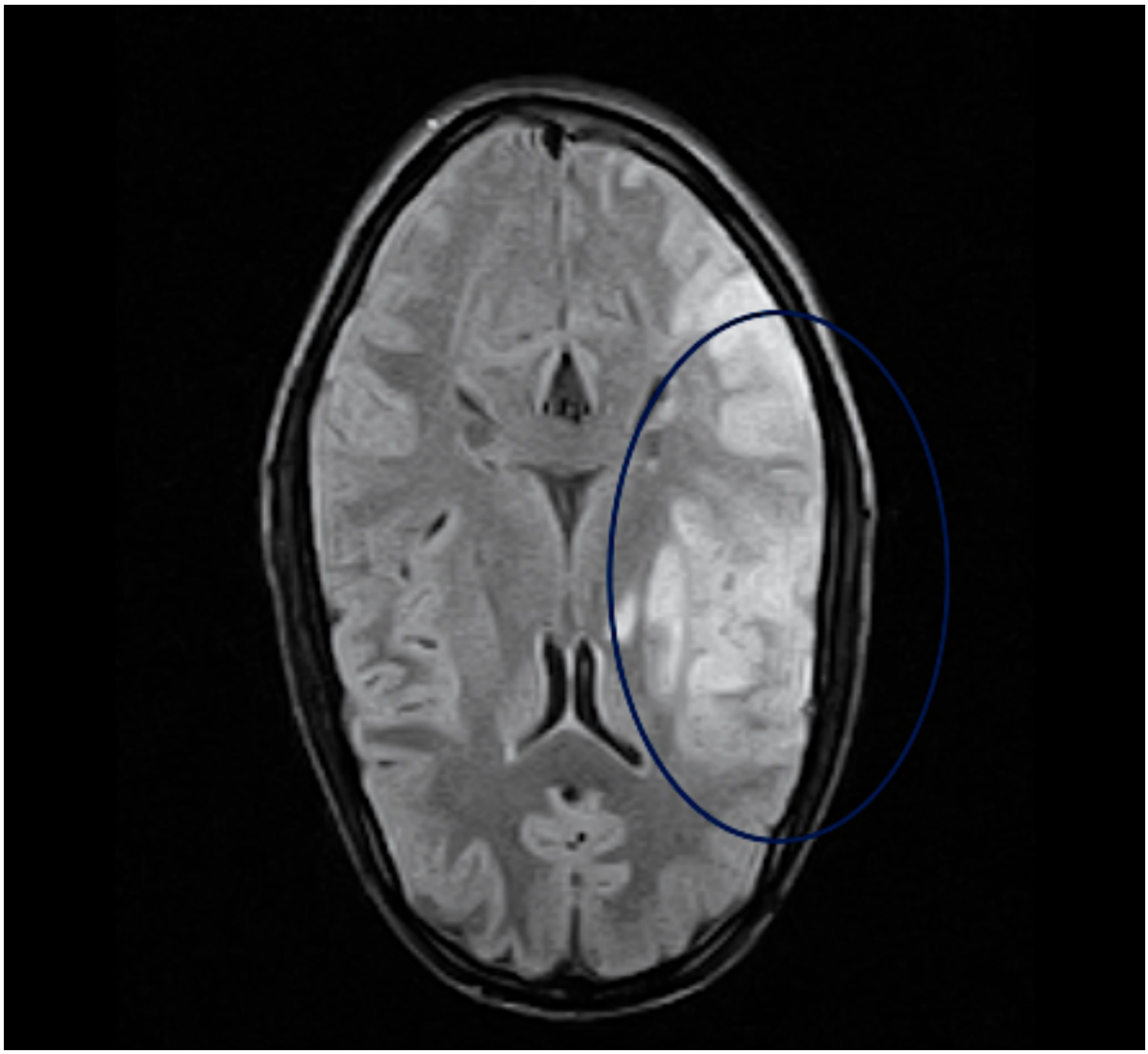

Fig. 1. Infarct in the left Parieto-Temporal Region corresponding to the area of Left Posterior Cerebral Artery.

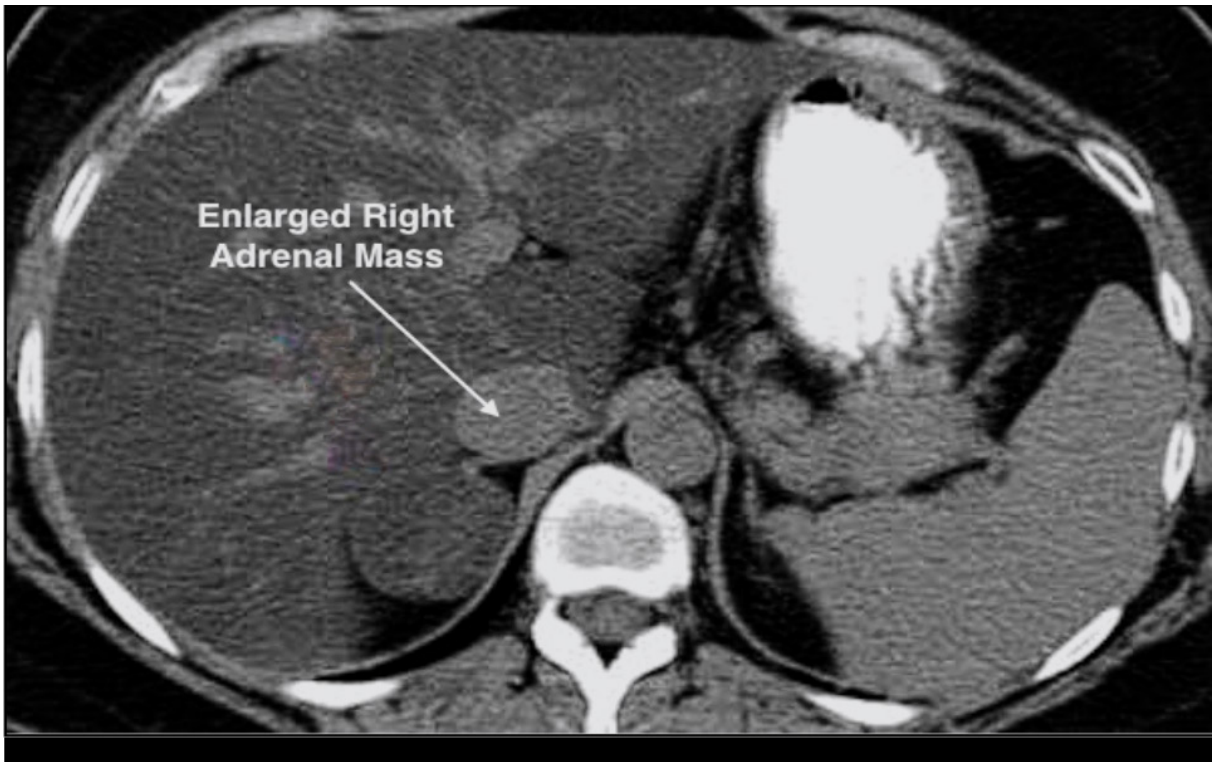

Fig. 2. Reveals an enlarged right adrenal mass, s/o Pheochromocytoma

Positive findings included motor aplasia with 0/5 power in the RUL across all joints, but normal in all other limbs. Hypertonia was present, and deep tendon reflexes were exaggerated in the RUL. The right plantar was extensor.

General and systemic findings were within normal limits, with no symptoms of meningeal irritation. The patient's BMI was 21 mg/kg^2. Routine investigations were normal, and an MRI of the brain suggested acute infarction of the left parieto-temporal region.

Renal Doppler and carotid intima media thickness were normal, and a cerebral angiogram did not reveal any vascular anomaly. A 2D E.C.H.O. and fundoscopy were immaculate.

General blood chemistry was normal, except for slightly elevated levels of platelet count with a normal coagulation and bleeding profile. The Antinuclear Antibody test was negative.

A contrast CT of the abdomen revealed a right adrenal mass suggestive of Pheochromocytoma.

The MRI of the brain showed an acute left parietal temporal infarct (Figure 1). A contrast CT of the abdomen revealed a right adrenal mass suggestive of Pheochromocytoma (Figure 2). These findings were biochemically confirmed by a raised positive Vanyl-Mandelic Acid level of 12.50 mg/24 hr urine output. The MR Angiography of cerebral vessels was normal.

There was no evidence of multiple endocrine neoplasia type 2, von Hippel-Lindau syndrome, or neurofibromatosis type 1. Thus, the patient was diagnosed with a solitary adrenal pheochromocytoma, and no signs of distant metastases were identified.

The patient was managed conservatively for 4 weeks, after which he underwent total tumorectomy. The tumor, measuring 4.0 × 4.8 cm, was resected, and histopathological findings of the resected tumor corresponded to those of pheochromocytoma without any signs of malignancy. After the operation, his systolic blood pressure was 140-150 mmHg without antihypertensive drugs, and his inotropic and other supportive therapy normalized within 2-3 days post-operation. He was discharged on the 15th postoperative day with bi-monthly follow-ups and post-stroke rehabilitation guidance. His follow-ups confirmed the improvement of non-neurological pheochromocytoma features.

At 5 months post-operation, the patient's blood

pressure (128/66 mm Hg) and metanephrine levels were normal. However, the neurological symptoms of aphasia and facial deviation, although improved, persist.

Discussion

Ischemic stroke in younger adults is far less common than that among older adults, yet the underlying pathogeneses and risk factors are more diverse. Almost all strokes in adults aged 18 to 50 years are most associated with high incidence rates of hypertension (20%), diabetes mellitus (11%), dyslipidemia (38%), and smoking (34%) [5].

The most common sign of pheochromocytoma is hypertension, found in approximately 95% of patients and related to catecholamine excess [6].

Pheochromocytomas may occur at any age, however, they are commonly presented in the fourth to fifth decade of life [7]. Their presence at an early age is a matter of concern as was in our patient.

This unique case of Stroke in young with Occult pheochromocytoma sheds light on the association between these two entities. Pheochromocytoma produces enormous amounts of catecholamines due to mutation of succinate dehydrogenase by oxidative phosphorylation deficit. However, in non-functional/ silent pheochromocytoma, metanephrine levels are elevated instead of catecholamines [9], although both can be increased during acute phases.

Complications of pheochromocytoma in a hypertensive crisis include sustained hypertension due to continuously elevated levels of catecholamine causing vasoconstriction, and orthostatic hypertension due to reduced blood volume resulting in vasoconstriction, postural tachycardia, and postural hypotension [8]. Neurological complications are hypertensive encephalopathy, hemorrhage (due to paroxysmal hypertension), and acute ischemic stroke (due to postural hypertension) [6].

Catecholamines generate moderately elevated levels of platelet count, which enhance the risk of thrombosis in the body, as was evident in this patient with no other discernible explanation for the same [9].

Patients with pheochromocytomas have a potentially curable cause of endocrine hypertension and, if undetected, pheochromocytomas confer a high risk for morbidity and mortality [10]. Young adults (less than 40 years old) are reported to have a prevalence of secondary hypertension of 30%.

Pheochromocytomas are usually benign, but may also present as or develop into a malignancy. The diagnosis can be established by measuring free plasma or fractionated urinary metanephrines (metanephrine and normetanephrine). However, predicting such behavior is notoriously difficult, and in such conditions with no previous symptoms, a sharp eye and screening play a pivotal role. The 2014 Endocrine Society clinical practice guideline recommends that all patients with pheochromocytoma paraganglioma should be engaged in shared decision making for genetic testing, however, the cost and availability for these become a difficulty.

If Pheochromocytoma is suspected, more than four times elevation of plasma metanephrines and elevated 24-h urinary fractionated metanephrines should be analyzed. If results are equivocal, a clonidine suppression test should be performed followed by a CT scan. An MRI can be done to avoid radiation or in metastatic diseases. This is followed by (123I)-MIBG (Metaiodobenzylguanidine Scintigraphy) and finally FDG-PET (fluorodeoxyglucose (FDG)-positron emission tomography (PET)) scans [11, 12].

Not much is available for medical treatment, and surgical intervention as soon as possible is the gold standard. The Endocrine Society, the American Association for Clinical Chemistry, and the European Society of Endocrinology have released clinical practice guidelines recommending preoperative blockade of hormonally functional Pheochromocytoma to prevent cardiovascular complications, along with medication for normalization of blood pressure as well as heart rate. Alpha-adrenergic blockade (i.e., doxazosin, prazosin, or terazosin) followed by a β-adrenergic blockade (i.e., propranolol, atenolol) is recommended for preoperative preparation. It is also suggested to administer a high-sodium diet and fluid intake to prevent low blood pressure after surgery [11].

The key lies in early recognition and identification of risk factors and their proper correlation.

Conclusion

Catecholamine excess states, especially endocrine hypertension, are a diagnostic challenge due to heterogeneous clinical presentation like fluctuating hypertension in young individuals, which may not attract enough clinical and laboratory attention. However, since endocrine hypertension is a reversible and preventable cause of stroke in young people, a sharp eye and timely screening can prevent its associated morbidity and mortality.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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