

# An atypical manifestation of pheochromocytoma crisis: Acute delirium

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### ABSTRACT

Pheochromocytoma is a rare neuroendocrine tumor presenting with a classical triad of symptoms. In 10% of the cases, the presentation can be atypical, and the diagnosis is often missed for several years. Most common neurological manifestations are haemorrhage, seizures, etc., but pheochromocytoma crisis presenting as delirium has been infrequently reported. We present a case of a middle-aged female who presented with hypertensive emergency and an acute confusional state. Other causes of delirium were ruled out in the patient and a timely diagnosis of pheochromocytoma was made with CT abdomen showed a large right suprarenal mass which was confirmed on <sup>123</sup>I-MIBG scan and supported by elevated plasma metanephrines. She responded to alpha and beta blockers following which her blood pressure spikes were controlled, and subsequently, her sensorium improved significantly. Patient underwent surgical resection of the tumor and was followed up after 2 weeks with her blood pressure controlled without any medications. **Conclusion:** A high degree of clinical suspicion is essential in such rare presentations of pheochromocytoma. Early diagnosis, adequate preoperative preoperative stabilization followed by a definitive surgical excision offers a complete cure to such patients.

**Keywords:** Delirium, hypertension, metaiodobenzylguanidine (I-131 MIBG) scan, neuroendocrine tumour, pheochromocytoma, plasma metanephrines

### Introduction

Pheochromocytoma is a rare catecholamine-secreting neuroendocrine tumour with an estimated annual incidence of 0.8 per 100,000 person-years<sup>[1]</sup> and is a rare cause of endocrine hypertension, representing <0.2% of the total cases in the general population. Although pheochromocytomas may occur at any age, they are commonest in the fourth to fifth decade with equal male and female preponderance.<sup>[2]</sup>

The clinician must keep in mind the possibility of endocrine emergencies which can present with seizures, delirium, or coma.

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Apart from commonly seen conditions like hypoglycaemia, diabetic ketoacidosis and hyperosmolar hyperglycaemic state, the treating physician should also consider other conditions like pheochromocytoma, thyroid storm and myxoedema, which would be life threatening when missed.<sup>[3]</sup> Prompt diagnosis and early treatment in such conditions will be life saving for the patient. We present one such scenario of a patient with pheochromocytoma coming to us with acute delirium.

Pheochromocytoma has a classic triad of symptoms consisting of episodic headache, diaphoresis and tachycardia<sup>[4]</sup> but most do not present with this. It has atypical presentations in 9%–10% of cases. Even with classical presentations, the diagnosis is often missed for several years because the clinical manifestations are diverse and may mimic other disorders like headache syndromes or panic attacks. Prompt diagnosis and treatment cure the condition, but delay in diagnosis can result in serious cardiovascular and neurological complications.

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Most common neurological manifestations are haemorrhage, seizures, etc. There have been reports of pheochromocytoma causing cerebral infarctions due to cerebral vasoconstriction.<sup>[5]</sup> However, pheochromocytoma crisis presenting as delirium has been reported in only a handful of cases. We present a case of a middle-aged female with hypertension who presented with hypertensive emergency and acute confusional state.

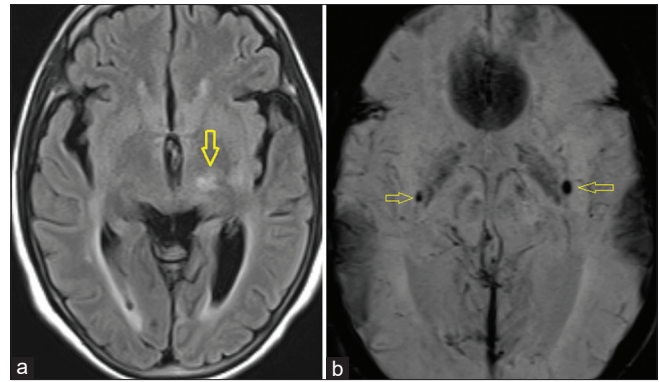
## Case Presentation

A 55-year-old female with a history of hypertension and diabetes presented with altered behaviour in the form of agitation, refusal to food and acute confusional state for the last 2 days. There was no history of fever, headache, seizures or loss of consciousness in the past. No history of substance abuse. Patient's past medical history was significant for an episode of ischemic stroke 7 years ago followed by complete recovery. The patient was on regular oral hypoglycaemic agents and antihypertensive drugs. She has had three hospital visits in last 1 year for intractable headaches; however, detailed evaluation was not done.

Upon presentation to the Emergency, the patient was conscious, but confused, and not following verbal commands. Her Glasgow Coma Scale was 13/15 (E4V4M5), pulse rate 130/min, BP 230/130 mm Hg and axillary temperature was 98.2 F. Examination showed bilaterally equal and reactive pupils and systemic examination was unremarkable. Fundus examination revealed nonproliferative diabetic retinopathy. Electrocardiogram showed findings of left ventricular hypertrophy. Rest of the blood investigations including workup for endocrine hypertension like serum electrolytes, thyroid function tests and early morning fasting serum cortisol were within normal range.

Random blood glucose obtained by finger prick method was 67 mg/dl. Keeping a possibility of hypoglycaemic encephalopathy intravenous dextrose was administered. Despite the correction of hypoglycaemia, there was no improvement in the sensorium of the patient. Considering the likelihood of hypertensive encephalopathy, we started her on intravenous labetalol along with an oral angiotensin receptor blocker and later added a diuretic. We monitored the blood pressure closely with repeated readings showing episodic spikes in blood pressure with no significant decline. Contrast imaging (MRI) of the brain [Figure 1] ruled out acute cerebrovascular accident and posterior reversible encephalopathy. Electroencephalography was normal.

Ultrasound scan of the abdomen showed a large (around 11 × 9 cm) well-encapsulated right supra renal heterogeneous lesion with vascularity. With suspicion of pheochromocytoma, we sent fasting plasma metanephrines and normetanephrines which were 80.8 and 1890 pg/ml, respectively (reference range below 195 pg/ml). Contrast-enhanced computed tomography (CECT) of the abdomen showed a well-defined heterogeneously enhancing right suprarenal mass [Figure 2] with absolute and relative washout values of 50 and 25, respectively, suggestive of pheochromocytoma. The patient was started on



**Figure 1:** (a) Axial T2W FLAIR image at the level of thalami shows small chronic infarct in the left thalamus (arrow). (b) Axial MIP susceptibility-weighted MRI image shows foci of microbleed in bilateral basal ganglia (arrows)

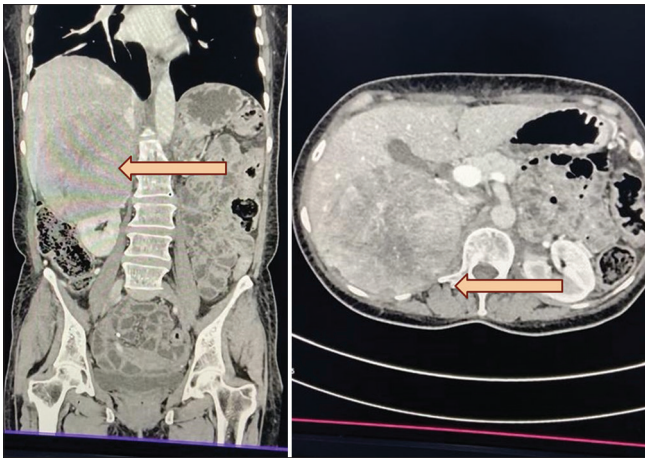
alpha- blocker (prazosin) for optimal blood pressure control. Over the next 24 h with the normalization of blood pressure spikes, her sensorium gradually improved and she comprehended normally.

The patient was planned for surgical excision of the tumour. A preoperative metaiodobenzylguanidine (I-131 MIBG) scan was performed which confirmed the diagnosis of pheochromocytoma [Figure 3]. Preoperative optimization of blood pressure was done using alpha and beta blockade. The right adrenal mass was excised [Figure 4]. During the intraoperative period, the patient had hypotension along with significant hypoglycaemia, requiring inotropes which were gradually tapered off over the next 48 h. She was discharged with normal blood pressure and no residual focal neurologic deficit. The patient was followed up after 2 weeks, and her sugar levels and blood pressure controlled without any medications.

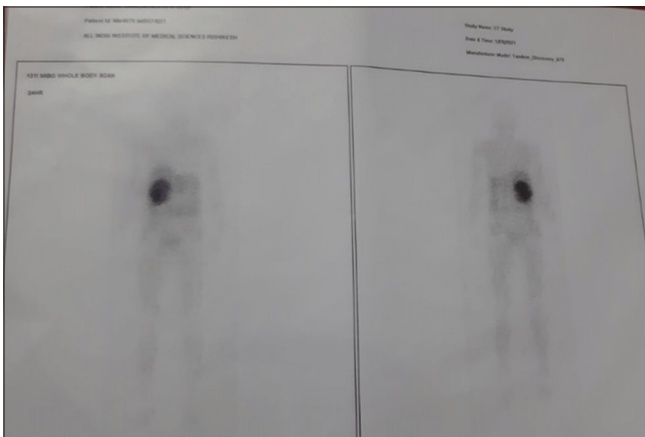
## Discussion

Pheochromocytoma can present with diverse clinical manifestations, hence also known as a ‘Great Masquerader’.<sup>[6]</sup> Neurological symptoms including thunderclap headache, seizures, strokes have been reported during acute pheochromocytoma crisis. These symptoms are mainly due to cerebral ischemia caused due to catecholamine surge during the crisis. Pheochromocytoma crisis manifesting as an acute delirium state has been very rarely reported in literature as most of the cases reported stroke as the main neurological complication, which was ruled out in our case.

In a study by Anderson *et al.*,<sup>[7]</sup> out of 28 patients who presented with pheochromocytoma crisis, 39% were associated with neurological symptoms. Severe headache was the most common neurological symptom (10 patients). Two patients sustained an ischaemic stroke. Other complications were seizures (five patients), intracerebral haemorrhage and cortical blindness. Only three patients had a clinical picture of delirium. In all the cases, blood pressure was significantly elevated during the acute crisis (range 170/90–290/130 mm Hg), which was consistent



**Figure 2:** CECT abdomen showing a well-defined hyperenhancing right suprarenal mass (arrow)



**Figure 3:** I-131 scan showing MIBG avid soft tissue density mass lesion arising from the upper pole of the right kidney. Two images are of the same patient from front and back



**Figure 4:** A large well-circumscribed mass 12 × 10 cm right suprarenal mass

with our clinical finding. Previous studies have also reported pheochromocytoma causing multiple cerebral infarctions by inducing reversible cerebral vasoconstriction.<sup>[5]</sup> In a review

of 200 cases of pheochromocytoma by Y Ando *et al.*,<sup>[8]</sup> the most common presenting symptom was headache, and the most commonly damaged organ was the heart. There have been reports of the tumour presenting with diffuse alveolar haemorrhage, acute respiratory distress syndrome or mimicking acute coronary syndrome.<sup>[9-11]</sup> Being a great masquerade, the tumour can manifest in varied ways. Our case highlights one such unique presentation as acute delirium.

Pheochromocytoma is provisionally diagnosed by elevated 24-h urine catecholamine metabolite levels. Radiologically, a CT scan with adrenal protocol is carried out to locate the adrenal tumour. If it is undetected by conventional imaging or if metastasis must be ruled out, a secondary imaging modality is used, which includes I-MIBG scan as done in our patient.

Surgical excision remains the treatment of choice.<sup>[12]</sup> If the patient presents in crisis, surgery must be deferred until the patient is hemodynamically stable which is achieved by adequate alpha and beta blockade. Our patient was operated 1 week after the presentation and was rendered normotensive thereafter.

## Conclusion

It is important for clinicians to diagnose pheochromocytomas at an early stage to prevent catastrophic complications. Not always do patients present with the classic triad of symptoms and the presentations can be atypical. Sometimes the presentation is only uncontrolled hypertension and fluctuating blood sugar levels with episodic worsening of symptoms attributing to excess catecholamines during the crisis. With advancement in diagnostics, many atypical presentations of pheochromocytoma are being reported in literature; however, the key is to extract detailed history with prudent investigations to rule out other causes of delirium and approach the case with a clinical suspicion of pheochromocytoma in such settings. Our patient responded both hemodynamically and clinically with appropriate alpha and beta blockade. With the definitive treatment being surgical, meticulous preoperative assessment is important as an intraoperative crisis can be fatal and life threatening.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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