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***Case Report***

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# Hypertensive encephalopathy as the initial manifestation of Cushing's syndrome

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## Abstract

A 65-year old lady was rushed into the accident and emergency department with a two-day history sudden onset severe generalized throbbing headache associated with restlessness, irritability, irrational talk, projectile vomiting and loss of consciousness of three hours duration. On examination, she had moon face, buffalo hump, and truncal obesity with body mass index was 45.84kg/m$^2$. Her blood pressure was 190/120 mmHg. Serum cortisol done at 0800 hrs the next day was elevated with a value of 511 ng/ml. 1 mg overnight dexamethasone was 148 ng/ml. The diagnosis of hypertension secondary to Cushing's syndrome should be strongly considered in any hypertensive obese patients regardless of age with typical 'cushingoid facies'. An assessment of serum cortisol in such patients would be beneficial in diagnosing this condition and optimizing treatment outcomes.

**Keywords:** Cushing's, Hypertension, Encephalopathy.

**INTRODUCTION**

Cushing's syndrome is the constellation of a large group of signs and symptoms resulting from prolonged pathologic hypercortisolism caused by excessive adrenocorticotropic hormone (ACTH) secretion by tumors in the pituitary gland or elsewhere, or by ACTH-independent cortisol secretion from adrenal tumors[1]. It is one of the endocrine causes of hypertension with profound cardiovascular and neurological effects. It is very rare with a prevalence of 2 to 5 cases per million[2]. It is associated with hypertension in about 80% of cases[3].

There are very few reports in the literature describing the association of Cushing's syndrome with hypertensive encephalopathy. To the best of our knowledge, there has been no such report from our environment. In this report, we describe a very rare presentation of hypertensive encephalopathy as the first presentation of Cushing's syndrome. We also highlight the importance of diagnosing secondary causes of hypertension in patients as a conventional treatment for hypertension would not be effective without recognizing and treating the underlying cause.

**CASE REPORT**

A 65-year old lady was rushed into the accident and emergency department with a two-day history sudden onset severe generalized throbbing headache associated with restlessness and loss of consciousness of three hours duration. On regaining consciousness, she had five episodes of projectile vomiting. She was also very restless, irritable and talked irrationally. There was no history of seizures, neck pain, photophobia, fever or focal limb weakness. Prior to her presentation, she had been experiencing intermittent palpitations, with easy fatigability and breathlessness on exertion. She was neither previously hypertensive nor diabetic.

On examination, she had moon facies, buffalo hump, and truncal obesity. She was conscious but extremely restless. Her body mass index was 45.84kg/m$^2$. She did not have neck stiffness or any focal neurology. She had tachycardia of 100/min with the complete irregularity of her pulse rhythm; blood pressure was 190/120 mmHg and apex beat was displaced to the sixth left intercostal space, lateral to the midclavicular line with a heave. Abdomen was distended with multiple striae. She had a firm non-tender hepatomegaly of 8 cm. The spleen was not enlarged and her kidneys were not palpable. Our initial consideration was hypertensive encephalopathy with heart disease in a morbidly obese woman to exclude

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cushing's syndrome.

Random blood sugar was 11.1 mmol/l. Fasting blood sugar and 2 hour value of the oral glucose tolerance test were 5.1mmol/l (3.3-5.5 mmol/l) and 6.8 mmol/l (<7.8 mmol/l) respectively. Serum cortisol at 0800 hrs was 511 nmol/l (60-230 nmol/l). A 1mg overnight dexamethasone suppression test had a value of 148 nmol/l (<50 nmol/l). Her fasting lipid parameters were: triglycerides-1.2 mmol/l (0.3-1.8 mmol/l); total cholesterol-5.9 mmol/l (<5.2 mmol/l); high density lipoprotein cholesterol-1.0 mmol/l (>1.2 mmol/l) and low density lipoprotein cholesterol-4.4 mmol/l (<2.6 mmol/l) respectively.

Chest radiograph showed unfolded aorta, cardiomegaly of left ventricular preponderance with significant elevation of right hemi-diagphragm. Electrocardiogram showed tachycardia of 100-150/min, first-degree heart block with prolonged PR interval of 0.24s (normal:0.12-0.20s), left axis deviation, left atrial enlargement, left ventricular hypertrophy and left bundle branch block. Abdominal ultrasound scan done revealed hepatomegaly with a normal echotexture. There was intrahepatic or extrahepatic duct dilatation. Gall bladder was of normal size but had thickened wall with multiple calculi with posterior acoustic shadowing. Other intraabdominal organs were sonographically normal. She was unable to do a brain magnetic resonance imaging due financial constraints.

She responded rapidly and remarkably to cerebral decongestion with intravenous mannitol. Her blood pressure was optimized with anti-hypertensives, digoxin was given to regularize cardiac rhythm. She was also received statins and anti-platelets. She was counseled with respect to her condition and its underlying cause with further advice on the need for further follow-up and definitive treatment. She was eventually discharged in good condition on antihypertensives and ketoconazole tablets. Ketoconazole is an imidazole antifugal agent that blunts ACTH-induced cortisol release. It also blocks glucorcorticoid synthesis in the adrenal gland[4,5]. She, however, was lost to follow-up.

**DISCUSSION**

Hypertension results from the interplay of several pathophysiological mechanisms controlling plasma volume, cardiac output and peripheral vascular resistance, all of which may be increased[6]. Glucocorticoids cause hypertension through several mechanisms: through activation of the renin-angiotensin-aldosterone system; by their intrinsic mineralocorticoid activity; by causing suppression of the vasodilatory systems and also by enhancement of vasoactive substances[7].

The clinical manifestations of Cushing's syndrome can be quite variable and are frequently mistaken, with consequently delayed diagnosis and significant morbidity and mortality. A complete history, physical examination with a very high index of suspicion enhances the pre-test likely hood of making a diagnosis of Cushing's syndrome. Patients present with a wide range of signs and symptoms, and no single symptom is necessary to the diagnosis. Many of the clinical manifestations of Cushing's syndrome are common in the general population. However, if multiple and progressive features are present (particularly worsening hypertension or diabetes), then a diagnosis of Cushing's syndrome should be entertained.

Our patient had some stigmata of Cushing's syndrome. These included moon face, buffalo hump, and abdominal striae. However, these could be misleading as these features are now common in the general population with the rising prevalence of obesity. Altered mental status is a common presentation in the emergency department, and can be caused by other endocrine disorders like diabetes mellitus and myxoedema[8]. Neurologic manifestations of Cushing's syndrome include myopathy, headache, neuropsychiatric disturbances including particularly mood disorders and cognitive impairment[9,10].

She also had features of hypertensive target organ damage as seen from her chest radiologic and electrocardiogram results. The absence of features that would point to bronchogenic carcinoma on her chest radiograph would exclude oat-cell carcinoma as the cause of her hyper-cortisolism. A chest computerized tomographic scan or magnetic resonance imaging would have been most suitable for this. One milligram overnight dexamethasone suppression test failed to suppress serum cortisol to the expected values. This procedure involves the administration of 1 mg dexamethasone between 2300 and 2400 h and blood sampling between 0800 and 0900 hours the following morning for the measurement of serum cortisol. A normal response is adequate suppression of serum cortisol to less than 50 nmol/l[11]. The presence of non-suppressible hypercortisolism is associated with a very poor prognosis[12]although therapy of the hypercortisolism may improve some of the clinical manifestations and the patient's quality of life. The diagnosis of Cushing's syndrome depends on the demonstration of increased cortisol production and failure to suppress cortisol secretion normally when dexamethasone is administered. Once the diagnosis is established, further testing is designed to ascertain the etiology. One shortfall in our management of this patient was her inability to perform brain magnetic resonance imaging due to financial constraint. This would have boosted our treatment objectives by finding and removing the cause of excess her glucocorticoids, which, in most cases of endogenous Cushing's syndrome, is achieved surgically.

**CONCLUSION**

The diagnosis of hypertension secondary to Cushing's syndrome should be strongly considered in any hypertensive obese patients regardless of age with typical 'cushingoid facies' of unknown etiology. An assessment of serum cortisol in such patients would be beneficial in diagnosing this condition and optimizing treatment outcomes. It is very important as clinicians to always identify secondary causes of hypertension and treat appropriately.

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