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Case Report

Adrenocorticotropic Hormone (ACTH) Independent Cushing's Syndrome Presenting as Hypertension in the Young: A Case Report from Kumasi, Ghana

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ABSTRACT

The endogenous cause of Cushing's syndrome is very rare with an incidence of 0.7–2.4 per million population per year. Diagnosis of this syndrome may pose a challenge on the clinician for the fact that it is rare and also shares many features with the more common condition metabolic syndrome. We present the case of a 31 year old overweight male with no known chronic disease presenting with abdominal pain, moon face, striae, acne and hypertension. A post dexamethasone suppression cortisol level was >1750 nmol/l. The ACTH levels were 1 pg/ml which was below the lower limit of the reference range. An abdominal CT scan showed a well-defined enhancing mass arising from the lateral limb of the left adrenal gland measuring 2.6 × 2.1 cm with features consistent with an adrenal adenoma. Patient was treated with eplerenone, ketoconazole, hydralazine and losartan and he is currently doing well.

Keywords: Adrenocortoco tropic hormone; Cushing's syndrome; hypertension

INTRODUCTION

Cushing's syndrome is a clinical condition caused by chronic exposure to cortisol. It is caused by either chronic exposure to exogenous or endogenous cortisol/glucocorticoids or both but more commonly from exogenous causes. The endogenous cause of Cushing's syndrome is very rare with an incidence of 0.7–2.4 per million populations per year [1-3]. Diagnosis of this syndrome may pose a challenge on the clinician for the fact that it is rare and also shares many features with the more common condition metabolic syndrome. Cushing's syndrome is clinically characterised by moon face, weight gain, buffalo humps, truncal obesity, striae, acne, alopecia, hypertension, glucose intolerance, proximal muscle weakness, decreased libido and depression or psychosis. The condition is generally more common in females than in males with a ratio of 3:1 respectively [3].

Cushing's syndrome can be classified into 2 groups namely: ACTH dependent and ACTH independent. 15%–20% of endogenous Cushing's syndrome in adults is due to ACTH independent causes of which 90% is due to unilateral adrenal tumour [4]. Among the adrenal tumours, adrenal adenoma is the most common constituting about 60% of all cases [2,5]. The remaining 40% is caused by adrenocortical carcinoma which is often an aggressive tumor [5]. Detection of ACTH independent causes of Cushing's syndrome has markedly improved with the invent of imaging modalities such as Computed Tomography (CT scan) and Magnetic Resonance Imaging (MRI) [6]. Thus in delineating the endogenous causes of Cushing's syndrome these imaging modalities may be indispensable. We present the case of young male with ACTH independent Cushing's syndrome who presented with secondary hypertension.

Case study

We present the case of a 31 year old overweight male with no known chronic disease who presented with intermittent abdominal pain of 3 months duration associated with heart burns. On examination his BP=149/109 mmhg, BMI=28.1 kg/m^2, had moon face, striae and acne. There was tenderness in the epigastrum. Chest was clinically clear with normal heart sounds. Initial labs showed normal WBC count (8.46 × 103/ul)

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and absolute neutrophil count but increased neutrophil percentage (72.6%, ref=37%-72%), high cholesterol 5.61 mmol/l (ref 3.90-5.20 mmol/l), HbA1c=6.1%, normal renal function test and liver function test. An initial impression of systemic hypertension, gastroesophageal reflux disease and dyslipidemia was made with differential of Cushing's syndrome. He was put on tab losartan 100 mg, tab artorvastatin 40 mg nocte, cap omeprazole 20 mg bd, syrup antacid 10 mls.

Serum cortisol, Na, K, Cl were then requested for review in 1 month. On review patient was generally stable with no complaints of abdominal pains. BP=120/90 mm Hg, Na=143 mmol/l, K=4.0 mmol/l, serum cortisol=852 nmol/l, (elevated). He was then admitted for the dexamethasone suppression test which was done with IV dexamethasone 8 mg at 11 pm. The serum cortisol of the patient was repeated the next day at 8 am which showed a post suppression cortisol level of >1750 nmol/l. Serum ACTH levels was 1 pg/ml which was below the lower limit as indicated in Figure 3 . An abdominal CT scan showed a well-defined enhancing mass arising from the lateral limb of the left adrenal gland measuring 2.6 × 2.1 cm with features consistent with an adrenal adenoma.

The patient was kept on eplerenone 20 mg, tab hydralazine 25 mg, tab ketoconazole 200 mg bd × 30. The urology team was informed to plan the definitive treatment which is the resection of the tumour (Figures 1-3).

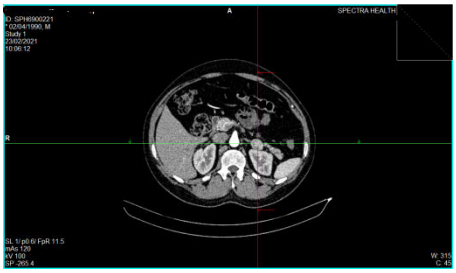
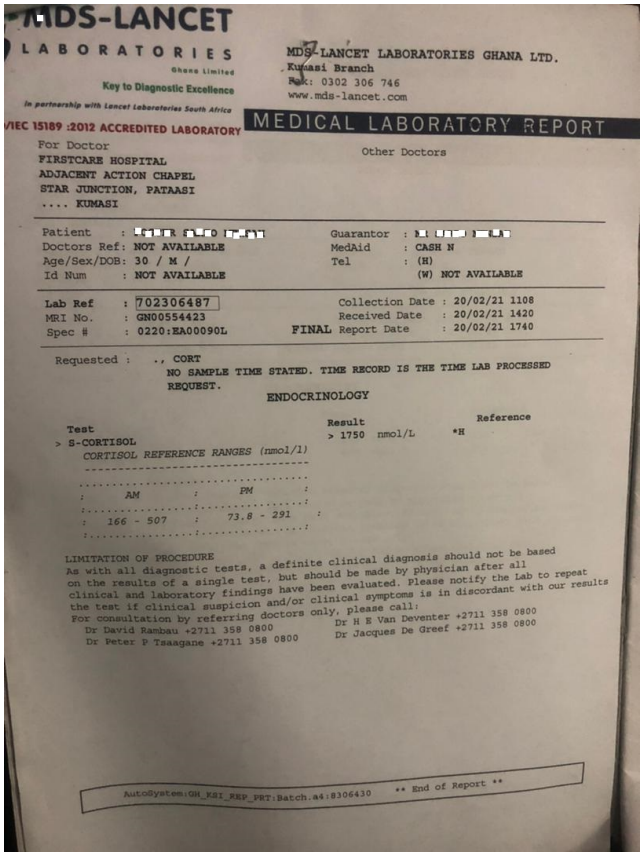


Figure 1: Indicates the Abdominal CT scan image showing a well-defined enhancing mass arising from the lateral limb of the left adrenal gland measuring 2.6 × 2.1 cm with features consistent with an adrenal adenoma.



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Patient : [redacted]
Doctors Ref: NOT AVAILABLE
Age/Sex/DOB: 30 / M /
Id Num : NOT AVAILABLE

Guarantor : [redacted]
MedAid : CASH N
Tel : (H)
(W) NOT AVAILABLE

Lab Ref : 702306487
MRI No. : GN00554423
Spec # : 0220:EA00090L

Collection Date : 20/02/21 1108
Received Date : 20/02/21 1420
FINAL Report Date : 20/02/21 1740

Requested : ., CORT
NO SAMPLE TIME STATED. TIME RECORD IS THE TIME LAB PROCESSED REQUEST.

ENDOCRINOLOGY

Test	Result	Reference
> S-CORTISOL	> 1750 nmol/L	*H

CORTISOL REFERENCE RANGES (nmol/l)

AM	PM
166 - 507	73.8 - 291

LIMITATION OF PROCEDURE
As with all diagnostic tests, a definite clinical diagnosis should not be based on the results of a single test, but should be made by physician after all clinical and laboratory findings have been evaluated. Please notify the Lab to repeat the test if clinical suspicion and/or clinical symptoms is in discordant with our results
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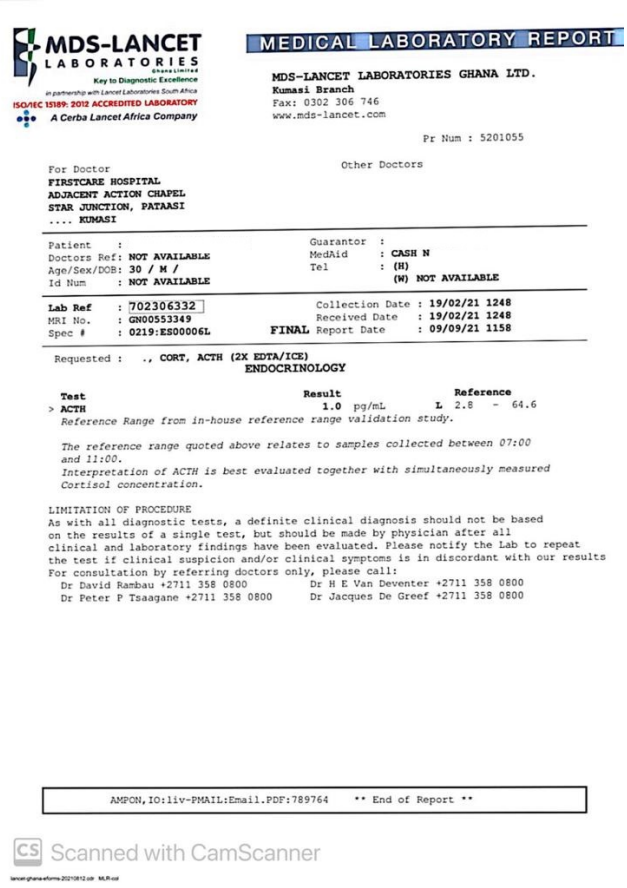
AutoSystem:GH_KSI_REP_PRT:Batch.a4:8306430 ** End of Report **

Figure 2: Shows image indicating the cortisol levels at 11 pm after dexamethasone suppression test.



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Doctors Ref: NOT AVAILABLE
Age/Sex/DOB: 30 / M /
Id Num : NOT AVAILABLE

Guarantor :
MedAid : CASH N
Tel : (H)
(W) NOT AVAILABLE

Lab Ref : 702306332
MRI No. : GN00553349
Spec # : 0219:ES00006L

Collection Date : 19/02/21 1248
Received Date : 19/02/21 1248
FINAL Report Date : 09/09/21 1158

Requested : ., CORT, ACTH (2X EDTA/ICE)

ENDOCRINOLOGY

Test	Result		Reference
> ACTH	1.0 pg/mL	L	2.8 - 64.6

Reference Range from in-house reference range validation study.

The reference range quoted above relates to samples collected between 07:00 and 11:00.
Interpretation of ACTH is best evaluated together with simultaneously measured Cortisol concentration.

LIMITATION OF PROCEDURE
As with all diagnostic tests, a definite clinical diagnosis should not be based on the results of a single test, but should be made by physician after all clinical and laboratory findings have been evaluated. Please notify the Lab to repeat the test if clinical suspicion and/or clinical symptoms is in discordant with our results
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AMPON,IO:liv-PMAIL:Email.PDF:789764 ** End of Report **

Figure 3: Shows Adreno Cortoco Tropic Hormone (ACTH) levels of patient.

DISCUSSION

The presentation of Cushing's syndrome vary depending on the duration and severity of the exposure of the patient to increased cortisol levels and as such there no one pathognomonic presentation for this condition [7]. Moreover the condition shares many characteristics with the more common condition, metabolic syndrome. Patients with long standing exposure may develop many characteristics of the syndrome while patients at the early stage of the disease may not show any symptoms or signs. Due to rarity of the condition the diagnosis may require a high index of suspicion especially at the early stages. Cushing's syndrome should be suspected in every individual who chronically uses exogenous steroids. In this case report the patient was an overweight young man who presented with high blood pressure (149/109 mmHg). The diagnosis of Cushing's syndrome was initially suspected based on the presentation of hypertension, moon face and striae. The findings of moon face, striae, acne may point to long standing duration or excessive exposure of the patient to increased cortisol levels.

Physiologic cortisol levels are under the control of our biologic clock and thus varies during the day and night. Cortisol levels are high in the morning usually about 30 mins upon waking up and decline steadily in the course of the day till bed time reaching its lowest levels around midnight [8]. This diurnal variation is disrupted in Cushing's syndrome. It is important to consider this diurnal variation when taking samples for cortisol levels and the timing of such samples must be indicated on the laboratory request to enable good interpretation of results. Dexamethasone Suppression Test (DST) is used in the evaluation of endogenous Cushing Syndrome (CS) by giving exogenous corticosteroid and evaluating the level of suppression of the Hypothalamic-Pituitary-Adrenal (HPA) axis [9]. ACTH secreting tumours and adrenal tumours are not affected by this suppression and so the cortisol levels are not altered. In this patient, his initial serum cortisol level was 852 nmol/l which was markedly elevated above the upper limit. This prompted us to the dexamethasone suppression test.

A high dose dexamethasone suppression test with 8 mg dexamethasone was administered around 11 pm. Serum cortisol levels obtained around 8 am in the morning revealed a cortisol level of >1750 nmol/l. Our diagnosis of Cushing's syndrome was certain at this stage but the underlying cause of the condition remained undetermined. The ACTH levels was 1 pg/ml which was below the lower limit of the reference range. Abdominal CT scan revealed an adrenal Adenoma thereby ascertaining the cause of Cushing's syndrome in this patient. Unilateral adenoma is the most common cause of ACTH independent Cushing's syndrome [4].

Prompt treatment of Cushing's syndrome and comorbidities are essential to prevent complications and reduce mortality. Complications include metabolic syndrome, musculoskeletal disorders such as osteoporosis, fractures and myopathy, neuropsychiatric and reproductive function impairments [10].

The treatment of choice of Cushing's syndrome due to a tumour is surgical removal. Medical management may be instituted before surgery in patients with comorbidities and/or severe hyper cortisolism [11]. Our patient was initially started on losartan, atorvastatin and omeprazole with addition of ketoconazole, eplerenone and hydralazine when Cushing's syndrome was confirmed.

Ketoconazole is a potent inhibitor of steroido genesis *via* cytochrome P450 inhibition which was approved for treatment of endogenous Cushing syndrome by the European medications agency in 2014 [12]. It has potential benefits in dyslipidemia due to its inhibition of cholesterol synthesis [11]. A systematic review and meta-analysis by Broersen et al. [13] showed normalization of hyper cortisolism in up to 71% of patients with Cushing's syndrome of all etiologies treated with ketoconazole [13]. Treatment is recommended at 400-600 mg/day in two or three divided doses at initiation with maintenance dosage titrated based on cortisol level monitoring [12]. Other current and novel therapies include metyrapone, etomidate, mifepristone, osilodrostat and pasireotide [12]. Glucocorticoids are associated with activation of the renin angiotensin aldosterone system which leads to the hypertension usually seen in Cushing's syndrome. Blockade of the renin angiotensin system with ACE-I, ARBs and mineralocorticoid antagonist such as eplerenone and spironolactone have been shown to be effective BP normalization agents in Cushing's syndrome. More than one agent is usually required [14].

CONCLUSION

Not with standing the rarity of Cushing's syndrome, the diagnosis of the condition should be suspected in any obese or overweight young patient presenting with hypertension. Clinicians should have high index of suspicion for this condition to enable early detection and prompt management.

Funding

There was no funding for this case study.

Conflict of Interest

Authors declare no conflict of interest.

Informed Consent

Informed consent was obtained from the patient. Patient's data is available for verification.

Author's Contribution

Prince Yaw Boahene, Solomon Gyabaah, Prince Addo Ameyaw, Lisa Annabelle Agyei- Mensah: drafting and revising the article, concept and design. Prince Yaw Boahene, Solomon Gyabaah: Final revision of the article, concept and design.

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