Case Report

# Primary Hyperaldosteronism in a 58-Year-Old Nigerian Man with Difficult to Treat Hypertension

**Uduagbamen PK[1,2], Ogunmola MI[2], Falana TE[2], Alao OJ[2]**

[1]Division of Nephrology and Hypertension, Department of Internal Medicine, Babcock University, [2]Division of Nephrology and Hypertension, Department of Internal Medicine, Babcock University Teaching Hospital, Ilisan-Remo, Nigeria

## ABSTRACT

Conns syndrome is a known cause of secondary hypertension. It is not commonly reported in low-income nations like Nigeria and many cases could be wrongly managed as primary hypertension due to low index of suspicion on the part of the clinicians, inadequate diagnostic tests or non-availability of funds for these tests. This could lead to poor treatment outcome. We present the case management of the patient and reviewed the literature. A 58-year-old male with history of poor blood pressure control, recurrent body weakness and palpitation was referred to the nephrology unit for further management. Examination revealed thickened arterial wall, elevated blood pressure, an enlarged heart and a fourth heart sound. The serum potassium was low, this was corrected. Laboratory investigations revealed elevated urine potassium and serum aldosterone-to-renin ratio. Ultrasound scan showed normal-sized echogenic kidneys, electrocardiogram showed left ventricular hypertrophy (LVH) and echocardiogram showed LVH, mild left ventricular dilatation and mild aortic valve regurgitation. Computed tomography revealed bilaterally enlarged adrenal glands. He was managed for Conns syndrome and responded well to salt restriction, eplerenone and other BP-lowering drugs. This case confirms that with a very high index of suspicion and the availability of specific laboratory tests and advance radiological investigations, more cases of Conns would be diagnosed and patients are more likely to receive better treatment with more favourable outcome.

**Key words:** Adrenal hyperplasia, aldosterone-to-renin ratio, Conns, hypokalaemia, left ventricular hypertrophy, metabolic alkalosis

**How to cite this article:** Uduagbamen PK, Ogunmola MI, Falana TE, Alao OJ. Primary hyperaldosteronism in a 58-year-old Nigerian man with difficult to treat hypertension. Niger J Health Sci 2020;20:64-8.

## INTRODUCTION

Conn syndrome is a cause of secondary hypertension which could be difficult to treat. It results from excessive aldosterone production from the adrenal glands leading to heightened sodium and water absorption and potassium secretion (loss) through its actions on the sodium–potassium exchanger at the late distal tubules.[1] Hypokalaemia, metabolic alkalosis often with supranormal sodium levels and elevated urinary potassium are common in Conns.[2] The risk of progression from hypertension to chronic kidney disease (CKD) could be high in Conns due to aldosterone's role in renal tissue fibrosis.[3]

Conns is well reported, accounting for 10%–15% of cases of hypertension.[1] However, in Nigeria and in many low-income nations, it is less commonly reported due majorly to the low index of suspicion among the clinicians as reported by Uchenna and Unachukwu.[4] The non-availability and high cost of specific tests needed for diagnostic precision also contribute to this diagnostic challenge. We present a 58-year-old male with bilateral adrenal hyperplasia and difficult to treat hypertension.

## CASE REPORT

A 58-year-old male, known hypertensive for 25 years, was referred to the nephrology unit on account of poor blood pressure control, recurrent palpitation, headache, body weakness and hypokalaemia. He also had nocturia, polyuria and had been treated with amlodipine, hydrochlorothiazide,

**Submitted:** 17-Apr-2020 **Revised:** 30-May-2020
**Accepted:** 02-Jul-2020 **Published:** 22-Sep-2022

Access this article online

Quick Response Code:

Website: www.chs-journal.com

DOI: 10.4103/njhs.njhs_6_20

**Address for correspondence:** Dr. Uduagbamen PK, Division of Nephrology and Hypertension, Department of Internal Medicine, Babcock University/Babcock University Teaching Hospital, Ilisan-Remo, Nigeria.
E-Mail: petr.uduagbamen@gmail.com

ramipril, atenolol, spironolactone and aspirin in various combinations since diagnosis. His father was also hypertensive.

He was calm, not pale, not cyanosed and had no pedal oedema. He had gynaecomastia but no anterior neck swelling. His body mass index was 34.7 kg/m$^2$, pulse was 90/min with thickened arterial wall and blood pressure was 158/96 mmHg. His precordium was hyperactive and cardiac apex was displaced to the left, heaving and a fourth heart sound was heard.

Assessment – Hypertensive heart disease. To rule out secondary causes like Conns syndrome.

He had grade 2 hypertensive retinopathy. Urinalysis showed specific gravity of 1.010 and PH of 7.0. Serum potassium was 2.5 mmol (3.5–5.0). His potassium deficit was calculated to be 36 mmol/l. Hydrochlorothiazide was stopped and potassium was corrected with tablet potassium chloride 600 mg thrice daily for 1 week, in addition to increasing the intake of high potassium containing food. He was commenced on tablet amlodipine 10 mg daily, tablet ramipril 10 mg daily and tablet atenolol 100 mg daily. The serum potassium rose up to 4 mmol. Urinary and blood findings on admission and after correcting hypokalaemia are shown in Tables I and II. Renal ultrasound scan showed echogenic, normal-sized kidneys. As shown in Table III, with serum potassium at 4.0 mmol/l, the two point (blood sample for aldosterone and plasma renin were taken at rest in supine position and after 1 h of standing erect) renin–aldosterone system assessment showed elevated aldosterone-to-renin ratio, 64.1(<20) and 83.6 (<20), respectively. Computed tomography scan in Figure 1 shows bilateral smooth and enlarged adrenal glands (right – 11.3 mm [6.1 mm] and left – 14.1 mm [7.6 mm]). The electrocardiogram (ECG) in Figure 2 shows left ventricular hypertrophy (LVH), whereas echocardiogram in Figure 3 shows LVH with high-voltage complexes. Ejection fraction was 61% and the left ventricular internal diastolic diameter was 5.2 cm (4.2–5.5 cm), mild aortic regurgitation was present, but no abnormal wall motion nor intracardiac thrombus.

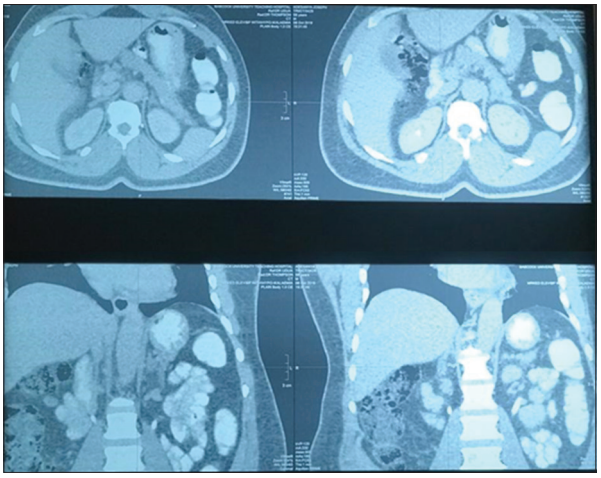

**Figure 1:** Computed tomography of the adrenal glands of a 58-year-old male with bilateral smooth glandular enlargement: Upper panel showing smooth right gland with width of 11.3 mm (6.1 mm) and a smooth left gland with width of 14.1 mm (7.6 mm). Lower panel shows width of the medial limb of the right gland (3.3 mm) and width of the lateral limb of the right gland (3.3 mm), width of the medial limb of the left gland (3.8 mm) and width of the lateral limb of the left gland (3.7)

### Electrocardiogram showed left ventricular hypertrophy with left axis deviation

Tablet spironolactone was stopped and he was commenced on tablets eplerenone 25 mg daily, nifedipine 60 mg in the morning and 30 mg evening, indapamide 1.5 mg daily, rosuvastatin 10 mg nocte and clopidogrel 75 mg daily. His daily urine output throughout admission ranged between 1.6 and 2.2 l. He was counselled on lifestyle changes, intake of high potassium containing food and was discharged with BP – 132/82 mmHg and potassium – 4.2 mmol/l.

When reviewed a week later, he had no complaints, BP was 150/88 mmHg and potassium was 3.7 mmol/l. Tablet eplerenone was increased to 50 mg daily. Two weeks later, blood pressure was 124/76 mmHg and K – 4.0 mmol/l. His clinical parameters and serum potassium have remained normal in subsequent visits.

## DISCUSSION

We reported a 58-year-old male with difficult to treat hypertension and recurrent hypokalaemia. He had been managed for primary hypertension since diagnosis. The poor blood pressure control coupled with the recurrent hypokalaemia triggered a search for an underlying cause. His symptoms which were recurrent could be attributed to elevated serum aldosterone, the body main mineralocorticoid hormone, produced from the zona glomerulosa of the adrenal cortex that mediates sodium absorption and potassium loss.[1] In Conns, high normal to supranormal plasma sodium, elevated BP, low potassium and metabolic alkalosis are classical as was seen in the index case.[2] Unilateral disease is usually an adenoma, whereas bilateral disease commonly shows bilateral enlargement (seen in this index case) or could be from genetic changes (familial hyperaldosteronism Types 1, 2 and 3). Rare malignant adrenal tumour can also be the source of aldosterone production. A case of glucocorticoid remediable hypertension (GRH) which is a monogenic form of hypertension secondary to familial hyperaldosteronism type 1 was reported by Chikladze et al. in a Russian woman.[5]

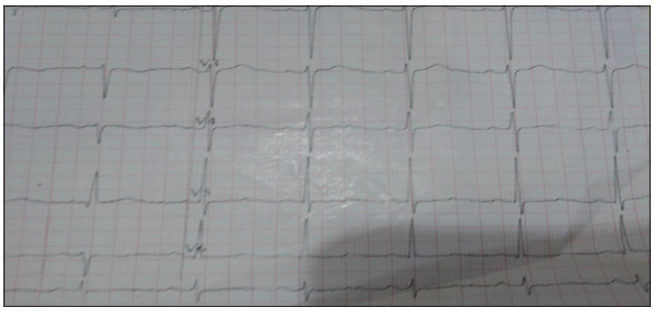

**Figure 2:** Echocardiogram showing heart rate, 63/min, high-voltage complexes, left ventricular hypertrophy and U wave

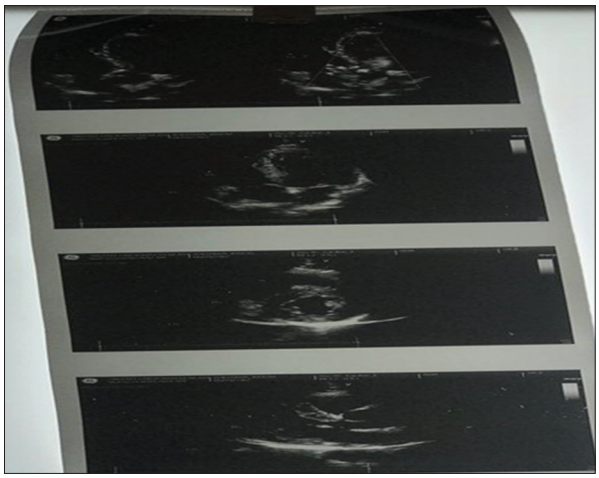

**Figure 3:** Echocardiogram showing hypertensive heart disease with left ventricular hypertrophy, mild aortic regurgitation. The ejection fraction was 61% and the left ventricular internal diastolic diameter was 5.2 cm. There were plaques on the aortic valve leaflets, no abnormal wall motion and no intramural thrombus was detected

Majority are unilateral and small. Extraadrenal cause is commonly associated with bilateral cortical nodular hyperplasia (BCNH).[4] Hypertension from bilateral cortical disease, as seen in the index case, could be difficult to treat and to differentiate from volume-dependent hypertension found in Africans. Furthermore, bilateral disease tends to have lower serum potassium and aldosterone with lesser radiological features compared to adenoma. BCNH make up about 70%–80% of Conns population and 10% of secondary hypertension and it is found in 6%–12% of the US population. Conns syndrome is the most common endocrine cause of hypertension, more common in women and between 30 and 50 years.[6] Similar figures are seen in Asian and European nations, but reported cases in Nigeria like most low-income countries are few.[4]

Recurrent weakness, as seen in the index case, is very common in Conns and could be due to low serum potassium.[2,4] Potassium is a cardiac muscle cell membrane stabiliser, hypokalaemia could lead to cardiac myocyte instability, increased negativity of the cardiac myocyte membrane potential, generation of ventricular fibrillation, cardiac arrest, with asystole and death. In Nigeria, Uchenna and Unachukwu reported a case of cardiac arrest in a middle-aged woman who had an adrenal adenoma.[4] Renal hypoperfusion states like standing and dehydration cause an increase in renin and aldosterone release.[7] However, the negative feedback loop from angiotensin II decreases the renin; hence, the ratio of aldosterone-to-plasma renin activity (ARR) is ultimately reduced in standing and other hypovolemic states.[7] The ARR has been used as a screening test for Conns in suspected cases and in first-degree relatives of persons with Conns. When ARR is >20, with elevated plasma aldosterone, confirmatory test is usually warranted, either radiologic and/or salt (sodium) loading test.

Screening for Conns is needed in first-degree relatives, moderate-to-severe hypertension, resistant hypertension,

**Table I: Urinary findings after correcting hypokalaemia (5 September 2019)**

| Variables | Results (normal) |
|---|---|
| Spot urine potassium (mmol/l) | 10.09 (<10) |
| 24 h urine potassium (mmol/l) | 133 (25-125) |
| 24 h urine aldosterone (µg/day) | 16 (<10) |

hypertension with hypokalaemia with/without diuretic use, early-onset hypertension, cerebrovascular disease and suspected secondary hypertension.[8] Even when diuretic treatment was discontinued in the index case, hypokalaemia was still present hence the necessity of evaluating for Conns. Diagnostic criteria for hyperaldosteronism include: decreased renin not corrected by volume depletion, increased diastolic BP without oedema and aldosterone secretion not volume suppressed. Oedema absence results from escape phenomenon from mineralocorticoid sodium retaining properties. However, rare pretibial oedema could be found in complicated Conns with nephropathy in up to 40%–50% of Conns, particularly when hypertension progresses to CKD.[9] Urinalysis often reveals urinary concentrating defects as was seen in the index case. Urine PH is hardly acidic, commonly >7 due to compensatory ammonium generation and bicarbonate loss, though urinary findings are less prominent in bilateral disease compared to adenoma. Concomitant polyuria could prevents hypernatraemia in Conns as was the presentation in this case.[6,9]

Confirmatory tests were not carried out in our patient to avoid possible consequences of uncontrolled blood pressure surge coupled with the fact that some researchers have reliably diagnosed Conns from urine potassium and aldosterone, serum potassium and ARR and radiological evidence of enlargement or hyperplasia of the adrenal glands as both glands were markedly enlarged compared to.[9-11] The index patient presented with diastolic hypertension associated with severe headache and palpitation similar to that reported by Strandgaard Paulson.[12] LVH which was reported as ECG and ECHO findings in the index patient could be more common than in other causes of hypertension due to aldosterone's role in fibrogenesis and cardiac remodelling.[7,8] With diagnostic challenges, it might be necessary for patients to undergo percutaneous transfemoral adrenal vein catheterisation and adrenal vein sampling which gives a unilateral 2–3 fold increase in aldosterone in adenoma unlike in bilateral disease.[13] Autonomous secretion is diagnosed by none aldosterone suppression with volume expansion. Ectopic Adrenocorticotropic hormone (ACTH) production, hypermineralocorticoid states and Bartter and Gitelman syndromes are differentials that can be ruled out by the presence or not, of oedema, hypertension, hypomagnesaemia, hyperreninaemia and elevated aldosterone level.[5,6] Suppressed renin even with continued RAAS inhibition in our patient significantly contributed to our reliance on the diagnosis of hyperaldosteronism.[7]

**Table II: Results of investigations**

| Variables | Admission (29 August 2019) | Discharge (6 September 2019) | 1 month after discharge (8 October 2019) |
|---|---|---|---|
| Sodium (mmol/l) (135-145) | 136 | 137 | 143 |
| Potassium (mmol/l) (3.5-5) | 2.5 | 4.0 | 3.5 |
| Chloride (mmol/l) (97-107) | 96 | 103 | 100 |
| Bicarbonate (mmol/l) (22-30) | 22 | 22 | 22 |
| Creatinine (µmol/l) (60-110) | 122 | 138 | 126 |
| Urea (mmol/l) (3-7) | 5.4 | 5.5 | 3.5 |
| Platelets (150-400×$10^9$) | 224 | | 219 |
| Packed cell volume (41-52%) | 39 | 40 | 41 |
| White cell count (4-11×$10^9$) | 3.5 | 4.3 | 4.1 |

eGFR: Estimated glomerular filtration rate, CKD-EPI: Chronic kidney disease epidemiological collaboration

**Table III: Plasma aldosterone-to-renin ratio done between 11.00 am and 12.10 pm**

| Variables | Aldosterone ng/L (normal) | Renin ng/ml/h (normal) | ARR (normal) |
|---|---|---|---|
| Supine and on normal sodium diet | 338 (11.8-230) | 5.27 (1.7-24.0) | 64.1 (<20) |
| 1 h standing and on normal sodium diet | 399 (22.5-353) | 4.77 (2.6-27.7) | 83.6 (<20) |

ARR: Aldosterone-to-renin ratio

Conns' management involves normalising serum potassium, other electrolytes, aldosterone and blood pressure; treatment depends on underlying cause. In single benign tumour, laparoscopic removal is curative with a third achieving complete blood pressure normalisation, and of the rest, hypertension requires fewer drugs' treatment. Treatment in bilateral disease involves hypokalaemia correction and aldosterone inhibition. Hormonal side effects of aldosterone antagonist could limit their use in men.[14] Eplerenone has less anti-androgen effects compared to spironolactone; hence, it was used in our patient as a way of reducing gynaecomastia.[1] Sodium restriction forms a major part of Conns' management as it also reduces potassium loss. Surgery is indicated in large tumour, uncontrolled BP and severe hypokalaemia not responding to potassium replacement. Prognosis from surgical excision is good when done before 50 years.[10] First-degree relatives of Conns patients should be followed up with determination of urinary and serum potassium.

## CONCLUSION

Conns syndrome is the most common secondary cause of hypertension worldwide, but diagnosis in Nigeria and other low-income nations is not commonly made due to very low index of suspicion among clinicians. It commonly presents with weakness, difficult to treat hypertension, hypokalaemia, metabolic alkalosis and elevated ARR. The management essentially involves potassium replacement and blood pressure control. Screening programmes should be extended to first-degree relatives as early intervention could drastically reduce disease body.

### Acknowledgement

The authors would like to thank the entire nursing staff in the male medical ward of the Babcock University Teaching Hospital, Ilishan-Remo, Nigeria.

### 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.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Kerstens MN, Kobold AC, Volmer M, Koerts J, Sluiter WJ, Dullaart RP. Reference values for aldosterone-renin ratios in normotensive individuals and effect of changes in dietary sodium consumption. Clin Chem 2011;57:1607-11.
2. Corssmit EP, Dekkers OM. Screening in adrenal tumors. Curr Opin Oncol 2019;31:243-6.
3. Marzano L, Colussi G, Sechi LA, Catena C. Adrenalectomy is comparable with medical treatment for reduction of left ventricular mass in primary aldosteronism: Meta-analysis of long-term studies. Am J Hypertens 2015;28:312-8.
4. Uchenna DI, Unachukwu CN. Suspected conn's syndrome in a female adult hypertensive: A case report. Niger J Health Sci 2009;9:1-4.
5. Chikladze NM, Favorova OO, Chazova IE. Family hyperaldosteronism type I: A clinical case and review of literature. Ter Arkh 2018;90:115-22.
6. Williams SK, Ravenell J, Seyedali S, Nayef S, Ogedegbe G. Hypertension treatment in blacks: Discussion of the U.S. Clinical practice guidelines. Prog Cardiovasc Dis 2016;59:282-8.
7. Schilbach K, Junnila RK, Bidlingmaier M. Aldosterone to renin ratio as screening tool in primary aldosteronism. Exp Clin Endocrinol Diabetes 2019;127:84-92.
8. Yin G, Zhang S, Yan L, Wu M, Xu M, Li F, *et al*. One-hour upright posture is an ideal position for serum aldosterone concentration and plasma renin activity measuring on primary aldosteronism screening. Exp Clin Endocrinol Diabetes 2012;120:388-94.
9. Morera J, Reznik Y. Management of endocrine diseases: The role of confirmatory tests in the diagnosis of primary aldosteronism. Eur J Endocrinol 2019;180:R45-58.

10. Ismail F, Lockhat Z, van de Linde L. Conned by Conn's syndrome. SAJ Radiol 2008;12:2.
11. Vincent JM, Morrison ID, Armstrong P, Reznek RH. The size of normal adrenal glands on computed tomography. Clin Radiol 1994;49:453-5.
12. Strandgaard S, Paulson OB. Cerebrovascular consequences of hypertension. Lancet 1994;344:519-21.
13. England RW, Geer EB, Deipolyi AR. Role of venous sampling in the diagnosis of endocrine disorders. J Clin Med 2018;7:114.
14. Calhoun DA. Medical versus surgical treatment of primary aldosteronism. Hypertension 2018;71:566-8.