



HOSTED BY



ELSEVIER

Contents lists available at ScienceDirect

Journal of Acute Disease

journal homepage: www.jadweb.orgCase report <http://dx.doi.org/10.1016/j.joad.2016.03.020>

Primary hyperaldosteronism presenting with rhabdomyolysis in emergency room – Case report

Ilkay Cakir^{1*}, Serkan Senol², Yasin Simsek³, Zuleyha Karaca⁴, Kursad Unluhizarci⁴, Fatih Tanrıverdi⁴¹Department of Endocrinology, Bağcılar Training and Research Hospital, Istanbul, Turkey²Department of Radiology, Erciyes University Medical School, Kayseri, Turkey³Department of Endocrinology, Kayseri Training and Research Hospital, Kayseri, Turkey⁴Department of Endocrinology, Erciyes University Medical School, Kayseri, Turkey

ARTICLE INFO

Article history:

Received 30 Jan 2016

Accepted 18 Feb 2016

Available online 2 Apr 2016

Keywords:

Hypokalemia

Rhabdomyolysis

Primary aldosteronism

Adrenal adenoma

ABSTRACT

Primary hyperaldosteronism, is a well-known cause of secondary hypertension, mostly idiopathic hypertension or arising from aldosterone-producing adenomas. It is characterized with resistant hypertension, hypokalemia and metabolic alkalosis related with aldosterone production excess and plasma renin activity suppression. Hypokalemic rhabdomyolysis usually presents with muscle pain, cramps, fatigability and generalized weakness. Rhabdomyolysis due to hypokalemia is a rare complication of primary hyperaldosteronism reported within a limited number of cases in medical literature. Diagnosis and treatment of primary hyperaldosteronism is fundamentally important because of the probability of certain cure with accurate surgery. Here, we report a 38-year-old female with hypertension related with primary hyperaldosteronism who presented with rhabdomyolysis most likely due to profound hypokalemia.

1. Introduction

Primary hyperaldosteronism, is a well-known cause of secondary hypertension, which is characterized with resistant hypertension, hypokalemia and metabolic alkalosis, associated with plasma renin activity suppression and aldosterone production excess^[1]. In the case of severe hypokalemia, muscle weakness, cramping, headaches, palpitations and polyuria may be seen. In order to make a proper diagnosis, a high index of suspicion is needed^[2]. Rhabdomyolysis is a rare complication of primary hyperaldosteronism reported within a limited number of cases^[3–6]. Here we report a case of primary aldosteronism presented with rhabdomyolysis due to hypokalemia.

2. Case presentation

A 38-year-old female was admitted to emergency department with generalized muscle weakness. Her relatives reported an inability to walk unassisted since 10 days. Medical history was unremarkable except metformin use started 1 week ago by an

internal specialist with the diagnosis of type 2 diabetes mellitus (DM). Loss of appetite and sustained vomiting were present. The patient was obese with a body mass index of 32, found dehydrated and hypertensive (blood pressure was 190/110 mmHg) at clinical examination. Blood tests revealed hyperglycemia of 237 mg/dL (reference ranges of 70–115), metabolic alkalosis of pH 7.51, pO₂ 57.2 mmHg, pCO₂ 36.1 mmHg and cHCO₃ 28.7 mmol/L, severe hypokalemia (1.6 mmol/L, reference ranges of 3.3–5.5), mild renal insufficiency (urea 67 mg/dL, reference ranges of 0–50 and creatinine 1.58 mg/dL, reference ranges of 0–1.2), creatine phosphokinase and lactate dehydrogenase elevation (7666 IU/L, reference ranges of 0–167 and 534 IU/L, reference ranges of 140–280, respectively). She denied any other medication usage including insulin and herbal medicine. Based upon these clinical features, hypokalemia due to gastrointestinal loss and hypokalemia induced rhabdomyolysis were suspected as first diagnosis. After treatment with hydration and potassium replacement, muscle weakness was ameliorated dramatically and the blood glucose was controlled by basal-bolus insulin therapy. A series of laboratory examinations were performed for differential diagnosis of hypokalemia and hypertension. Twenty-four-hour urinary potassium excretion was 20.1 mEq. The overnight 1 mg dexamethasone screening test for Cushing's Syndrome yielded a suppressible plasma cortisol level of 1.79 µg/dL. Thyroid function tests were normal. Plasma renin activity (PRA) was suppressed (0.2 ng/mL/h, reference ranges of 0.5–1.9) while

*Corresponding author: Ilkay Cakir, Department of Endocrinology, Bağcılar Training and Research Hospital, Istanbul, Turkey.

Tel: +90 533 634 08 45

E-mail: drilkcakir@hotmail.com

Peer review under responsibility of Hainan Medical College. The journal implements double-blind peer review practiced by specially invited international editorial board members.

plasma aldosterone concentration (PAC) was upper than normal values (167.3 pg/mL, reference ranges of 10–160) and the ratio of PAC/PRA was 83 ng/dL/ng/mL/h. The patient underwent an abdominal computed tomography (CT) scan, which revealed two nodular lesions sized 27 and 20 mm in the right adrenal gland (Figure 1). Spironolactone treatment provided an excellent improvement in her general condition so that the patient refused surgical removal. She remains on treatment with spironolactone of 50 mg/day, metformin of 2 g/day and biphasic insulin of 3 × 20 units/day.

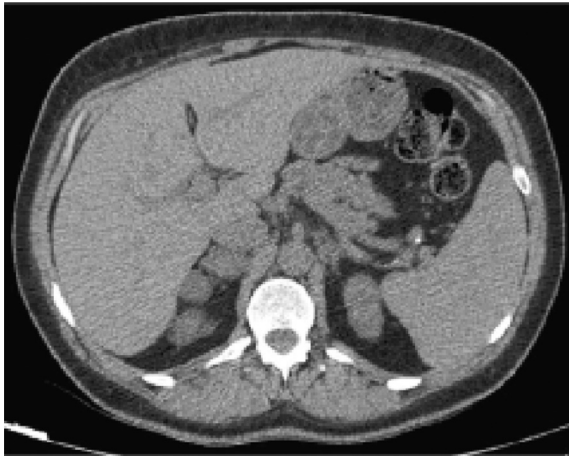


Figure 1. Nodular lesions sized 27 and 20 mm in the right adrenal gland.

3. Discussion

Here, we report a case of primary hyperaldosteronism presented with rhabdomyolysis due to profound hypokalemia. Potassium is the most abundant cation in the body which is predominantly (98%) restricted to the intracellular compartment and serum level is regulated around a narrow range of 3.5–5.0 mmol/L. Insulin and catecholamines are physiological short-term regulators that act in a shift of potassium and deposit it primarily in the liver and striated muscle cells. β_2 -stimulation results in a shift of potassium into the cell, while α -stimulation has an opposite effect^[7].

The kidney is the primary actor in long-term potassium homeostasis by matching potassium intake with its excretion. The filtered potassium is largely reabsorbed by proximal nephron segments and again excreted by distal segments. The secretion of potassium in these nephron segments is indirectly but tightly coupled to sodium reabsorption^[8].

Hypokalemia is a common electrolyte disorder encountered in clinical practice, that may result from insufficient potassium intake, shift to intracellular space from extracellular space or excessive loss either renal or extrarenal. Intake of drugs including β_2 -mimetics, barium, chloroquine known to cause internal cellular potassium shift was excluded. Insulin administration might be reasonable when the recent diagnosis of DM was taken in account, but both patient and her relatives denied insulin usage. Normal thyroid function tests and negative family history removed the prediagnosis of acquired and/or familial hypokalemic periodic paralysis. Gastrointestinal losses may be the underlying cause of hypokalemia. The patient reported sustained vomiting may result from stress or metformin intolerance. In further investigation 24 h urinary potassium excretion was found at some degree confusing. Usually low urinary

potassium concentrations <20 mEq/L favour extrarenal fluid losses such as diarrhoea, vomiting. Besides concentrations >40 mEq/L are considered compatible with urinary losses such as mineralocorticoid excess, Bartter's syndrome^[7]. The concentration of urinary potassium lower than expected in primary hyperaldosteronism may be interpreted as a compensatory effect of kidneys to the sustained vomiting in presented case.

Rhabdomyolysis is a rare complication of primary hyperaldosteronism reported within a limited number of cases in medical literature^[3–6]. The exact mechanism of rhabdomyolysis remains obscure, but hypokalemia is considered causative derangement via inducing inadequate vasodilatation of arterioles and capillaries that perfuse exercising muscle, suppression of glycogen synthesis and storage and deranged ion transport across the cell membrane^[9]. The main clinical manifestations of hypokalemic rhabdomyolysis are muscle pain, cramps, fatigability and generalized weakness as seen in our patient. Although a large series of pH reported severe muscle weakness to be a classic clinical manifestation that is usually related to coexistent hypokalemia in another review study of 30 patients, findings were on the contrary^[10,11]. Overall majority of patients with pH tend to be normokalemic^[12].

Hyperglycemia was another confounding factor in our patient's clinical picture. Chow *et al.* described a 70-year-old male diagnosed as having Conn's syndrome, hypokalemia, rhabdomyolysis and mild hyperglycemia^[5]. Correction of hypokalemia resolved rhabdomyolysis rapidly and hyperglycemia reversed by definite resection of the aldosterone secreting adenomas^[5]. A significant inverse relationship as lower potassium values are associated with higher glucose values which was demonstrated previously^[13]. The exact mechanism by which hypokalemia may cause glucose intolerance is still not known, but it is probably related to defects in insulin release or insulin sensitivity. It is interesting to note that angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists (angiotensin receptor blockers) drugs that results in an increase in serum K^+ , which has the lowest rates of new-onset diabetes and has been advocated as improve insulin sensitivity. The evidence of the importance of hypokalemia of data from studies over the past 40 years suggest that K^+ replacement should minimize the occurrence of new-onset diabetes observed with thiazide diuretics^[14]. Our patient was an obese female prone to impaired glucose tolerance with a positive family history of DM, but it would not be completely wrong to speculate a triggering effect of hypokalemia in newly onset hyperglycemia.

Primary aldosteronism is a well-known cause of secondary hypertension resulted from excessive or inappropriately elevated aldosterone production from the adrenals^[1]. Although reported prevalence varies considerably between different studies, depending on patient selection, diagnostic methodology employed and severity of arterial hypertension, it is estimated to be 4.6%–16.6% in unselected hypertensive populations and 17%–23% in patients with resistant hypertension^[15]. Primary hyperaldosteronism may exist in several forms and the most common forms are idiopathic hyperaldosteronism (60%–66%) and aldosterone-producing adenoma (APA) (30%–35%). The remaining forms including primary adrenal hyperplasia, familial hyperaldosteronism syndrome type 1 or 2, adrenocortical carcinoma, or ectopic aldosterone production are seen extremely rare^[2]. Screening should be considered in the states like hypertension and hypokalemia, resistant and severe hypertension,

adrenal incidentaloma and hypertension, onset of hypertension at a young age (<20 years), family history of early onset hypertension or stroke at age <40, and in hypertensive patients with a first degree relatives of those with primary hyperaldosteronism^[16]. Due to the lack of specific symptoms and signs, clinician's awareness is of critical importance in diagnose, hypokalemia itself, while help in recognizing the disease is not required, just only 9%–37% of patients with plasma aldosterone (PA) present with hypokalemia^[2]. Presence of both hypokalemia and hypertension in a young patient marked the diagnosis of hyperaldosteronism, in presented case. The biochemical hallmarks of primary hyperaldosteronism are the high aldosterone, and the low renin. The initial screening test calculates the ratio of PAC/PRA after correcting hypokalemia if present. The ratio of aldosterone to PRA expressed in ng/dL and ng/mL/h, respectively, which exceeds 30 and indicates the diagnosis of PA^[17]. Confirmatory test is strongly recommended with intravenous saline loading, oral sodium loading and the fludrocortisone suppression test in order to exclude misdiagnoses derived from laboratory-dependent thresholds and we skipped that step when we considered the general status of patient suffered^[1]. Finally CT scan revealed two nodular lesions sized 27 and 20 mm in the right adrenal gland. The patient was opposite to another more intervention including adrenal venous sampling and/or adrenalectomy and at that point, medical treatment with aldosterone antagonist agent spironolactone was prescribed based on the reported data that unilateral macroadenomas (>1 cm), detected by CT is highly suggestive for (APA) in the cases of PA^[18]. Although treatment of choice for patients diagnosed with APA or unilateral hyperplasia is unilateral laparoscopic adrenalectomy^[1], some authors arguing for first-choice therapy of PA should be based on long-term administration of low-dose mineralocorticoid receptor antagonists (spironolactone, eplerenone) and the cause of PA is suspected to be the continuum of low-renin hypertension, regardless of the morphological type of PA^[19]. Our patient was discharged well-feeling with spironolactone (50 mg/day), metformin (2 g/day) and biphasic insulin 3 × 20 units/day. Left adrenalectomy might have a curable, at least ameliorated effect on her blood pressure and blood glucose levels.

4. Conclusion

We reported a case with primary aldosteronism not only with severe hypertension but also complicated with rhabdomyolysis, providing an important lesson to be aware about the whole clinical picture. Diagnosis of secondary causes of hypertension is significantly important which can cause the probability of certain cure with accurate surgery.

Conflict of interest statement

The authors report no conflict of interest.

References

- [1] Stowasser M. Update in primary aldosteronism. *J Clin Endocrinol Metab* 2015; **100**(1): 1-10.
- [2] Thomas RM, Ruel E, Shantavasinkul PC, Corsino L. Endocrine hypertension: an overview on the current etiopathogenesis and management options. *World J Hypertens* 2015; **5**(2): 14-27.
- [3] Tsai WT, Chen YL, Yang WS, Lin HD, Chien CC, Lin CL. Primary aldosteronism associated with severe hypokalemic rhabdomyolysis. *Hormones (Athens)* 2012; **11**(4): 505-6.
- [4] Wen Z, Chuanwei L, Chunyu Z, Hui H, Weimin L. Rhabdomyolysis presenting with severe hypokalemia in hypertensive patients: a case series. *BMC Res Notes* 2013; **6**: 155.
- [5] Chow CP, Symonds CJ, Zochodne DW. Hyperglycemia, lumbar plexopathy and hypokalemic rhabdomyolysis complicating Conn's syndrome. *Can J Neurol Sci* 1997; **24**(1): 67-9.
- [6] Goto A, Takahashi Y, Kishimoto M, Minowada S, Aibe H, Hasuo K, et al. Primary aldosteronism associated with severe rhabdomyolysis due to profound hypokalemia. *Intern Med* 2009; **48**(4): 219-23.
- [7] Gumz ML, Rabinowitz L, Wingo CS. An integrated view of potassium homeostasis. *N Engl J Med* 2015; **373**(1): 60-72.
- [8] Palmer BF. Regulation of potassium homeostasis. *Clin J Am Soc Nephrol* 2015; **10**(6): 1050-60.
- [9] Allison RC, Bedsole DL. The other medical causes of rhabdomyolysis. *Am J Med Sci* 2003; **326**(2): 79-88.
- [10] Ma JT, Wang C, Lam KS, Yeung RT, Chan FL, Boey J, et al. Fifty cases of primary hyperaldosteronism in Hong Kong Chinese with a high frequency of periodic paralysis. Evaluation of techniques for tumour localisation. *Q J Med* 1986; **61**(235): 1021-37.
- [11] Goh BK, Tan YH, Chang KT, Enq PH, Yip SK, Cheng CW. Primary hyperaldosteronism secondary to unilateral adrenal hyperplasia: an unusual cause of surgically correctable hypertension. A review of 30 cases. *World J Surg* 2007; **31**: 72-9.
- [12] Douma S, Petidis K, Doulmas M, Papaefthimiou P, Triantafyllou A, Kartali N, et al. Prevalence of primary hyperaldosteronism in resistant hypertension: a retrospective observational study. *Lancet* 2008; **371**(9628): 1921-6.
- [13] Zillich AJ, Garg J, Basu S, Bakris GL, Carter BL. Thiazide diuretics, potassium, and the development of diabetes: a quantitative review. *Hypertension* 2006; **48**(2): 219-24.
- [14] Carter BL, Basile J. Development of diabetes with thiazide diuretics: the potassium issue. *J Clin Hypertens (Greenwich)* 2005; **7**(11): 638-40.
- [15] Piaditis G, Markou A, Papanastasiou L, Androulakis II, Kaltsas G. Progress in aldosteronism: a review of the prevalence of primary aldosteronism in pre-hypertension and hypertension. *Eur J Endocrinol* 2015; **172**(5): R191-203.
- [16] Moraitis A, Stratakis C. Adrenocortical causes of hypertension. *Int J Hypertens* 2011; **2011**: 624691.
- [17] Kołodziejczyk-Kruk S, Januszewicz W, Pęczkowska M, Prejzbis A, Zgliczyński W, Januszewicz A. Primary aldosteronism-recent progress and current concepts. *Endokrynol Pol* 2013; **64**(4): 312-8.
- [18] Young WF Jr, Hogan MJ, Klee GG, Grant CS, van Heerden JA. Primary aldosteronism: diagnosis and treatment. *Mayo Clin Proc* 1990; **65**(1): 96-110.
- [19] Hyla-Klekot L, Kokot F. Primary aldosteronism: a new insight into pathogenesis, diagnosis, and treatment in hypertensive patients. *Pol Arch Med Wewn* 2013; **123**(10): 547-51.