Endocrinology & Metabolic Syndrome
ISSN: 2161-1017

Gen et al., Endocrinol Metab Synd 2012, 1:4
DOI: 10.4172/2161-1017.1000106

Case Report Open Access

Acromegaly Presented as Severe Hypertension due to Primary Hyperaldosteronism

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Abstract

The coexistence of acromegaly and primary hyperaldosteronism is very rare. We herein report a 30-year-old-woman with severe hypertension in patient with acromegaly. After the endocrine tests confirmed the active acromegaly, hypogonadotropic hypogonadism and autonomous secretion of aldosterone, then patients underwent pituitary and adrenal MRI. MRI of the sella revealed intra and suprasellar adenoma with extending to right and left cavernous sinus. Adrenal MRI revealed 20×15 mm ovoid left adrenal adenoma with normal right adrenal. Patient first undergo surgical removal of the pituitary tumor. Then patient underwent left open adrenalectomy. Following the adrenalectomy, her blood pressure and number of antihypertensive drugs reduced significiantly.

In conclusion clinicians should be aware that a acromegalic patient with severe hypertension needs to be evaulated carefully for the possible curable cause of secondary hypertension such as primary hyperaldosteronism.

Keywords: Acromegaly; Primary hyperaldosteronism; Severe hypertension

Introduction

Acromegaly is a rare disease caused by excess secretion of growth hormone (GH), which is characterized by acral enlargement, maxillofacial changes, excessive sweating, arthralgias, visceromegaly, endocrinopathy, respiraory dysfunction, cardiovascular distrubances, insulin resistance and diabetes [1]. Acromegaly is associated with 2-5 times increased mortality risk, which is mostly due to cardiovascular and cerebrovascular disease [1]. Hypertension is an important complication of acromegaly, contributing to the increased morbidity and mortality of this condition. Prevalence of hypertension is up to 40% in acromegaly [1]. Exact mechanisms behind the development of the high blood pressure in pateints with acromegaly remains obscure [2]. Chronic hypervolemia, endotelial dysfunction, insulin resistance, diabetes and sleep apnea are likely to contribute to the pathogenesis of hypertension in acromegaly [2]. Previous studies showed that aldosterone level was increased in patients with active acromegaly [3,4]. High blood pressure in acromegaly may be due to increased aldosterone secretion.

Primary hyperaldosteronism (PA) is caused by the autonomous secretion of aldosterone from adrenocortical lesions which is associated with hypertension due to sodium retention with hypokalemia and metabolic alkalosis due to increased potassium excretion [5]. PA is commonly caused by adrenal hyperplasia (65–70%), aldosterone-producing adenomas (30–35%), and in rare cases by the inherited condition of glucocorticoids-remediable aldosteronism [5].

The coexistence of acromegaly and PA is very rare [6,7]. We herein report a severe hypertension due to PA in a patient with acromegaly.

Case Report

A 30-year-old-woman was admitted to the hospital with complaints of severe hypertension, cramps in both upper and lower limbs, headache, marked fatigue and weakness. She had recieved olmesartan 20 mg/day and nifedipine 30 mg/day for hypertension. She reported symptoms of acral changes, thickened lips, prognatism, exsessive sweating, headache, amonerrhea, cramps in both upper and lower limbs and muscle weakness over the two years. On the physical examination, body temperature was 36.8°C, pulse rate was 84/min, blood pressure was 200/100 mm/Hg and respiratory rate was 17 breathes/min. Physical examination revealed typical physical signs of acromegaly such as frontal bossing, thickened lips, macroglossia, prognatism, acral enlargements, coarse facial features. No abnormal findings were observed in her chest and abdomen.

Laboratory data showed marked hypokalemia (2.8 mEq/L) with elevated GH level (55 ng/ml) and IGF-1 level (1400 ng/ml) (Table 1). She was treated conservatively with potassium supplementation (180

	Patient's Serum Level	Reference Range
K (meq/L)	*2,8*	3,5-4,5
GH (ng/ml)	*55*	0-7
IGF-1 (ng/ml)	*1400*	115-317
24-hour urine VMA (mg)	*4,6*	1,4-6,5
24- hour urine normetanephrine (µg)	*438*	88-444
24- hour urine metanephrine (µg)	*150*	52-341
24-hour urine cortisol (nmol)	*278*	100-379
Cortisol (nmol/L)	*352*	171-536
ACTH (pg/ml)	*32*	0-46
FSH (mIU/ml)	*0,3*	3,5-12,5
LH (mIU/ml)	*0,25*	2,4-12,6
Estradiol (pg/ml)	*14,7*	24,5-195
FT4 (pmol/L)	*16,5*	12-22
TSH (µIU/ml)	*0,44*	0,27-4,2
Plasma Aldosterone (ng/dl)	*48*	1-16
Plasma Renin Activity (ng/ml/h)	*0,7*	1,2-3,5
Aldosterone Renin Ratio (ARR)	*68,7*	
1 mg dexamethason supression test cortisol	*22*	<50
0 minute GH (ng/ml)	*48*	<1
30 minute GH (ng/ml)	*62*	<1
60 minute GH (ng/ml)	*48*	<1
90 minute GH (ng/ml)	*39*	<1
120 minute GH (ng/ml)	*42*	<1

Table 1: Hormonal Parameters of Patients.

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Received August 07, 2012; **Accepted** September 12, 2012; **Published** September 13, 2012

Citation: Gen R, Akbay E, Akbay E (2012) Acromegaly Presented as Severe Hypertension due to Primary Hyperaldosteronism. Endocrinol Metab Synd 1:106. doi:10.4172/2161-1017.1000106

mEq/day) and carvedilol 25 mg added on her hypotension drugs. After the potassium level recovered fully (potassium was 4.1 mEq/L) and her blood pressure was 130/85 mm/Hg, patient underwent endocrine work up for acromegaly and secondary hypertension (Table 1). After the endocrine tests confirmed the active acromegaly, hypogonadotropic hypogonadism and autonomous secretion of aldosterone, then patients underwent pituitary and adrenal MRI.

MRI of the sella revealed intra and suprasellar adenoma with extending to right and left cavernous sinus (Figure 1). Adrenal MRI revealed 20×15 mm ovoid left adrenal adenoma with normal right adrenal (Figures 2A and 2B).

She was followed with spironolactone 100 mg/day, olmesartan 20 mg/day , carvedilol 25 mg/day and nifedipine 60 mg/day for hypertension. After her potassium level has became normal range (4.5 meq/L), she underwent transsphenoidal surgery for removal of the pituitary tumor. Microscopical examination of the resected tumor specimens was consistent with acidophilic adenoma which immunostaining with GH, but not with FSH, LH, ACTH, TSH and PRL. After the transsphenoidal surgery, her basal GH level was 38 ng/mL and IGF-I level was 944 ng/mL and there was no supression of GH after oral glucose tolarence test indicating the unsuccessful removal of the pituitary tumor. After transphenoidal surgery, MRI of sella revealed residual intrasellar adenom with extending to right and left caverneous sinus (Figure 3). Then the patient was treated with long acting depot lanreotide 90 mg/month and cabergoline 2 mg/week. At the three month follow up her serum IGF-1 levels was remained high (IGF-1 789 ng/ml), administration of lanreotide increased to 120 mg/month and patient underwent gamma knife radiotheraphy for residual pituitary adenoma. One year following the treatment with gamma knife and lanreotide 120 mg/month, her IGF-1 level remained high (IGF-1 677 ng/ml), then we added on pegvisomant 10 mg/day to lanreotide 120 mg/month and cabergoline 4 mg/week. Since her IGF-1 level was remained high (IGF-1 477 ng/ml), adminsitration of pegvisomant dose gradually increased to 40 mg/day. Three month following the treatment with pegvisomant her IGF-1 level was normal (IGF-1 277 ng/ml).

6 months after her transsphenoidal operation, she was admitted to Department of Urology for adrenalectomy. Then patient underwent left open adrenalectomy. Microscopical examination of the resected tumor specimens was consistent with adrenal adenoma on immuno-staning with melan A, synaptophysin, inhibin and vimentin. Following her adrenalectomy, the plasma aldosterone was 12 ng/dl, plasma renin activity was 1.4 ng/ml/h, ARR was 8.5 and plasma potassium level was 4.1 mEq/L. The patient now has excellent control over her hypertension with the aid of one hypotensive drugs. Follow-up at 6 months showed that the patient remained normotensive with olmesartan 20 mg/day and normokalemic.

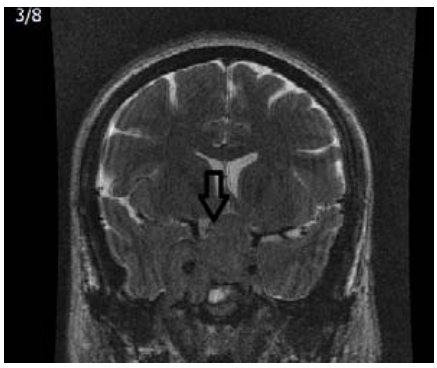

Figure 1: Pre operative coronal MRI of sella.

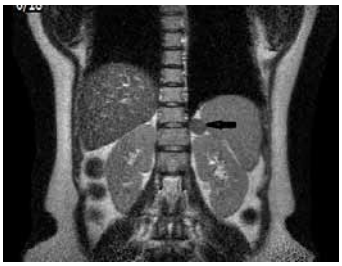

Figure 2A: Sagittal MRI of adrenal.

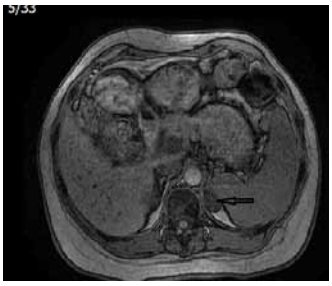

Figure 2B: Coronal MRI of adrenal.

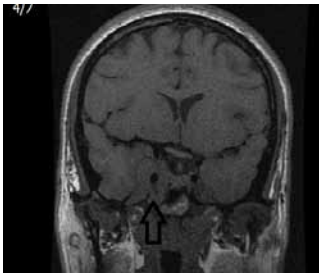

Figure 3: Post operative coronal MRI of sella.

Discussion

The coexistence of acromegaly and PA due to adrenal adenoma in the same individual is rare. Exact mechanisms behind the development of the high blood pressure in pateints with acromegaly remains obscure but may include several factors depending on the chronic exposure to GH and/or IGF-I excess. The growth hormone induced reduction in the ANP causing expansion of the extracellular fluid volume; may be the possible mechanism for the hypertension in acromegalic patients [2]. Insulin resistance and hyperinsulinemia which may induce hypertension by stimulating renal sodium absorption and sympathetic nervous activity may contribute to the pathogenesis of hypertension in acromegaly [2]. The increased sympathetic tone could play a role in development of elevated blood pressure in patients with acromegaly [2]. But data about the potential implication of the renin aldosterone axis on the pathogenesis of the high blood pressure in acromegaly are not obvious. Strauch et al. [8] showed that the renin–angiotensin–aldosterone system was normal in normotensive acromegalic patients but renin–angiotensin system was supressed with increased aldosterone secretion rates in hypertensive acromegalic patients. In contrast to this study, Cain et al. [9] showed that decreased aldosterone secretion rates in hypertensive patients with acromegaly. Recent study found that in

both humans and mice, chronic GH excess is associated with increased aldosterone levels, which is likely to be independent of systemic renin secretion [3]. But in this study aldosterone levels were within the reference range in both mice and humans with chronic growth excess [3]. In addition, adrenal morphological alteration in patients with acromegaly have been reported. Scaroni et al. [10] demostrated an increased prevalence of adrenal morphological alterations in patients with acromegaly which the baseline hormonal profile and testing of cortisol and aldosterone hypersecretory status with overnight 1 mg dexamethasone and ARR did not reveal any adrenal functional autonomy. Smilarly Pappa et al. [4] also demonstrated an increased prevalance of adrenal morphological alteration in patients with acromegaly with significant association of adrenal morphology and arterial hypertension. In contrast, they demonstrated that among patients with adrenal morphological changes exhibited autonomous cortisol and aldosterone secretion [4]. High blood pressure in acromegaly may be caused by increased aldosterone secretion and alteration of adrenal morphology.

Present case had early onset of severe hypertension (200/100 mm/Hg) with marked hypokalemia (2.8 mEq/L). Conditions that make the search for primary hyperaldosteronism mandatory in a hypertensive patient; unexplained hypokalemia, resistant hypertension and Grade 2 or 3 hypertension, early onset hypertension and/or stroke, incidentally discovered apparently nonfunctioning adrenal mass, evidence of organ damage particularly if disproportionate for the severity of hypertension and obstructive sleep apnea syndrome [11].

When a solitary unilateral macroadenoma (larger than 1 cm) and normal contralateral adrenal morphology are found on CT or MRI in a patient with primary who is younger than 40 years, unilateral adrenalectomy is reasonable option for PA [5]. Present case was 30-year-old woman which her plasma aldosterone level 48 ng/dl and ARR 68.7 with 20 mm ovoid left adenoma and normal right adrenal. For this reason patient underwent open left adrenalectomy. Then we could reduce the hypotensive drugs of our case by half in the post-operative phase. The patient now has excellent control over her hypertension with the aid of one hypotensive drug. After adrenalectomy, hypertension is cured in around 50% of patients with aldosterone producing adenoma with the remaining patients showing a significant reduction in blood pressure and number of antihypertensive drugs [5].

Conclusion

We report the case of acromegaly in a patient with concurrent PA at the time of initial presentation. Clinicians should be aware that a acromegalic patient with severe hypertension needs to be evaulated carefully for the possible curable cause of secondary hypertension such as primary hyperaldosteronism.

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