Hyperaldosteronism Associated with Bilateral Macronodular Adenomas and a Renal Mass in the Left Kidney

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As first reported by Conn [1], pripmary aldosteronism is a syndrome characterized by hypertension, hypokalemia, suppressed plasma renin activity and increased aldosterone secretion. Approximately two-thirds of the cases are known to be caused by an aldosterone-producing adenoma, and the remaining one-third by hyperplasia [1]. On the other hand, incidentally discovered adrenal tumors, so-called incidentalomas, have been shown to be associated with subtle autonomous cortisol production, which although insufficient to cause clinically overt Cushing's syndrome are usually considered as preclinical or subclinical Cushing´s syndrome.

The literature contains few cases of aldosterone-producing adenoma complicated with Cushing's syndrome or preclinical Cushing's syndrome [2]. Also rarely reported – in less than 5% of the reported APA cases – are bilateral nodular adenomas of the adrenals associated with hyperaldosteronism. We describe a case of bilateral macronodular adenomas of the adrenals with concurrent presence of a left renal mass proven to be benign after resection.

APA = aldosterone-producing adenoma

PATIENT DESCRIPTION

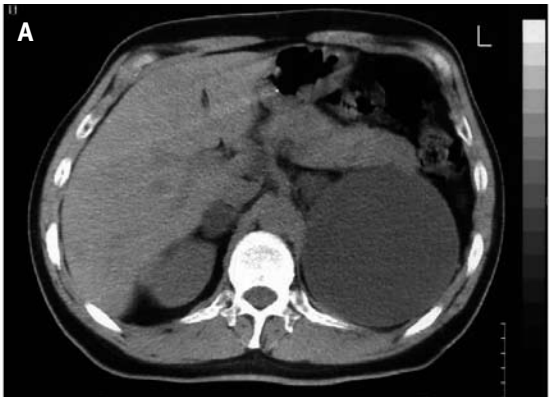
A 55 year old man with a 10 year history of severe hypertension was referred to our department due to repeated episodes of headache, diaphoresis and uncontrolled blood pressure. On presentation, blood pressure was 220/110 mmHg. The patient was hyperactive, and complained of repeated episodes of muscle weakness of the extremities, nocturia and, on occasion, tenderness in the left lower back. On clinical examination, he had a temperature of 36.8^{0}C, pulse rate of 80 beats/min and his weight and height were 75 kg and 1.82 m, respectively. No clinical symptoms of Cushing's syndrome were present. He had previously undergone partial thyroidectomy due to nodular hyperplasia. Clinical examination of the lungs, heart and abdomen was normal. An area of tenderness in the left kidney was noted, although Giordano sign was negative. Neurological examination was normal except for hyperactive deep tendon reflexes. He was on antihypertensive medication with calcium channel blockers (nifedipine 60 mg once a day) and prazosin (2 mg 3 times a day). Fluctuations of blood pressure measurements did not allow discontinuation of the antihypertensive drugs, and due to the potential risk of acute volume overload the saline loading test was not performed.

Laboratory data of blood tests on admission showed low serum potassium with increased urinary potassium secretion, normal serum and urinary sodium, slightly increased serum urea levels and normal creatinine levels. Proteinuria or hematuria was not observed and urinary creatinine excretion was normal. The hormonal data revealed urinary 24 hour cortisol and aldosterone levels marginally elevated with normal vanillymandelic acid levels. Morning and midnight serum cortisol and plasma ACTH levels were all within the normal range. Normal suppression of serum cortisol was observed after a 1 mg overnight dexamethazone test. Serum aldosterone levels were in the normal range in the supine position with suppressed plasma renin activity levels. On the 4 hour postural stimulation test, serum aldosterone exhibited marked elevation with suppression of plasma renin activity.

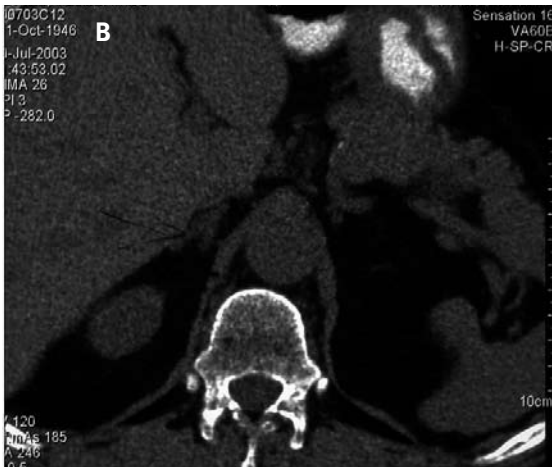
X-ray of the chest showed torsion of the thoracic portion of the aorta, asbestosis of the aortic arc and an elevation of the right hemidiaphragm due to a translucent lesion. Computed tomography of the abdomen showed the presence of a 4.5 cm nodule in the right adrenal, two nodules measuring 2 cm and 3 cm respectively in the left adrenal, and a large mass, 10 x 12 cm, with cystic components in the upper part of the left kidney [Figure A]. Adrenal scintigraphy with l31I-6-β-iodomethyl-norcholesterol, following administration of cortisol in order to suppress the zona fasciculata, showed significant uptake in the right adrenal but inhibition of the contralateral left adrenal gland. Kidney scintigraphy with 99MTC-DTPA showed a homogenous radioactive distribution with the left renal mass appearing as a cold (or photopenic) lesion.

During surgery, both nodules in the

[A] Radiological findings of the adrenals by plain CT scan before surgery, showing the macronodules of the adrenals and the large homogenous renal mass.



[B] CT scan of the adrenals post-surgery, showing only the right adrenal with postoperative connective tissue growth in the area of the left adrenal.



left and right adrenals, as well as the left renal cystic mass were removed. Additionally, due to adhesions of the cystic mass to the surrounding tissues only the right adrenal was preserved. Histological examination of the nodules confirmed the presence of clear cells, characteristic of APA, and showed paradoxical hyperplasia of the adjacent zona glomerulosa. Moreover, the left renal mass was composed primarily of collagenized hyalinized fibrous tissue with many inflammatory cells surrounding necrotizing tissue with blood and cholesterol crystals. Twenty-four hours after surgery blood pressure normalized without the use of any antihypertensive medication. Five days after surgery plasma renin activity, aldosterone and electrolytes were measured and found to be normal. Two months after surgery, a Synacten (ACTH) 250 μg test showed inadequate adrenal reserve (baseline cortisol levels were 9.6 μg/dl and 30 minutes after the test 11.5 μg/dl). For that reason cortisol supplementation was recommended. CT scan of the adrenals showed the presence of the right adrenal and postoperative connective tissue growth in the area of the left adrenal [Figure B].

COMMENT

We report the case of a male patient with APA and bilateral macronodular hyperplasia with a concurrent finding of a left extrarenal mass proven to be of benign origin.

Recently, Sugawara et al. [3] suggested that the occurrence of postoperative adrenocortical insufficiency should be included in the differential diagnosis of patients with large APA, even when no physical signs of autonomous cortisol overproduction are present. In our case, cortisol urine levels were slightly elevated while plasma cortisol levels were normally suppressed after an overnight 1 mg dexamethasone test. Histopathological data were consistent with APA since the right and left nodules comprised mainly clear cells. Additionally, there was hyperplasia of the zona reticularis in both nodules, a finding that in such cases must be taken into account for the final endocrinological evaluation of the hypothalamic-pituitary-adrenal axis.

Although adrenal vein sampling was not achieved, we managed to perform adrenal scintigraphy with radioactive cholesterol, which is known to provide a reliable measure of adrenocortical function, in addition to being a localizing technique for adenomas larger than 1.5 cm in diameter [4]. In the present study, pretreatment with cortisol was conducted before the administration of Il31-6-β-iodomethyl-norcholesterol, which is known to suppress zona reticularis and enhance the function of the outer zona glomerulosa. For that reason, it is quite interesting that although the histopathological examination revealed cells known to be due to APA in both adrenal nodules, a strong uptake compatible with aldosterone production was demonstrated only in the right adrenal, while the left adrenal showed complete suppression. Moreover, in both nodules hyperplasia of the zona reticularis was evident. Our findings might be explained by the fact that a different portion of the zona glomerulosa is over-expressed in the right adrenal. To the best of our knowledge this is the first report of such findings.

That the renal mass was cystic in nature was not unexpected [5]. It could have arisen as a hereditary developmental abnormality or it may have been an acquired lesion. The possibility that hypertension was a contributing factor – in the sense of causing renal dysfunction eventually leading to the development of a renal cyst – cannot be ruled out.

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