

CASE REPORT

Functioning Adrenal Adenoma in Association with Congenital Adrenal Hyperplasia

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SUMMARY

We report a case of a young hypertensive male who was first seen in 1998 with a right thalamic haemorrhage and uncontrolled hypertension. CT abdomen showed a right adrenal tumour and a hyperplastic left adrenal gland. Laparoscopic adrenalectomy performed followed by histopathological examination confirmed the diagnosis of adrenal adenoma. He subsequently presented to us again a year later with persistent hyperkalaemia and asymptomatic hyponatraemia. Further investigations strongly suggested the presence of isolated mineralocorticoid deficiency with normal cortisol levels. This was confirmed to be due to partial or late-onset congenital adrenal hyperplasia (CAH). We discuss the association of partial CAH and adrenal tumours and the unmasking of the mineralocorticoid deficiency following adrenalectomy.

KEY WORDS:

Late-onset congenital adrenal hyperplasia (CAH), Conn's adenoma, Mineralocorticoid deficiency, Adrenalectomy, Fludrocortisone

CASE REPORT

We report a case of a 53 year-old Chinese gentleman who was first seen in our medical institution in 1998. He had a background history of hypertension, diagnosed at the age of 33 for which he subsequently defaulted follow up. At the age of 38 he presented to a private medical institution with a sudden onset of left-sided hemiparesis, slurring of speech and impaired conscious level. A computer tomographic (CT) scan of the brain confirmed a right thalamic haemorrhage. He was then referred to our institution for further follow up.

On further examination there was no history to suggest thyrotoxicosis, pheochromocytoma or any other relevant diseases. There was no other medical or surgical history and no family history of similar illness or of consanguinity, ambiguous genitalia or virilisation. Childhood history was

unremarkable. He was a lorry driver, single, did not consume alcohol and ceased smoking a few years prior to admission. On examination he was thin but well kempt. He weighed 65kg with height of 160cm. Blood pressure (BP) was 170/100 mmHg and pulse rate (PR) 82 bpm. There was comprehensible slurring of speech. Neurological examination was consistent with a right thalamic lesion with left 7th and 9th cranial nerve palsies. Other examinations were normal including the genitalia. Blood investigations revealed hypokalaemia with serum potassium of 2.2 mmol/L and sodium 138 mmol/L. This was subsequently associated with serum aldosterone of 244.077pg/nL(N:34-273) and low serum renin of <7.5IU/mL(N:upright 7-76, supine 5-47). He responded well to treatment with ACE inhibitor, beta-blocker and spironolactone. A CT scan of the abdomen revealed a right adrenal mass measuring 2.7cm x 1.4cm and a hyperplastic left adrenal gland (radiological images lost during follow up). He underwent a laparoscopic right adrenalectomy in January 1999, which was uncomplicated. Histopathological examination confirmed an adrenal adenoma. Post-operatively he required anti-hypertensive medications, with stable BP of 130/80mmHg on oral Atenolol 100mg od and Prazosin 0.5mg bd.

One year post adrenalectomy he was admitted for investigations of hyponatraemia and hyperkalaemia (Na 122mmol/L, K 5.4mmol/L). He was asymptomatic with no symptoms to suggest hypocortisolism. His BP was 150/100mmHg and normal PR. Random blood sugar was 5.8mmol/L and there was no metabolic acidosis. A short synacthen test was done with good response (cortisol 0' 383, 30' 658, 60' 712 nmol/L). Further tests showed an elevated renin level of 728.319µU/mL (N:upright 7-76, supine 5-47). Serum aldosterone was normal 100pg/mL (N supine 70-180, standing 90-270). ACTH was unremarkable of <10pg/mL (N random 0-46). A frusemide challenge test was subsequently done, which involved administration of 40 mg of intravenous frusemide which showed good renin but inadequate aldosterone response.

Table I: Frusemide challenge test showing serum renin, aldosterone and ACTH response

| | Baseline | After frusemide | Normal range |
|---------------------|----------|-----------------|----------------------------------|
| Renin (µU/mL) | 16.1 | 276 | Upright 7-76 Supine 5-47 |
| Aldosterone (pg/mL) | 18.2 | 32.3 | Supine 70-180 Standing 90-270 |
| ACTH (pg/mL) | <10 | 23.3 | Random 0-46 |

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Serum 17-hydroxyprogesterone with ACTH stimulation revealed persistently elevated levels at baseline, 30 minutes and 60 minutes (10.7, 17.5 and 23.5 nmol/L respectively) (N range for male 1.5-6.4 nmol/L). Genotyping facilities are unavailable to us.

The patient was started on oral Fludrocortisone 0.1mg daily for treatment of the hyperkalaemia and remained well.

DISCUSSION

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder comprising of several groups of patients deficient in the synthesis of either cortisol, aldosterone or both. The most common form of CAH is due to 21-hydroxylase deficiency, with mutation in the cytochrome p450 protein CYP21 having being detected in more than 90% of cases of CAH but other mutations of CYP 11B1 and CYP17 are also recognized¹. However, the defect in cortisol or aldosterone synthesis may occur partially and patients present as late-onset or adult onset CAH with features of glucocorticoid or mineralocorticoid insufficiency. 21-hydroxylase deficient CAH has been suggested to be associated with a higher incidence of adrenal incidentaloma than the general population¹. However, in our literature search, the association of adrenal adenoma and partial CAH as in our patient remains a rare entity.

The clinical manifestations of the classic CAH are due to the unopposed oversecretion of the hypothalamic CRH and pituitary ACTH resulting in overproduction of active androgens, the precursors and hyperplastic adrenals. However, in partial hormonal synthesis defect, either one of cortisol or aldosterone production is normal, with normal levels of androgens and phenotypically normal patients. Therefore, patients often remain undetected and present only in adulthood with mere electrolyte abnormalities. This condition is characterized by a high basal level of cortisol biosynthesis precursors such as 17-hydroxyprogesterone, or elevation of the precursors after ACTH stimulation² as illustrated in this patient.

Our patient did not undergo chromosomal analysis due to limited availability of the test but the fact that he remained hypertensive after the adrenalectomy is most likely due to the

effect of deoxycorticosterone resulting in sodium retention and hypertension making the probable partial hormonal defect to be of 11-hydroxylase deficiency.

The association between CAH and adrenal tumours has been recognized with a detection of clinically silent macronodular adrenal hyperplasia and adrenocortical adenomas in 82% of homozygous and 45% of heterozygous CAH¹. It has been postulated that the formation of adrenal tumour is due to hyperplastic adrenal tissue with increased stimulation of the adrenal cortex¹ and further supported by the exaggerated response of 17-hydroxyprogesterone after ACTH stimulation in 30-70% of patients with incidentally detected adrenal tumours³. However, these tumours were detected incidentally and patients remained asymptomatic. Furthermore, numerous studies have identified a predisposition of adrenal tumours in 21-hydroxylase deficiency patients and little data is available on any other CAH disorders.

In conclusion, we report an extremely interesting case of an adrenal tumour with overt manifestation of mineralocorticoid excess. The patient subsequently underwent an adrenalectomy and unmasked his underlying aldosterone deficiency which is most likely of 11-hydroxylase abnormality. The tumorigenesis of the adrenal tumour in this population remains poorly understood and until more data is available, screening for cortisol or aldosterone synthesis deficiency in patients with adrenal tumours is still a controversial issue.

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