Familial Conn's syndrome

Nicholas London, John Swales¹, Ken Hollinrake², Peter Bell and Anthony Heagerty¹

Departments of Surgery and ¹Medicine, Leicester University, Clinical Sciences Building, Leicester Royal Infirmary, PO Box 65, Leicester LE2 7LX, and ²Nuneaton Hospital, UK

Summary: We describe the occurrence of primary hyperaldosteronism in two sisters. Although this is only the second published report of familial Conn's syndrome, it does have implications for the relatives of patients with Conn's syndrome and these are discussed.

Introduction

We describe the occurrence of primary hyperaldosteronism (Conn's syndrome) in two sisters. It is important that practitioners should be aware of a familial variant because it has important implications for the management of the relatives of patients with Conn's syndrome. Indeed, had a familial form of Conn's syndrome been described prior to the presentation of our second case, the management of this patient would almost certainly have been different.

Case 1

A previously fit 45 year old woman presented in August 1984 with generalized muscle weakness, hypertension (200/120 mmHg) and hypokalaemia (1.4 mmol/l). Plasma renin was 3.3 pmol/l in the lying position (normal range 1–14) and 2.3 pmol/l in the standing position (normal 11–41). Plasma aldosterone levels were raised at 1358 pmol/l in the lying position (normal 30–201) and 1534 pmol/l in the standing position (normal 47–710). A computed tomographic (CT) scan showed a 1.5 cm diameter lesion in the right adrenal and 6 β -¹³¹I-iodomethyl-19-norcholesterol (NP-59) scan showed that the uptake by the right gland was twice that of the left. At surgical exploration a right subtotal adrenalectomy was performed and histology showed features typical of an adrenal adenoma. She made an uncomplicated postoperative recovery.

Case 2

A 54 year old woman, presented to her general practitioner in March 1989 with labile hypertension and generalized weakness. She explained that her sister (Case 1) had undergone surgery for Conn's syndrome. Examination revealed a blood pressure of 180/120 mmHg and her serum potassium was found to be 2.6 mmol/l. Further investigation revealed a serum renin of 5.9 mmol/l/hour (normal 0.3–2.7) with a serum aldosterone of 3425 pmol/l (normal 28–4440). Selective renal venous renin levels were 1.0 mmol/l/hour for the left renal vein and 0.2 mmol/l/hour for the right side. Subtraction angiography showed a well-defined vascular lesion in the upper part of the left kidney. On the basis of these investigations she was thought to have a renin-secreting tumour of the left kidney and therefore underwent a left nephrectomy; the adrenal gland was not removed.

Postoperatively, however, she remained hypertensive and hypokalaemic. Further investigations revealed a greatly raised supine serum aldosterone level at 2200 pmol/l (100–500) in the presence of a suppressed serum renin, 0.2 pmol/l/hour (1.2–4.3). A CT scan was normal but a selenium-75 cholesterol scan showed uptake in the right adrenal twice that of the left, which suggested an adrenal adenoma of the right. At surgical exploration the left adrenal gland appeared normal, the right, however, contained a 1.5 cm diameter adenoma. The right adrenal was excised and histology confirmed an adrenal adenoma. She made an uncomplicated postoperative recovery, becoming normotensive and normokalaemic.

The parents, sib and progeny of the two sisters are normotensive.

Discussion

Conn first described the syndrome of primary aldosteronism resulting from an aldosterone-producing adenoma in 1955.¹ Other causes of primary aldosteronism include adrenal carcinoma,² adrenal hyperplasia³ and glucocorticoid-suppressible hyperaldosteronism.⁴ Although it is established that glucocorticoid-suppressible hyperaldosteronism^{4,5} and adrenal hyperplasia may be familial,⁶ it is only very recently^{5,7} that a familial form of aldosterone-producing adenoma has been described in four families. It has been suggested that familial glucocorticoid-suppressible hyperaldosteronism should be called type I and familial adenomatous hyperaldosteronism type II familial hyperaldosteronism. Stowasser *et al.*⁷ have noted that both angiotensin-responsive and angiotensin-unresponsive aldosterone-producing adenomas

can occur in the same family. Unfortunately, neither of our two patients were assessed by angiotensin infusions, although the elevated aldosterone in Case 1 was unresponsive to upright posture.

In conclusion, we describe a further case of familial Conn's syndrome and would agree with Gordon *et al.*⁵ that, although the mode of inheritance is uncertain, relatives of patients with primary aldosteronism should be examined for hypertension and affected individuals screened with plasma aldosterone/renin ratios.

Acknowledgement

We are grateful to Professor R. Wilkinson for allowing us to report Case 1.

References

1. Conn, J.W. Primary aldosteronism, a new clinical syndrome. *J Lab Clin Med* 1955, **45**: 3–17.
2. Conn, J.W., Knopf, R.F. & Nesbit, R.M. Clinical characteristics of primary aldosteronism from an analysis of 145 cases. *Am J Surg* 1964, **107**: 200–206.
3. Irony, I., Kater, C.E., Biglieri, E.G. & Shackelton, C.H.L. Correctable subsets of primary hyperaldosteronism: Primary adrenal hyperplasia and renin responsive adenoma. *Am J Hyperten* 1990, **3**: 576–582.
4. Sutherland, D.J.A., Ruse, J.L. & Laidlaw, J.C. Hypertension, increased aldosterone secretion and low plasma renin activity relieved by dexamethasone. *Can Med Ass J* 1966, **95**: 1109–1119.
5. Gordon, R.D., Stowasser, M., Tunny, T.J., Klemm, S.A., Finn, W.L. & Krek, A.L. Clinical and pathological diversity of primary aldosteronism, including a familial variety. *Clin Exp Pharm Physiol* 1991, **18**: 283–286.
6. Greco, R.G., Carroll, J.E., Morris, D.J., Grekin, R.J. & Melby, J.C. Familial hyperaldosteronism, not suppressed by dexamethasone. *J Clin Endocrinol Metab* 1982, **55**: 1013–1016.
7. Stowasser, M., Gordon, R.D., Tunny, J.T., Klemm, S.A., Finn, W.L. & Krek, A.L. Primary aldosteronism: implications of a new familial variety. *J Hypertension* 1991, **9** (Suppl 6): S264–S265.