et al: Acute leukemia after alkylating-agent therapy of ovarian cancer. *N Engl J Med* 297: 177, 1977
3. Leukaemia and cytotoxic drugs. *Lancet* 1: 70, 1971
4. Kaslow RA, Wisch N, Glass JL: Acute leukemia following cytotoxic chemotherapy. *JAMA* 219: 75, 1972
5. Greenspan EM, Tung BG: Acute myeloblastic leukemia after cure of ovarian cancer. *JAMA* 230: 418, 1974
6. Kyle RA, Pierre RV, Bayrd ED: Multiple myeloma and acute leukemia associated with alkylating agents. *Arch Intern Med* 135: 185, 1975
7. Rosner F, Grunwald H: Multiple myeloma terminating in acute leukemia. *Am J Med* 57: 927, 1974
8. Shaw MT, Twele TW, Norquist RE: Plasma cell leukemia: detailed studies and response to therapy. *Cancer* 33: 619, 1974
9. Pruzanski W, Platts ME, Ogryzlo MA: Leukemic form of immunocytic dyscrasia (plasma cell leukemia). *Am J Med* 47: 60, 1969
10. Sypkens Smit CG, Meyler L: Acute myeloid leukemia after treatment with cytostatic agents. *Lancet* 2: 671, 1970
11. Puri HC, Campbell RA: Cyclophosphamide and malignancy. *Lancet* 1: 1306, 1977
12. Chabner BA: Second neoplasm — a complication of cancer chemotherapy (E). *N Engl J Med* 297: 213, 1977

Remission of primary hyperaldosteronism consequent on adrenal venography

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The diagnosis of hyperaldosteronism is not without problems despite recent advances in biochemical and radiologic techniques.[1] An uncommon complication of adrenal venography has been necrosis of the adrenal gland associated with partial or complete remission of hyperaldosteronism and, in several patients, deficient secretion of cortisol.[2-7]

This report describes remission of hyperaldosteronism following adrenal venography without associated adrenal insufficiency. Hypertension, probably essential, recurred, with normal biochemical findings, and associated nonsignificant renal artery stenosis was demonstrated.

Case report

In October 1971 a 43-year-old woman presented with hypertension of 9 years' duration. There was associated headache and polyuria. Investigations in 1969, including measurement of serum concentration of potassium, had yielded normal results. She had not recently received therapy.

The only physical abnormality was a blood pressure of 180/110 mm Hg. Pronounced hypokalemia with inappropriately high urinary excretion of potassium was the main clinical finding. Other findings included a diabetic glucose tolerance test, normal concentration of plasma cortisol, normal excretion of urinary protein and vanillylmandelic acid, and a normal intravenous pyelogram. Hyperaldosteronism, suggested by the hypokalemia, was confirmed by the elevated urinary excretion of aldosterone when the patient was given a diet with unrestricted sodium intake, and was further defined as primary by the blunted response of plasma renin activity to dietary restriction of sodium.

Adrenal venography demonstrated a normal left adrenal gland but the right adrenal gland was not visualized. On this evidence a right-sided adrenal adenoma was considered likely but bilateral adrenal hyperplasia was not excluded. Exploratory laparotomy was advised but the patient refused to undergo an operation. She started taking spironolactone in increasing doses and was discharged taking 800 mg/d.

As an outpatient she became asymptomatic and her blood pressure and serum potassium concentration decreased to within normal limits. The dose of spironolactone was reduced sequentially and maintained at 200 mg/d.

In September 1974 further investigation was conducted with respect to the hyperaldosteronism. Again a normal left adrenal gland was visualized but the right adrenal gland was not demonstrated by adrenal venography. Blood samples taken at the time of adrenal venography showed that the concentration of plasma aldosterone was 1140 ng/dL in the left adrenal vein, 134 ng/dL in the inferior vena cava above the left renal vein and 96 ng/dL in the inferior vena cava below the left renal vein. These samples were taken while the patient was receiving spironolactone. At the time of venography she experienced severe pain in the right loin; it lasted 2 weeks. Aortography and renal angiography demonstrated moderate stenosis of the left renal artery but did not define further the anatomic features of the adrenal glands. There was no difference in plasma renin activity in the renal veins between the two sides. This was regarded as evidence for a nonfunctional renal arterial lesion.

In March 1975 spironolactone therapy was discontinued and for approximately 15 months the patient remained asymptomatic, with normal blood pressure, serum potassium concentration, plasma renin activity, plasma aldosterone concentration and urinary excretion of aldosterone.

In June 1976 hypertension recurred without biochemical evidence of hyperaldosteronism or evidence of significant renal artery stenosis from intravenous pyelography or renal scintiscanning. She refused further angiographic examination. A 24-hour urine specimen contained a normal concentration of free cortisol.

Adrenal scintiscanning after administration of iodine-131 (^{131}I)-iodocholesterol, performed in February and September 1976, failed to demonstrate either adrenal gland. The patient has since been treated with methyldopa and her hypertension has been controlled readily.

Discussion

The prevalence of primary hyperaldosteronism in an unselected hypertensive population is approximately 1%.[8] Our patient illustrates one aspect of the natural history of this condition: her serum potassium concentration was normal in February 1969 but she had severe hypokalemia in October 1971. Conn and colleagues[9] suggested the existence of normokalemic primary hyperaldosteronism; this might have been revealed in our patient if urinary aldosterone excretion and plasma renin activity had been measured in 1969. In October 1971 the clinical features and biochemical abnormalities clearly indicated primary hyperaldosteronism.

Adrenal venography was undertaken to delineate the cause of the primary aldosteronism and to locate any adenoma. Depending on diagnostic criteria it is generally accepted[10] that adrenal adenoma and bilateral adrenal hyperplasia are the most common causes of primary aldosteronism, the former being three times as frequent a cause as the latter; other causes are less frequent.[11] The treatments of choice are resection for the adrenal adenoma and therapy with spironolactone for the adrenal hyperplasia. The profound biochemical abnormalities in our patient favoured an adrenal adenoma[12] but she refused abdominal exploration. The high dose of spironolactone given initially was that usually found necessary to overcome the effects of aldosterone on blood pressure and serum potassium concentration.[1]

Twice adrenal venography showed a normal left adrenal gland but failed to demonstrate the right adrenal gland. Venography is most frequently unsuccessful on the right side.[13] The severe pain in the right loin is characteristic of adrenal necrosis during venography and has been reported previously.[2-7]

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The result of the presumed adrenal necrosis on the side of the probable adrenal adenoma was remission of the hyperaldosteronism, as documented by normal blood pressure, serum potassium concentration, plasma renin activity, plasma aldosterone concentration and urinary aldosterone excretion during 15 months of observation without therapy. The remission was not accompanied by hypocorticism;[4-6] the urinary excretion of free cortisol was normal and no clinical manifestations of hypocorticism were observed.

Measurement of plasma aldosterone concentration in blood samples from both adrenal veins has been found more reliable than adrenal venography both in elucidation of the cause of the hyperaldosteronism and in localization of an adenoma.[13] The aldosterone concentration in the plasma from the left adrenal gland in our patient was higher than that reported by Horton and Finck.[13] However, none of their patients were receiving spironolactone at the time of venous sampling, and this agent is known to increase the rate of secretion of aldosterone from the adrenal glands in healthy subjects.

Adrenal scintiscanning after administration of iodocholesterol labelled with ^{131}I was not available to us before 1976 and therefore the well attested diagnostic help from this procedure was not forthcoming.[14] However, scanning 17 and 24 months after the probable adrenal necrosis showed no adrenal image on either side. This is surprising since, biochemically, the patient showed normal adrenal function in terms of aldosterone and cortisol excretion.

Adrenal examination by aortography and selective renal angiography did not define further the cause of the primary aldosteronism beyond the information given by venography; this is consistent with previous reports.[7] The examination did, however, reveal left-sided renal artery stenosis. The incidence of concurrence of hyperaldosteronism and renal vascular stenosis has been reported recently as approximately 7.5%.[15] This rate is similar to that for hypertension in general. Bilateral estimation of plasma renin activity in the renal veins has shown no evidence of differential function, nor has intravenous pyelography, isotope renography or renal scanning.

The recurrence of hypertension in our patient 15 months after spironolactone therapy was discontinued is not an unusual finding. Previous reports have shown elevated blood pressure in up to 40% of patients with an adrenal adenoma treated surgically.[16] Investigation in our patient did not show a new cause for her hypertension. In particular, the known renal artery stenosis was not believed to be the cause and no recurrence of hyperaldosteronism was documented.

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References

1. Horton R: Aldosterone: review of its physiology and diagnostic aspects of primary hyperaldosteronism. *Metabolism* 22: 1525, 1973
2. Bookstein JJ, Conn J, Reuter SR: Intra-adrenal hemorrhage as a complication of adrenal venography in primary aldosteronism. *Radiology* 90: 778, 1968
3. Fisher CE, Turner FA, Horton R: Remismission of primary hyperaldosteronism after adrenal venography. *N Engl J Med* 285: 334, 1971
4. Eagan RT, Page IM: Adrenal insufficiency following bilateral adrenal venography. *JAMA* 215: 115, 1971
5. Castleman B, Scully RE, McNeely BU (eds): Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 39-1972. *N Engl J Med* 287: 656, 1972
6. Taylor HC, Sachs CR, Bravo EL: Primary aldosteronism: remission and development of adrenal insufficiency after adrenal venography. *Ann Intern Med* 85: 207, 1976
7. Kahn PC, Kelleher MD, Egdahl RH, et al: Adrenal arteriography and venography in primary aldosteronism. *Radiology* 101: 71, 1971
8. Kaplan N: Commentary on the incidence of primary aldosteronism: current estimations based on objective data. *Arch Intern Med* 123: 152, 1969
9. Conn JW, Rovner DR, Cohen EL, et al: Normokalemic primary aldosteronism: its masquerade as "essential" hypertension. *JAMA* 195: 111, 1966
10. Biglieri EG, Stockigt JR, Schambelan M: Adrenal mineralocorticoids causing hypertension. *Am J Med* 52: 623, 1972
11. Sutherland DJA, Ruse JL, Laidlaw JC: Hypertension, increased aldosterone secretion and low plasma renin activity relieved by dexamethasone. *Can Med Assoc J* 95: 1109, 1966
12. Ferriss JB, Brown JJ, Fraser R, et al: Hypertension with aldosterone excess and low plasma renin: pre-operative distinction between patients with and without adrenocortical tumour. *Lancet* 2: 995, 1970
13. Horton H, Finck E: Diagnosis and localization in primary aldosteronism. *Ann Intern Med* 76: 885, 1972
14. Hogan MJ, McCrae J, Schambelan M, et al: Location of aldosterone-producing adenomas with ^{131}I-19-iodocholesterol. *N Engl J Med* 294: 410, 1976
15. Beevers DG, Brown JJ, Ferriss JB, et al: Renal abnormalities and vascular complications in primary hyperaldosteronism: evidence on tertiary hyperaldosteronism. *Q J Med* 44: 401, 1976
16. Biglieri EG, Schambelan M, Slaton PE: The intercurrent hypertension of primary aldosteronism. *Circ Res* 27 (suppl I): 1195, 1970

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continued from page 786

UROLOGIC PATHOLOGY: The Prostate. Myron Tannenbaum. 419 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1977. $34.95. ISBN 0-8121-0546-X

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