Primary aldosteronism

The signs and symptoms of primary aldosteronism are non-specific and common. The disease is characterized by hypertension and hypokalaemia, caused by excessive aldosterone secretion. Differential diagnosis between the various subgroups of primary aldosteronism remains a problem in endocrinology. The first reported patient with hyperaldosteronism had an adrenocortical adenoma and was cured after unilateral adrenalectomy. Initially, it was believed that 10–20 per cent of hypertensive patients might have primary aldosteronism which could be improved by operation, but more recent studies have estimated the prevalence of primary aldosteronism among hypertensives at between 0.05 and 2 per cent. Such a rare disease is easily overlooked. A mean duration of hypertension of 7–8 years before diagnosis of primary aldosteronism demonstrates the importance of clinical awareness. Furthermore, several subtypes of primary aldosteronism have been recognized which need to be distinguished from each other and which require different treatments.

Classification of the different forms of primary aldosteronism is based on endocrinological and radiological evaluation. Patients must be potassium repleted, have an adequate sodium intake, and antihypertensive drugs should be withheld to remove their influence on the renin–angiotensin–aldosterone system. For a patient with suspected hyperaldosteronism, investigation is best started by determining 24-h urinary aldosterone excretion and plasma renin activity. High urinary aldosterone excretion and low plasma renin activity are consistent with primary aldosteronism. At this stage, a more sophisticated endocrinological investigation should be initiated.

The six subgroups of primary aldosteronism so far recognized are: (1) adrenocortical adenoma; (2) bilateral adrenocortical hyperplasia (idiopathic hyperaldosteronism (IHA)); (3) adrenocortical carcinoma; (4) glucocorticoid-suppressible hyperaldosteronism; (5) renin-responsive adrenocortical adenoma; and (6) primary adrenocortical hyperplasia. More than 60 per cent of patients with primary aldosteronism have a single benign adrenocortical adenoma; about 20 per cent have IHA.

The adenomas are usually adrenocorticotrophic hormone (ACTH) dependent while IHA is renin–angiotensin dependent. Thus, patients with adenomas have a cortisol-like plasma aldosterone diurnal variation. The ACTH-dependent disease can also be demonstrated by a postural test showing decreased or constant levels of plasma aldosterone when changing from rest to ambulation. A postural increase of plasma aldosterone favours a renin–angiotensin-dependent disease. An aldosterone-producing adrenocortical carcinoma responds to neither ACTH nor angiotensin; it is usually > 5 cm in diameter and has a pathological steroid production. Glucocorticoid-suppressible hyperaldosteronism is identified by a dexamethasone suppression test and the two last subgroups are extremely rare.

Localization should not be undertaken until the diagnosis is established, as non-hyperfunctioning adrenal tumours are common in the hypertensive population. A majority (80 per cent) of aldosterone-producing adrenocortical tumours are > 1 cm in diameter and are detectable by computed tomography, magnetic resonance imaging and ultrasonography. However, small (< 1 cm in size) intraglandular aldosterone-producing adenomas do exist, and so in many cases of primary aldosteronism it is advisable to perform localization not only of a tumour, but also of hyperfunction. A high aldosterone:cortisol ratio in the adrenal venous effluent provides the best localizing accuracy, with a precision of up to 95 per cent. Adrenal scintigraphy using 68Ga-131I jodomethyl-19-norcholesterol during dexamethasone inhibition of the adrenal cortex provides a functional localization of just over 70 per cent in primary aldosteronism.

For patients with a unilateral adrenocortical adenoma, a unilateral ACTH-dependent hyperplasia, or an adrenocortical carcinoma, adrenalectomy should be performed. We prefer an extraperitoneal approach using a flank incision. Resecting the 11th or 12th rib offers excellent exposure for smaller benign lesions, and a thoracoabdominal incision is reserved for large and often malignant tumours. Patients with IHA and glucocorticoid-suppressible hyperaldosteronism should be managed medically, with spironolactone and glucocorticoids respectively.
The typical aldosterone-producing adrenocortical adenoma has a golden-yellow colour and may be completely or partially encapsulated. Large, lipid-laden, clear zona fasciculata-like cells dominate, and the adjacent cortex is slightly atrophic. In atypical cases adenosomas, nodules and hyperplasia may coexist and a definite histopathological diagnosis cannot always be obtained.

Most patients with an aldosterone-producing adrenal adenoma become normotensive within a few days of operation and long-term cure rates vary from 69 to 89 per cent. Those with persistent hypertension respond favourably to conventional antihypertensive treatment. The results of adrenal surgery for primary aldosteronism depend mainly on the accuracy of preoperative biochemical evaluation and tumour location.

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