primary aldosteronism [created by Paul Young 05/12/07]

general

- primary aldosteronism is recognized to be the most common form of secondary hypertension. Using the plasma aldosterone to plasma renin activity ratio as a case-finding test, followed by aldosterone suppression confirmatory testing, has resulted in much higher prevalence estimates of 5-13% of all patients with hypertension.

subtypes

Aldosterone-producing adenoma (APA) – 35% of cases
Bilateral idiopathic hyperplasia (IHA) – 60% of cases
Primary (unilateral) adrenal hyperplasia –2% of cases
Pure aldosterone-producing adrenocortical carcinoma – < 1% of cases
Familial hyperaldosteronism (FH)
Glucocorticoid-remediable aldosteronism (FH type I) – < 1% of cases
FH type II (APA or IHA) –?% of cases
Ectopic aldosterone-producing adenoma or carcinoma – < 0·1% of cases

features

- Patients with marked hypokalaemia may have muscle weakness and cramping, headaches, palpitations, polydipsia, polyuria, nocturia, or a combination of these. The polyuria and nocturia are a result of hypokalaemia-induced renal concentrating defect and the presentation is frequently mistaken for prostatism in men.
- The degree of hypertension is usually moderate to severe and may be resistant to usual pharmacological treatments.
- Hypokalaemia is frequently absent; thus, all patients with hypertension are candidates for this disorder
- Because of a reset osmostat, the serum sodium concentration tends to be high-normal or slightly above the upper limit of normal. This clinical clue is very useful when initially assessing the potential for primary aldosteronism.

initial investigation

When to Consider Testing for Primary Aldosteronism:
- Hypertension and hypokalemia
- Resistant hypertension
- Adrenal incidentaloma and hypertension
- Onset of hypertension at a young age (< 20 y)
- Severe hypertension (≥ 160 mm Hg systolic or ≥ 100 mm Hg diastolic)
- Whenever considering secondary hypertension

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Morning blood sample in seated ambulant patient
- Plasma aldosterone concentration (PAC)
- Plasma renin activity (PRA or PRC)

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↑ PAC (≥ 416 pmol/l; ≥ 15 ng/dl)
↓ PRA (< 1·0 ng/ml per hour) or ↓ PRC (< lower limit of detection for the assay)

and

PAC/PRA ratio ≥ 555 pmol/l per ng/ml per hour (≥ 20 ng/dl per ng/ml per hour)

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Investigate for Primary Aldosteronism

- Mineralocorticoid receptor antagonists (e.g. spironolactone and eplerenone) and high-dose amiloride are the only medications that absolutely interfere with interpretation of the ratio and should be discontinued at least 6 weeks before testing.
- Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor antagonists (ARB) and diuretics have the potential to 'falsely elevate' PRA. Therefore, in a patient treated with an ACE inhibitor, ARB or diuretic the finding of a detectable PRA level or a low PAC:PRA ratio does not exclude the diagnosis of primary aldosteronism. However, a very useful clinical point is that when a PRA level is undetectably low in a patient taking an ACE inhibitor, ARB or a diuretic, primary aldosteronism should be highly suspect.
- Adrenergic inhibitors (e.g. beta-adrenergic blockers and central alpha-2 agonists) suppress renin secretion, but also in turn suppress aldosterone secretion (although to a lesser degree than renin) in normal individuals; thus, although the PAC/PRA may rise in hypertensive patients without primary aldosteronism treated with adrenergic inhibitors, the PAC remains less than 416 pmol/l (15 ng/dl) and the case finding test is not significantly affected.

confirmatory testing

- It is impossible to interpret data obtained from patients receiving treatment with mineralocorticoid receptor antagonists (e.g. spironolactone, eplerenone) or high-dose amiloride when PRA is not suppressed. Therefore, treatment with a mineralocorticoid receptor antagonist should not be initiated until the evaluation has been completed and the final decisions about treatment have been made
- Aldosterone suppression testing can be performed with orally administered sodium chloride and measurement of urinary aldosterone or with intravenous sodium chloride loading and measurement of PAC.

approach to primary aldosteronism

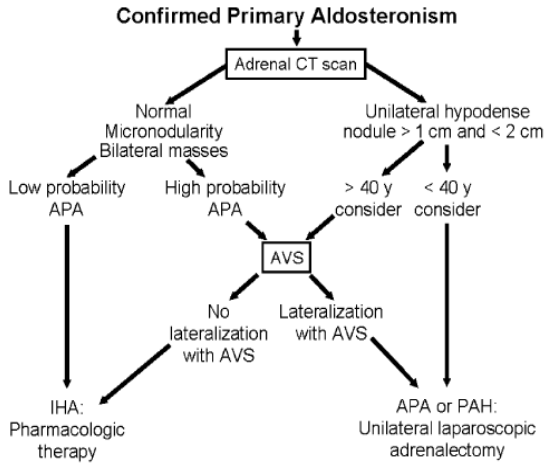

Fig. 2 Subtype evaluation of primary aldosteronism. See text for details. APA, aldosterone-producing adenoma; AVS, adrenal venous sampling; CT, computed tomography; IHA, idiopathic hyperaldosteronism; PAH, primary adrenal hyperplasia. (Modified from Young & Hogan.[64])

treatment

general
- Unilateral adrenalectomy in patients with APA or unilateral adrenal hyperplasia results in normalization of hypokalaemia in all these patients; hypertension is improved in all and is cured in approximately 30-60% of them.
- In bilateral adrenal forms of primary aldosteronism, unilateral or bilateral adrenalectomy seldom corrects the hypertension and they should be treated medically with a mineralocorticoid receptor antagonist.

surgical treatment
- Unilateral laparoscopic adrenalectomy is an excellent treatment option for patients with APA or unilateral hyperplasia. Although blood pressure control improves in nearly 100% of patients postoperatively, average long-term cure rates of hypertension after unilateral adrenalectomy for APA range from 30% to 72%.

Pharmacological treatment
(i) General
- IHA and GRA should be treated medically. In addition, APA patients may be treated medically if the medical treatment includes mineralocorticoid receptor blockade.
- No placebo controlled randomized trials have evaluated the relative efficacy of drugs in the treatment of primary aldosteronism.
(ii) Spironolactone
- Spironolactone has been the drug of choice to treat primary aldosteronism for more than three decades. The dosage is 12.5-25 mg per day initially and is increased to 400 mg per day if necessary to achieve normokalaemia without the aid of oral potassium chloride supplementation. Hypokalaemia responds promptly, but hypertension may take as long as 4-8 weeks to be corrected. After several months of therapy, this dosage often can be decreased to as little as 25-50 mg per day
(iii) Eplerenone
- Eplerenone is a steroid-based antimineralocorticoid that acts as a competitive and selective aldosterone receptor antagonist and was approved by the FDA for the treatment of uncomplicated essential hypertension in late 2003. The 9,11-epoxide group in eplerenone results in a marked reduction of the molecule's progestational and anti-androgenic actions compared with spironolactone
- Treatment trials comparing the efficacy of eplerenone vs. spironolactone for the treatment of primary aldosteronism have not been published.