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3

Screening for primary aldosteronism

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Normokalaemic manifestation of primary aldosteronism is a frequent cause of secondary hypertension. It occurs in approximately 5–12% of all patients with hypertension, primarily patients with severe and uncontrolled blood pressure. Main causes are bilateral adrenal hyperplasia (2/3 of cases) and aldosterone-producing adenoma (1/3 of cases). Screening is performed by measurement of the aldosterone/renin ratio, which is raised in affected patients. Suspicion of primary aldosteronism due to a pathological ratio requires confirmatory testing e.g. by saline infusion test or fludrocortisone suppression test. If the diagnosis is confirmed, the underlying cause of aldosterone excess needs to be identified because therapy differs. First, adrenal imaging (CT/MRI) is performed, which is followed by postural testing in cases with a unilateral lesion. Concordant results confirm the diagnosis of an aldosterone-producing adenoma and allow treatment to proceed to adrenalectomy. In cases of equivocal results or normal/bilaterally enlarged adrenal glands on imaging, adrenal venous sampling must be performed for subtype differentiation.

Key words: primary aldosteronism; Conn's syndrome; aldosterone; renin; secondary hypertension.

INTRODUCTION

By definition, primary aldosteronism is a state of aldosterone excess with subsequently suppressed renin levels and is the leading – and often only – symptom of hypertension. In the decades following its first description in 1954 by Jerome W. Conn[1], primary aldosteronism was considered to be a rarity and to occur only in patients presenting with the triad of hypertension, hypokalaemia and alkalosis. In recent years,

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this disorder has become accepted as a far more frequent, and hence more important, cause of hypertension than was previously thought.[2,3]

This is mainly due to the increasing detection of cases with normokalaemic primary aldosteronism, which present as the majority of cases.[4,5] About 5–12% of hypertensives are estimated to have primary aldosteronism depending on the study population and diagnostic tests. Taking into account the fact that about one-third of the European population has arterial hypertension[6], it is roughly estimated that 1.5–3% of the population might be affected by primary aldosteronism.

In recent years, aldosterone has been recognised as contributing to the pathogenesis of cardiovascular disease by cardiac remodelling and vasculopathy. These effects seem to be, in part, independent of the blood pressure effect.[7,8] Clinical findings show that patients with primary aldosteronism have more severe end-organ damage than comparable essential hypertensives.[9,10] The Randomized Aldactone Evaluation Study (RALES) demonstrated survival benefit in chronic heart failure by aldosterone blockade.[11,12]

Thus, the frequency of primary aldosteronism, as well as the increased risk of cardiac, vascular and renal consequences of this condition, emphasise its importance and are put forward as an argument in favour of widespread screening for primary aldosteronism among the hypertensive population.

CLINICAL PRESENTATION

Clinically, primary aldosteronism is mainly asymptomatic or presents with symptoms of hypertension such as headache. About two-thirds of patients have normal potassium levels[13,14], which may, in part, be the consequence of a low dietary sodium intake obscuring hypokalaemia. In patients with low potassium, further symptoms related to hypokalaemia including muscle weakness, polydipsia, polyuria, paresthesia and tetany can be present.[15] Impaired glucose tolerance, diabetes mellitus and other manifestations of the metabolic syndrome are associated with primary aldosteronism.[16] Oedema seldomly occurs. Primary aldosteronism mainly affects patients between 40 and 50 years of age and females slightly more frequently than males.[17]

Blood pressure is often found to be refractory to common antihypertensives. There is a correlation between prevalence of primary aldosteronism and the number of antihypertensives patients require to control hypertension. The prevalence of primary aldosteronism is highest in those patients with stage III hypertension (>190/110 mmHg).[18] Systolic blood pressure in untreated patients will often be found to be in the range of WHO stage II (>160/100 mmHg) and above. Cases of normotensive primary aldosteronism have been described but are usually of no clinical relevance.[19]

In routine laboratory testing, there are no indicative changes except for hypokalaemia. Most patients, however, will present with normal potassium values although most normokalaemic patients are expected to have periods of hypokalaemia as well. The latter not only depends on the amount of mineralocorticoid excess but also on comedication and sodium intake.

AETIOLOGY

The principle cause of primary aldosteronism is bilateral adrenal hyperplasia (idiopathic primary aldosteronism) which occurs in approximately 2/3 of cases. A further 1/3 are due to an aldosterone-producing adenoma. Less frequent subtypes of primary