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Übersicht

Dexamethasone-Suppressible Hyperaldosteronism: Pathophysiology, Clinical Aspects, and New Insights into the Pathogenesis

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Summary. A profile of dexamethasone-suppressible hyperaldosteronism (DSH), a variant of primary aldosteronism, is drawn by reviewing its pathophysiological and clinical aspects. Genetic studies show no HLA linkage and point to an autosomal dominant mode of inheritance, suggesting that the prevalence of this disease has been underestimated in the past. Hypertension, hypokalemia, suppressed renin, and high aldosterone values characterize DSH in the basal state, similar to the other forms of primary aldosteronism, i.e., aldosterone-producing adenoma (APA) or bilateral idiopathic adrenal hyperplasia (IAH). Biochemically DSH and APA can be differentiated from IAH since in both aldosterone does not respond to upright posture, to angiotensin II infusion, and to angiotensin-converting enzyme (ACE) captopril. In contrast, morphologically DSH is similar to IAH, since neither macroscopic nor histologic examinations of the adrenals give evidence of any unilateral abnormality. However, DSH is differentiated from APA and IAH by the hyperresponsiveness of aldosterone to acute ACTH administration as well as by the failure of aldosterone to escape from prolonged ACTH stimulation. The final diagnosis of DSH rests upon the prompt reversal of the features of mineralocorticoid excess by glucocorticoid therapy. In some cases hypertension is unresponsive to dexamethasone and needs alternative treatment. The main pathogenetic hypotheses point to a pituitary and/or an adrenal abnormality, but the intrinsic nature of the disease remains to be elucidated.

Key words: Dexamethasone-suppressible hyperaldosteronism – Pathogenesis – Diagnosis – Treatment

Aldosterone-producing adenoma (APA) and bilateral idiopathic adrenal hyperplasia (IAH) are the most common causes of primary aldosteronism [3, 4, 11, 56]. In 1966 Sutherland et al. described a variant of primary aldosteronism which appeared to be familial and completely reversed by dexamethasone administration [52]. Since then 33 cases with dexamethasone-suppressible hyperaldosteronism (DSH), also known as glucocorticoid-suppressible (responsive) hyperaldosteronism, have been well documented [6, 8, 15, 19, 20, 25, 37, 41, 44, 58]. A few details on 15 additional cases diagnosed in Japan are also available [38]. To draw a profile of DSH, useful for the diagnosis and treatment, its pathophysiological and clinical aspects will be reviewed. Different hypotheses on the pathogenetic mechanisms underlying this condition will also be discussed.

Pathophysiological and Clinical Aspects

Geography-Race

DSH is distributed worldwide with 7 cases reported in Europe, 16 in Japan, 3 in Australia, and 24 in North America (one of Mexican and one

Abbreviations: ACE = angiotensin-converting enzyme; ACTH = adrenocorticotrophic hormone; APA = aldosterone-producing adenoma; B = corticosterone; DOC = deoxycorticosterone; DSH = dexamethasone-suppressible hyperaldosteronism; IAH = idiopathic adrenal hyperplasia; 18-OH DOC = 18-hydroxydeoxycorticosterone; 18-OH B = 18-hydroxycorticosterone; PRA = plasma renin activity