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CUSING S SYNDROME AND HYPERTENSION

ABSTRACT

Endogenous Cushing's syndrome is a clinical state resulting from prolonged, inappropriate exposure to excessive endogenous secretion of cortisol and hence excess circulating free cortisol, characterized by loss of the normal feedback mechanisms of the hypothalamo-pituitary-adrenal axis and the normal circadian rhythm of cortisol secretion. The etiology of Cushing's syndrome may be excessive ACTH secretion from the pituitary gland, ectopic ACTH secretion by nonpituitary tumor, or excessive autonomous secretion of cortisol from a hyperfunctioning adrenal adenoma or carcinoma. A 31 year-old men with 6-month history of hyperpigmentation, weight gain and proximal myopathy was refereed to Institute of Endocrinology for evaluation of hypercortisolism. At admission, patient had classic cushingoid habit with plethoric face, dermal and muscle atrophy, abdominal strie rubrae and centripetal obesity, with hypertension ranging from 150/90 to 200/110mmHg. The standard laboratory data showed hyperglycaemia and hypokaliemia with high potassium excretion level. The circadian rhythm of cortisol secretion was blunted, with moderately elevated ACTH level, and without cortisol suppression after low-dose and high-dose dexamethasone suppression test. Urinary 5HIAA was elevated. Abdominal and sellar region magnetic resonance imaging was negative.CRH stimulation resulted in ACTH increase of 87% of basal, but without significant increase of cortisol level, only 7%. Thoracal CT scan revealed 14mm mass in right apical pulmonary segment. A wedge resection of anterior segment of right upper lobe was performed. Tumor cells were immunoreactive for synaptophysin and neuron-specific enolase. The postoperative course was uneventful and the patient was discharged on glucocorticoid supplementation. Signs of Cushing's syndrome were in regression,

and patient remained normotensive and normoglycaemic without therapy.

The prevalence of hypertension in Cushing's syndrome is approximately 80% with high diagnostic utility. The hypertension is characterized by an alteration in the blood pressure circadian rhythm with loss of the nocturnal drop, and clinical evidence of end-organ damage. The development of hypertension reflects interplay of factors regulating plasma volume, peripheral vascular resistance, and cardiac output, and all of them are increased in Cushing's syndrome. In patients with ACTH-dependent Cushing's syndrome hypertension is more frequent implying that, in addition to cortisol, hypersecretion of other steroid biosynthesis intermediates such corticosteron and DOC, contributes to hypertension. Glucocorticoides appear to cause hypertension by mineralocorticoid-independent mechanisms including: increased production of angiotensin II; enhanced glucocorticoid-mediated vascular reactivity to vasoconstrictors; inhibition of extraneuronal uptake and degradation of catecholamines; inhibition of vasodilatatory systems such as kinins and prostaglandin's, shift in Na+ from intracellular to extracellular compartment; and increased cardiac output from the increased production of adrenalin due to enhanced PNMT activity in adrenal medula. In addition, glucocorticoids may exert some hypertensive effects on cardiovascular regulation through the CNS, via glucocorticoid and mineralocortiocoid receptors. It is likely that the hypertension contributes to morbidity and mortality in Cushing's syndrome.