

Ectopic expression of serotonin receptors in Adrenocorticotropin-Independent Macronodular Adrenal Hyperplasia Causing Cushing's Syndrome

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OBJECTIVES

Cushing's syndrome is most often ACTH-dependent. ACTH-independent macronodular adrenal hyperplasia (AIMAH) is a rare peripheral form of Cushing's syndrome but is by far the most interesting. In AIMAH, cortisol secretion is controlled by illegitimate membrane receptors. In the normal adrenal gland, agonists of 5-HT₄ receptors have a powerful effect on aldosterone secretion but little effect on cortisol secretion in vitro. The aim of our study is to describe the clinical and hormonal features of patients diagnosed with aberrant serotonin receptor expression.

METHODS

We report the cases of three patients diagnosed with bilateral AIMAH with Cushing's syndrome. The identification of aberrant receptors was performed according to the protocol of Lacroix 2010.

RESULTS

Case 1:

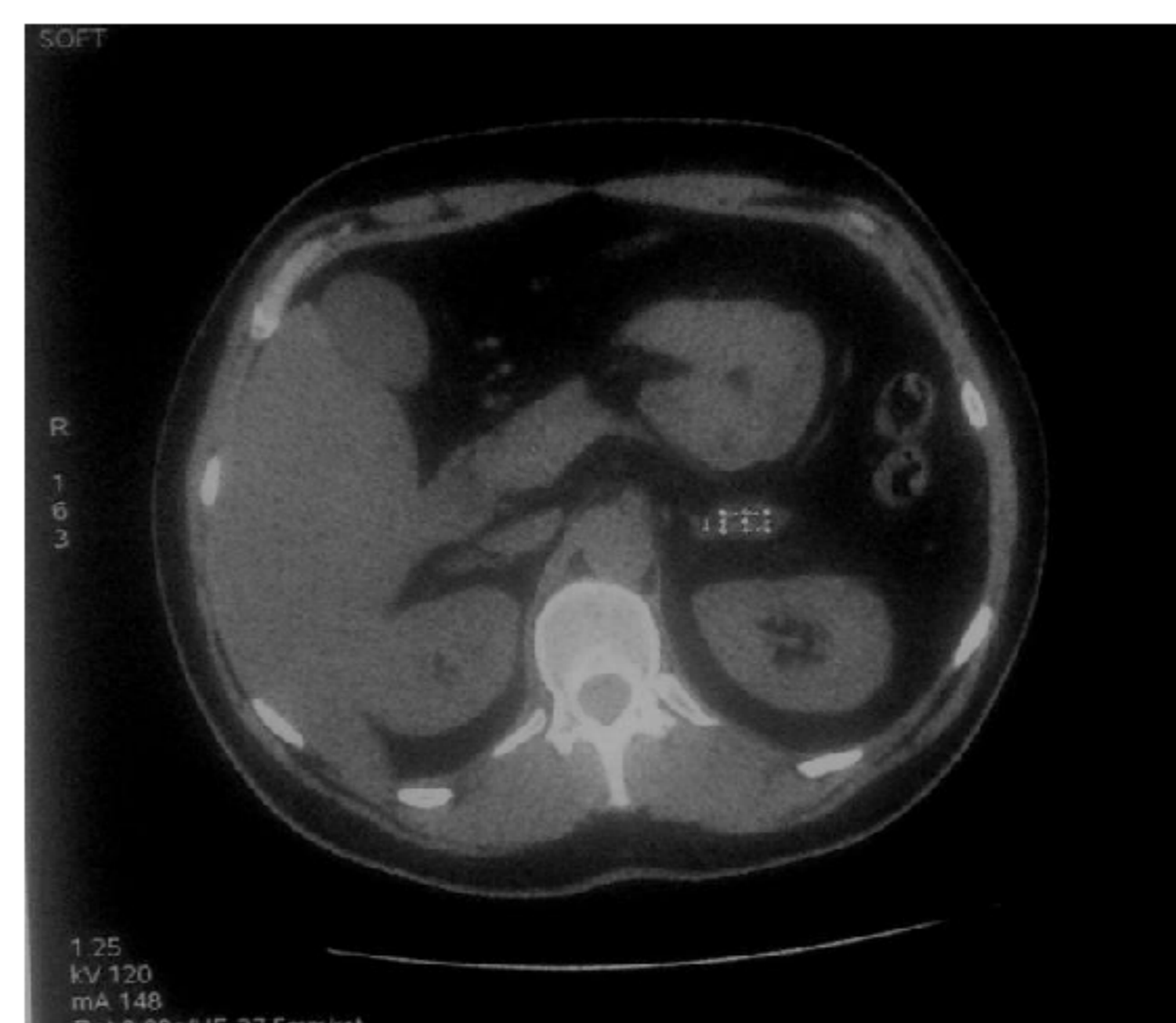
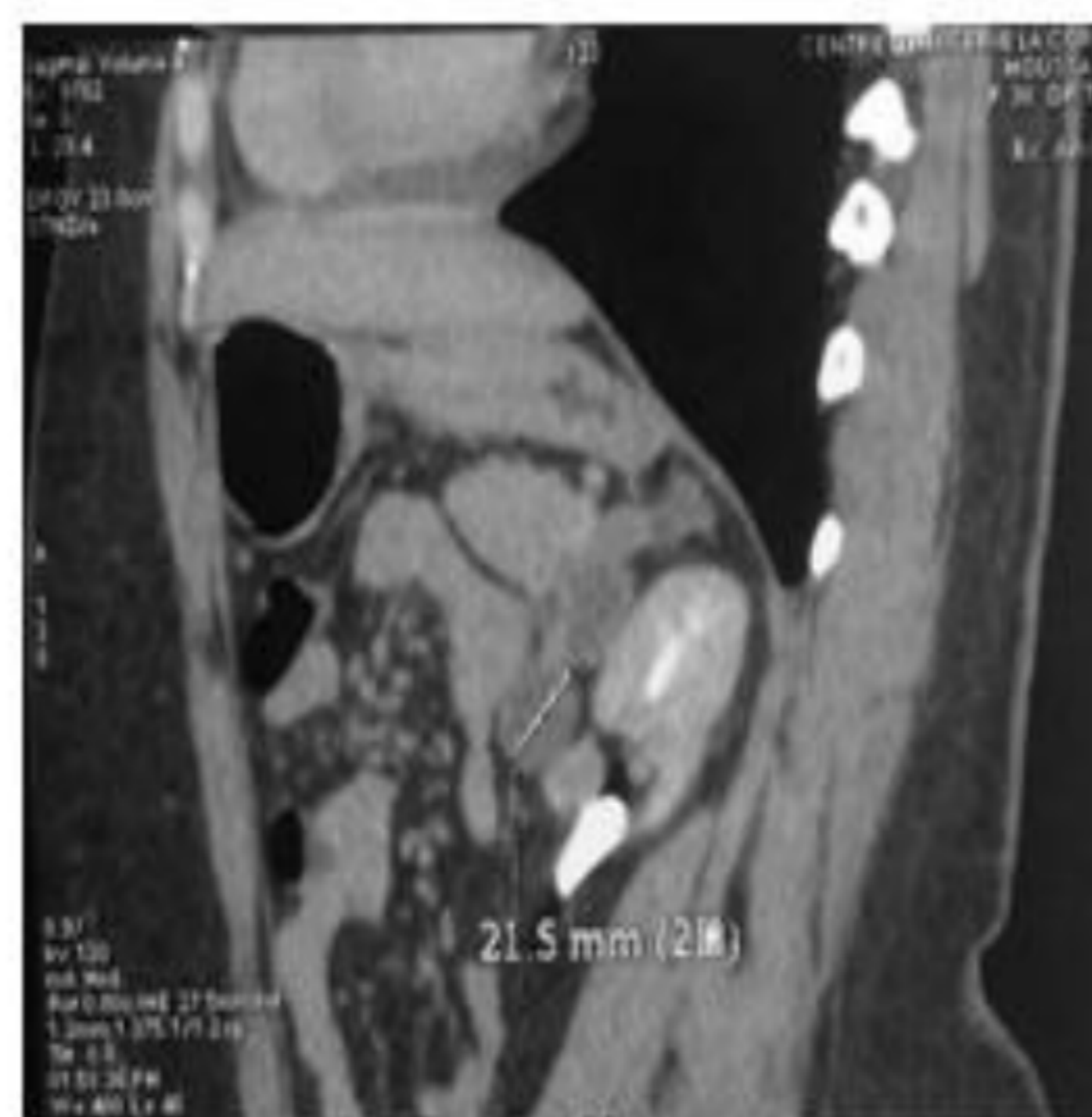
A 40 years old female patient presented with clinical Cushing's Syndrome. Hormonal investigations showed: serum cortisol = 260 ng/ml, ACTH = 10 pg/ml, post 1 mg dexamethasone suppression test cortisol level = 205 ng/ml. CT imaging showed a bilateral macronodular adrenal hyperplasia. The nodes measured 26 x 12 mm in the right and 15x 6 mm in the left adrenal gland. Identification of illegal receptors showed **aberrant receptors to serotonin and GIP.**

Case 2:

A 30 years old female patient presented with bilateral macronodular adrenal hyperplasia found in a CT scan. The adrenal nodes measured 12 mm and 26 mm in the right adrenal gland and 10 mm in the left adrenal gland. There was non clinical signs of Cushing's syndrome. The hormonal investigations showed: blood cortisol = 120 ng/ml, ACTH = 11 pg/ml and post 1 mg dexamethasone suppression test cortisol level = 18 ng/ml. Identification of illegal receptors showed **aberrant receptors to serotonin and Catecholamine.**

Case 3:

A 74 years old female patient presented with bilateral macronodular adrenal hyperplasia found in CT scan. The nodes measured 10 mm in the right and 12 mm in the left adrenal gland. There was no clinical signs of Cushing's syndrome. Hormonal investigations showed: blood cortisol = 230 ng/ml, ACTH = 9 pg/ml, and post 1 mg dexamethasone suppression test cortisol level = 35 ng/ml. Identification of illegal receptors showed **isolated aberrant receptors to serotonin.**



The radiological patterns of these three subtypes were similar, showing bilaterally enlarged adrenal glands with multiple nodules like ginger.

CONCLUSIONS

Serotonin receptors are probably the most functional receptors in AIMAH. Indeed their frequency is high in many published series. The simultaneous expression of several aberrant receptors linked to G protein makes difficult to identify the action of each receptor and the part of cooperation between the different receptors. The characterization of the pharmacological profiles of ectopic receptors in AIMAH provides opportunities for development of new pharmacological therapies. Because numerous adrenal hyperplastic tissues express more than one type of illegitimate receptor, drugs targeted to common transduction mechanisms of illegitimate receptors, including T-type calcium channel blockers, may prove to be useful for reducing cortisol synthesis and/or cellular proliferation in AIMAH.

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