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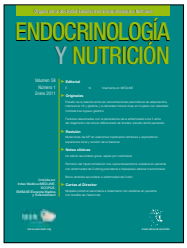

SCIENTIFIC LETTERS

Pathological thyroid uptake in Cushing's syndrome: An unexpected finding

Captación patológica tiroidea en síndrome de Cushing: un hallazgo inesperado

To the Editor:

Imaging tests indicated for the characterization of adrenal lesions include computed tomography (CT) scan and magnetic resonance imaging (MRI). Size, homogeneity, and lipid contents, as measured by Hounsfield units (HU), help distinguish benign from malignant lesions. There are however instances with indeterminate radiographic characteristics. Some studies support the use of positron emission tomography (PET) with 18-fluorodeoxyglucose (^{18}F-FDG) to assess these lesions.

However, what is used in principle to establish a diagnosis can become a tool for the diagnosis of unsuspected conditions.

We report a 34-year-old female patient with an unremarkable personal history except for carbohydrate intolerance. She was referred to the endocrinology clinic for abnormal thyroid function test results including free T4 levels of 0.79 ng/dL (0.9-1.7) and TSH levels of 0.84 µg/mL (0.27-4.5), which were not confirmed by repeat testing (free T4 1.14 ng/dL, TSH 0.64). The patient reported an increase in body hair, mainly in the limbs, over the previous two years and a weight gain of 16 kg in one year. She reported no hematoma, alopecia, or menstrual cycle changes.

Physical examination revealed blood pressure of 130-70 mmHg, heart rate of 74 bpm, moon face, and trunk obesity. Weight: 90.5 kg; height: 165.5 cm; BMI: 33.5 kg/m^2; waist circumference: 123 cm; and increased interscapular fat. Hirsutism, particularly in the face, was prominent (17 points on the Ferriman-Gallwey scale). Neck palpation found no goiter, thyroid nodules, or adenopathies. The examination was otherwise normal.

Cushing´s syndrome was suspected, and laboratory tests were performed with the following results: basal cortisol: 18.8 µg/dL (6.2-19.4); free cortisol in 24-h urine: 158 µg/24 h (22.2-128.5); plasma cortisol after dexamethasone 1 mg: 19.48 µg/dL; cortisol after dexamethasone 0.5 mg every 6 h for 2 days: 16 µg/dL; cortisol at 23 h: 12.75 µg/dL; cortisol after strong suppression with dexamethasone 8 mg: 14.48 µg/dL; ACTH: < 5 pg/mL; androstenedione: 1.5 (0.2-3.1 ng/mL), DHEA-S: < 15 (35-430 µg/dL).

Based on the diagnosis of a non ACTH-dependent Cushing's syndrome of adrenal origin, abdominal MRI was performed (Fig. 1). The image showed a left adrenal mass 3 cm in size with no signal loss in the opposite phase, which could not therefore be confirmed as being an adenoma. An abdominal CT scan showed the same lesion with indeterminate radiographic characteristics. Malignancy could not therefore be ruled out. An additional imaging test, a PET/CT with ^{18}F-FDG (Fig. 2), was thus requested. This showed the left adrenal nodule with a maximum standard uptake value (SUV) of 2.66, lower than SUV in the liver (3.4), and benign metabolic criteria. At neck level, a mild intensity deposit was seen in the left thyroid lobe with a maximum SUV of 2.76 (lower than maximum SUV in mediastinum), suggesting malignancy. Thyroid ultrasound examination confirmed a

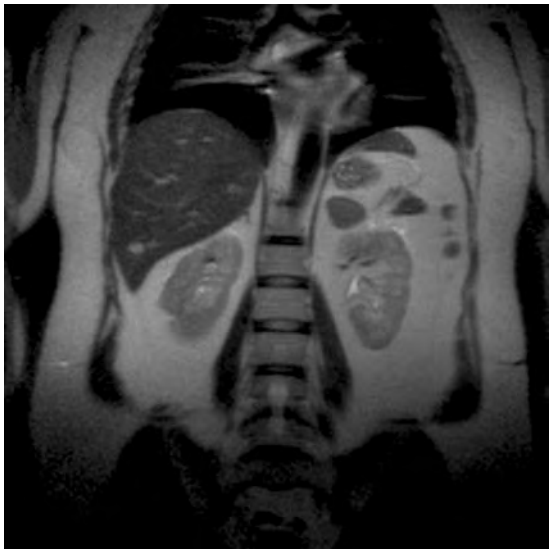

Figure 1 MRI of abdomen. Left adrenal mass 3 cm in size with indeterminate characteristics.

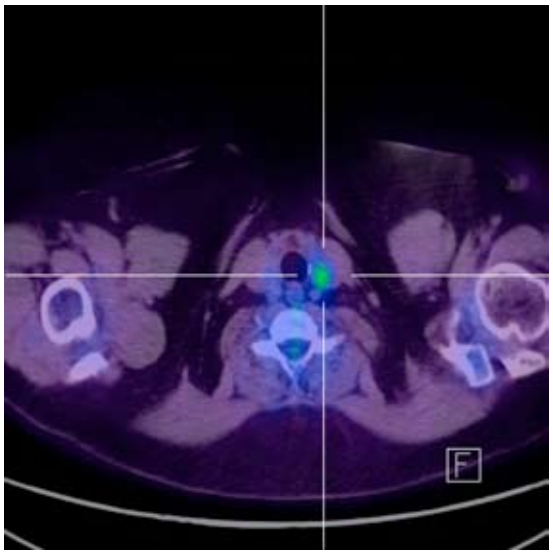

Figure 2 PET/CT with ^{18}F-FDG. Mild intensity deposit in left thyroid lobe.

1-cm hypoechogenic lesion, and FNA suggested papillary carcinoma.

Left laparoscopic adrenalectomy was performed, followed by pathological examination of the adrenal adenoma. Hydrocortisone was administered perioperatively and at hospital discharge. Subsequent total thyroidectomy with complete removal of the central neck lymph nodes revealed a stage pT3 papillary thyroid carcinoma, 1 x 0.9 x 0.9 cm in size, with no nodal involvement and focal extension to perithyroid soft tissues. An ablation dose of ^{131}I (150 mCi) was administered, and at the time of writing there is no trace of the disease. The patient is on replacement therapy with hydroaltesone and levothyroxine with good hormone control. She reports an improvement of hirsutism and a significant weight loss with normalization of carbohydrate metabolism.

Small (< 4 cm) homogeneous adrenal masses with smooth, rounded contours suggest a benign condition, particularly if they have a density lower than 10 HUs and show fast contrast elimination in CT, or are isointense with the liver in T1 and T2 in MRI. Irregular, heterogeneous lesions with calcification and > 4 cm in size suggest malignancy, especially if they also have a density higher than 20 HUs in CT and show irregular contrast uptake and delayed contrast elimination. Hypointensity as compared to liver in T1 and high density in T2 in MRI suggest a malignant lesion. However, diagnosis is not always easy, and the radiologist's report sometimes states: "adrenal lesion with indeterminate characteristics" or "malignancy cannot be ruled out". In the reported case, a Cushing's syndrome secondary to adrenal adenoma was suspected, but the nature of such a lesion could not be distinguished because, although uncommon, there are adrenal carcinomas which cause hormone overproduction, and the final radiographic diagnosis had both therapeutic and prognostic implications. A PET/CT with ^{18}F-FDG was therefore performed. This procedure provides metabolic information about the functional characteristics of lesions, but little morphological information[1]. When combined with CT, PET/CT allows for the merging and correlating of anatomical and functional images.

Adrenal glands do not take up FDG under normal conditions[2]. Malignant lesions show an increased uptake, but this may also occur in glands with benign conditions. There are studies supporting the value of ^{18}F-FDG PET/CT for differentiating malignant and benign adrenal lesions in patients with no history of neoplasm[3,4]. In the Tenenbaum et al. study[5], using the SUV index only, the predictive value of ^{18}F-FDG was good, but the authors recognized that it was imperfect. Using a cut-off point of 3.4 they achieved a 100% sensitivity for an accurate diagnosis of all malignant lesions, although specificity for differentiating adenoma from carcinoma was only 70%. Thus, a negative or fainter uptake in PET/CT is highly predictive of a benign lesion and may help prevent surgery or delay it if necessary. If surgery is indicated, PET/CT may help in the selection of a less invasive surgical approach[6].

On the other hand, mild diffuse and homogeneous uptake may be seen in the thyroid gland (although it is absent in most cases). In chronic thyroiditis of Graves-Basedow disease, a diffuse, symmetrical FDG metabolic increase may be seen. A more heterogeneous uptake is usually identified in multinodular goiter. Incidental focal uptake occurs in 1%-4% of PET/CT studies in oncological patients with no thyroid disease. This may represent autonomous hyperfunctioning nodules or benign tumors such as Hürthle cell adenoma and follicular adenoma. It is however important to rule out primary malignant disease because it has been found in a non negligible percentage of these uptakes (from 14% to 63% depending on the series)[7].

The studies so far conducted have not been able to conclude what uptake index is most helpful for discriminating benign from malignant thyroid lesions, but agreement exists as to the usefulness of studying all thyroid focal lesions found in PET/CT because of the high probability of a malignant lesion[8].

To conclude, the performance of PET/CT was helpful both in arriving at a more precise definition of the adrenal mass causing Cushing's syndrome, and in identifying a malignant subcentimetric thyroid lesion which would otherwise have been overlooked, and so changed the therapeutic approach to the patient.

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Pituitary apoplexy due to macroadenoma bleeding

Apoplejía hipofisaria por sangrado de macroadenoma

A 54-year-old male attended the emergency room for sudden bifrontal headache, nausea, and vomiting. Nine years previously, he had experienced a similar condition associated with diplopia and had been diagnosed a non-secretory pituitary macroadenoma (Fig. 1 A-B) with secondary panhypopituitarism (TSH 0.026 mcU/mL, T4 0.54 ng/dL, basal prolactin 1.88 ng/mL, FSH 1.01 mIU/mL, LH < 0.5 mIU/mL, ACTH < 10 pg/mL, cortisol < 1 µg/dL, GH < 0.3 ng/mL). The patient had refused any therapeutic intervention other than hormone replacement therapy.

Physical examination revealed partial paresis of the right third cranial nerve with no campimetric or visual acuity deficits. Both CT and MRI of the head showed a 2.6 x 2.3 cm pituitary adenoma which had increased in size since the previous examination, extending to the chiasm without compressing it and had recent intratumoral bleeding (Fig. 2 A-B). Based on a diagnosis of pituitary apoplexy (PA) due to macroadenoma bleeding, transsphenoidal hypophysectomy with evacuation of intratumoral hematoma was performed with no complications. The postoperative course was uneventful, with complete neurological recovery.

PA is an uncommon complication in the course of pituitary tumors. It is caused by a sudden expansion of the pituitary gland secondary to an ischemic or hemorrhagic infarction which almost invariably occurs in the presence of a pituitary adenoma. The true incidence of PA is difficult to establish because pituitary tumor bleeding is often asymptomatic. The reported data suggest that up to 25.7% of pituitary tumors exhibit some degree of surgically documented bleeding[1]. However, PA occurs as a syndrome in 0.6%-21% of the cases[2-5]. In addition, a vast majority of them occur in non-functioning adenomas (77% in the Semple et al series[6]). The rapid growth of sellar contents compresses both adjacent structures and pituitary vascularization and causes sudden headache, vomiting, disorders, oculomotor nerve palsy, meningism, impaired consciousness, and hypopituitarism. PA spontaneously occurs in 60%-80% of previously asymptomatic patients[7]. However, it has been reported as being associated with a number of triggering factors such as head trauma, arterial hypotension or hypertension, a history of irradiation, heart

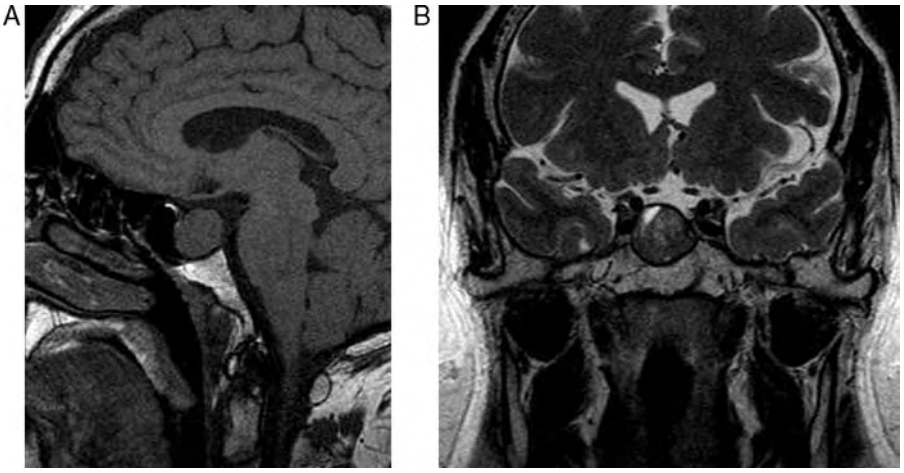

Figure 1