OPEN ACCESS

Saudi Journal of Medicine

Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) |ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Case Report

A Rare Case of Plurihormonal GH-ACTH Pituitary Adenoma Resulting in Acromegaly and Cushing's Disease: From a Case Report

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DOI: 10.36348/sjm.2021.v06i10.001 | **Received:** 22.08.2021 | **Accepted:** 29.09.2021 | **Published:** 02.10.2021

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Abstract

Plurihormonal pituitary adenomas are rare tumors that present cellular immunoreactivity for more than one pituitary hormone. The most common form is that combining growth hormone and prolactin, but the combination of growth hormone with adrenocorticotropic hormone causing Acromegaly and Cushing's disease is extremely rare and clinical signs may be subtle. We have demonstrated the clinicopathological characteristics of plurihormonal pituitary adenomas through the case of our 25-year-old patient who had a pituitary macroadenoma with an initial clinical picture dominated by acromegaly and mild cushingoid features.

Keywords: pituitary adenoma, plurihormonal, acromegaly, cushing's disease.

INTRODUCTION

Pituitary adenomas are well-differentiated benign tumors that may or may not be secreting. About half of pituitary adenomas secrete distinct pituitary hormones, most often prolactin (PRL), growth hormone (GH) or adrenocorticotropic hormone (ACTH) [1]. Plurihormonal adenomas represent approximately 10 to 15% of pituitary adenomas [2].

Immunohistochemistry can detect other anterior pituitary hormone-secreting cells among GH-secreting cells and the most observed association is GH-prolactin co-secretion. GH and ACTH adenomas are very rare although a few cases have been described. We report a case of a pituitary macroadenoma producing both GH and ACTH resulting in acromegaly and Cushing's disease.

PATIENT AND OBSERVATION

A 25-year-old woman, with no particular history, presented between 2007 and 2016 a change in morphotype with sign of the ring, change in shoe size, enlargement of the nose, bulging fingers and toes. In 2019, the patient reported the occurrence of retro-orbital headaches with reduced visual acuity and a change in the tone of the voice becoming deep. In early 2020, the patient consulted for the first time for primary amenorrhea, the clinical examination noted a dysmorphic syndrome (prominent nose, thickened lips, bulging fingers and toes), homogeneous obesity (BMI 35.7 kg / m²), facial acne with moderate hirsutism rated at 23 according to the Ferriman and Gallwey score, no overt cushingoid syndrome (no faciotruncular obesity, no slender limbs, no buffalo hump, no purple stretch marks). A complete hypophysiogram was performed; revealing hypogonadotropic hypogonadism, the rest of the hypophysiogram was normal, in particular normal testosterone level at 0.5ng / ml and morning cortisolemia at 14µg / dl. IGF-1 was 3 times normal and ACTH was 26.5ng / L (Normal values 10.3- 48.3). A complement of pituitary MRI objectified an intra and suprasellar process measuring 2.7 * 2.4 * 1.9 cm arriving in contact with the optic chiasma, suggesting a pituitary macroadenoma (Figures 1 and 2). Acromegaly was mentioned, a MEN1 (multiple endocrine neoplasia type 1) assessment was performed without specificity, the patient was quickly operated on by the transphenoidal way. The anatomopathology noted a morphological aspect compatible with a pituitary adenoma and the evolution was marked by a transient diabetes insipidus with the onset 3 months postoperatively of a frank cushing syndrome with significant weight gain (weight gain of more than 20kg in 3 months), purple stretch marks on the abdominal area and the root of the limbs. The control pituitary

MRI noted an 8 mm suprasellar ectopic pituitary microadenoma, the control IGF-1 remained high at 373.3ng / ml (Normal values 105- 311) and the complement of immunohistochemistry carried out noted the expression anti GH and anti ACTH antibodies.

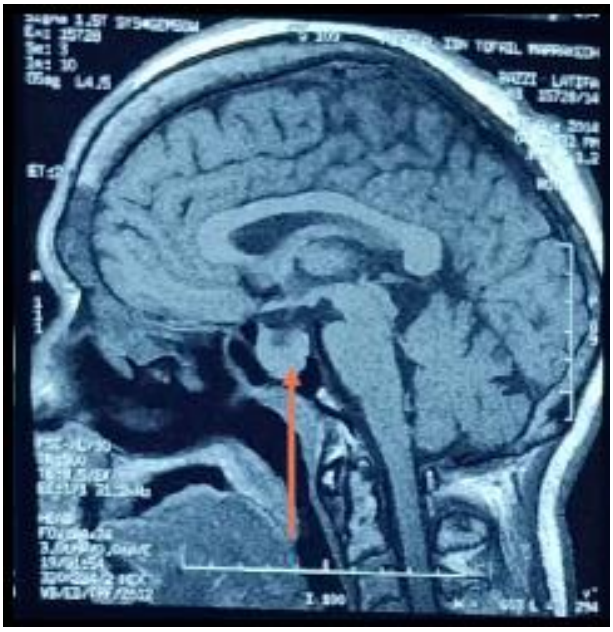

Fig-1: Macro pituitary adenoma on MRI, sagittal T1-weighted slice

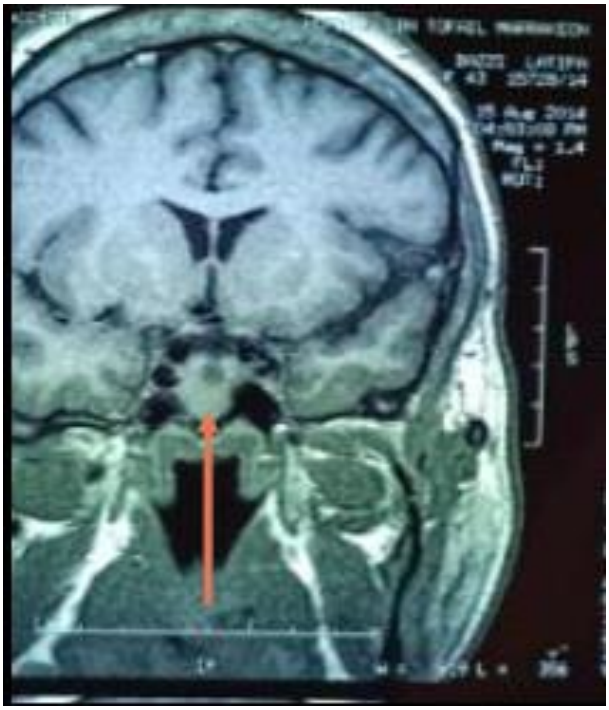

Fig-2: Macro pituitary adenoma on MRI, coronal T1-weighted slice

DISCUSSION

Pituitary adenomas may be revealed by pituitary tumor syndrome, hormonal hypersecretion syndrome, or anterior pituitary insufficiency. They are classified by immunohistochemical labeling, according to their somatotropic (GH), lactotropic (PRL), gonadotropic (FSH / LH), corticotropic (ACTH) or thyrotropic (TSH) contingent [3]. When at least 2 pituitary hormones are expressed, it is called a plurihormonal adenoma and the diagnosis is based on immunohistochemistry demonstrating significant and specific immunoreactivity to unrelated hormones using specific antisera, the positive transcription factor. Pituitary-specific 1 (PIT-1) regulates expression of GH, PRL and TSH, and steroidogenic factor 1 (STF-1) and endothelial transcription factor GATA 2 regulate expression of LH and FSH, ACTH expression is regulated by the tumor homeobox transcription factor19 (TBX 19, also called TPIT) [4]. Composite pituitary adenomas are macroadenomas in 80% of cases, with an invasive character in 50% of cases [2]. Our patient also presented a macroadenoma, with supra-sellar development coming into contact with the optic chiasma, leading to a pituitary tumor syndrome. Her IGF-1 was initially very high at 3 times normal, the level of GH was not measured, the levels of ACTH and cortisol were normal, but in Cushing's disease morning cortisol levels have no diagnostic value and ACTH may be normal or moderately elevated. The clinical picture was nevertheless very suggestive of acromegaly and there were no initially unequivocal signs of cushing's disease, apart from a few signs of hyperandrogenism such as facial acne, moderate hirsutism, deep voice. But hyperandrogenism can be observed both in Cushing's syndrome, in this case Cushing's disease, and in acromegaly, although more rarely, making this clinical picture of hyperandrogenism a non-decisive picture between the 2 pathologies. In addition, her obesity initially did not have the cushingoid characteristics in the sense that it was more a homogeneous obesity and not facio-truncal and was not accompanied by bison hump or purple stretch marks, leaving us thus in the diagnosis of acromegaly secondary to a pituitary macroadenoma. But when our patient developed very suggestive cushingoid features (purple stretch marks and very significant weight gain) in the postoperative period, the diagnosis of acromegaly alone was rediscussed a posteriori to include an association with Cushing's disease that was confirmed by the result of the immunohistochemistry that was requested in addition to the initial anatomopathology.

Plurihormonal adenomas can consist of one cell type secreting several hormones (monomorphs) or several cell types, each secreting a hormone (plurimorph) [5]. The clinical expression of plurihormonal adenomas does not always reflect the different hormonal secretions, in a series of 67 cases of multisecretory adenomas, only 7% had a pluri-secretory clinical expression [6]. Somatotropic adenomas often co-secrete prolactin, but ACTH co-secretion is rare and can be clinically difficult to diagnose because it is masked by the antagonistic effects of these hormones (GH and ACTH) on protein and lipid metabolism [7]. Generally in somatotropic and corticotropic

plurihormonal adenomas, the clinical picture is dominated by the secretion of GH because in all the reported cases of adenomas bi-secreting of GH and ACTH, the dominant clinical features were those of hypersecretion of GH [3], what we also found in our patient, and as in our patient in whom the initial clinical picture was more in favor of an overproduction of GH, it is frequent, in the rare cases reported, that plurihormonal pituitary adenomas co-secreting GH and ACTH do not present any clinical sign of cushing's syndrome, the authors refer to as subclinical cushing's disease [3]. A review of the literature based on a meta-analysis reported only 20 patients with a single pituitary adenoma simultaneously expressing GH and ACTH, of whom 4 had both clinical signs of acromegaly and Cushing's disease, 11 had only clinical signs of acromegaly and 2 presented only clinical signs of Cushing's disease, the 3 remaining presented pituitary apoplexy [8]. Our patient is therefore one of the very rare cases of plurihormonal GH-ACTH pituitary adenoma having presented clinical signs of acromegaly of cushing's disease although initially not very meaningful.

However, in our patient, we cannot completely exclude the absence of an initial clinical manifestation of ACTH hypersecretion; the signs of hyperandrogenism found such as moderate hirsutism could be part of the related clinical picture. Thus, the appearance in our patient at 3 months postoperatively of more obvious cushingoid clinical manifestations suggests that either that plurihormonal adenoma was predominantly GH and that the tumor residue is predominantly ACTH compared to the remaining cells, or the corticotropic secretion was a cyclic secretion with an initial eucorticism phase and which entered its hypercorticism phase from the tumor residue 3 months after surgery, or again the anabolic effects of GH masked the effects of hypercorticism on the metabolism explaining the mild preoperative cushingoid clinical characteristics.

CONCLUSION

It may be difficult to suspect the presence of a plurihormonal pituitary adenoma solely from preoperative clinical and biochemical features, but the absence of overt signs and symptoms does not indicate the absence of disease. Immunostaining remains the key diagnostic test. Our case is an additional case of plurihormonal GH-ACTH pituitary adenoma with both clinical signs of Acromegaly and Cushing's disease, thus completing a systematic review of the literature in 2018 which only documented about twenty cases of GH-ACTH plurihormonal pituitary adenomas, of which only about 20% showed clinical signs of both Acromegaly and Cushing's disease.

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