

## Gonadotropic pituitary adenomas: Two cases report

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### Abstract

The pituitary gonadotropic adenoma is an adenoma developed in the gonadotropic cells of the anterior pituitary. It can be secreting releasing in excess in blood and urine; the products of its secretion are gonadostimulines (F.S.H. and L.H.) or non-secreting in this case only histo- cytochemical analysis will be able to allow identification. We report two cases of macroadenoma with LH-FSH immunostaining. Pituitary magnetic resonance imaging revealed a macroadenoma. Transphenoidal surgery was incomplete. Immunohistochemical staining showed that the tumor cells were reactive to LH (70%) and FSH (30%). Control pituitary imaging revealed a residual macroadenoma and deficit replacement was started.

Hormonal testing for all patients with pituitary adenoma should be performed even in the absence of symptoms of hypersecretion. The treatment of gonadotropic adenomas is surgical. Complementary radiotherapy is usually indicated in case of postoperative tumor remnants with an effect on the prevention of recurrence. Medical treatment (dopaminergic agonists, somatostatin analogues, GnRH agonists and antagonists) is disappointing.

**Keywords:** Adénome gonadotrope; Immuno-cytochimie; Folliculostimulating hormone (FSH); Luteining hormone (LH)

### 1. Introduction

Gonadotropic adenoma occupies an important place in pituitary tumor pathology after prolactin, growth hormone and A.C.T.H adenomas [1]. Its diagnosis has benefited nowadays from radio-immunological assay of gonadostimulins, alpha and beta subunits and immuno- cytochemical studies [2]. Gonadotropic pituitary adenomas represent about 90% of non- functioning pituitary adenomas (NFPAs). They are most often macro adenomas, invasive in two thirds of cases, discovered during a pituitary tumor syndrome (visual impairment in more than half of the cases) or an anteropituitary insufficiency. They are exceptionally associated with clinical signs related to gonadotropin hypersecretion. We report the study of two cases of pituitary macroadenoma with positive follicle stimulating hormone (FSH), Luteining hormone (LH) immunostaining.

### 2. Observation 1

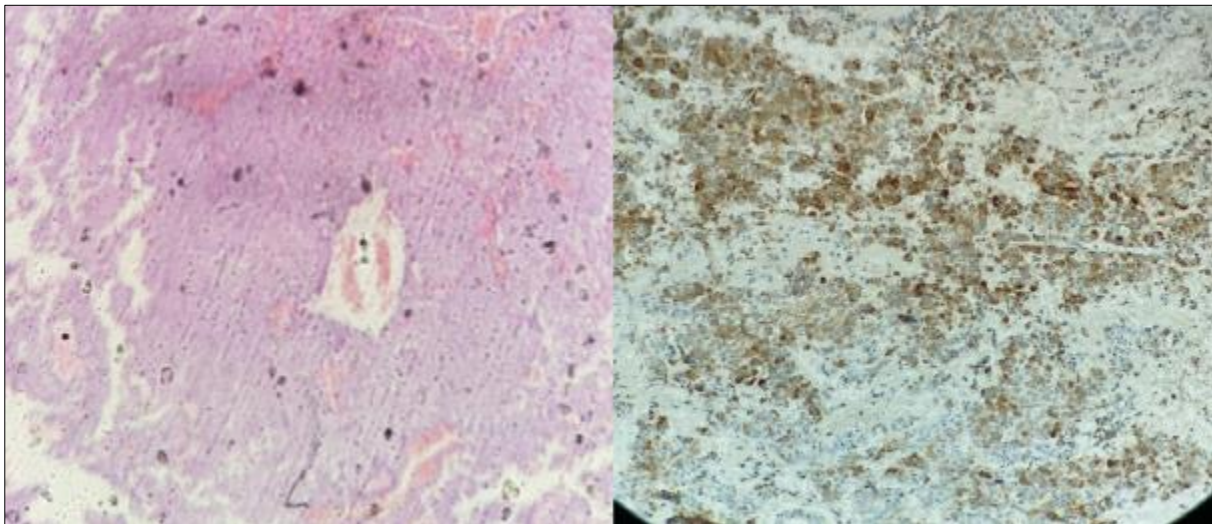
A 47-year-old female patient was referred to our hospital for a decrease in visual acuity predominantly in the right eye with frontotemporal headaches evolving for 3 years. Her medical history was unremarkable. On examination, she reported menstrual cycle disorders such as spaniomenorrhea and oligomenorrhea without any other signs of hypersecretion or antehypophyseal insufficiency. On physical examination, she had a heart rate of 83/minute, blood pressure of 114/81 mmHg, the initial hormonal assessment objectified a cortisolemia of 8h: 24.78ug/dl, follicle

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stimulating hormone (FSH) low: 9.88mUI /ml; luteinizing hormone (LH) low: 4. 89mUI /l; Low estradiol: 5pg/ml; Progesterone: 0.11ng/ml; Prolactin level: 25.3ng/ml; Normal TSH: 2.89 Uui/L; Thyroxine (T4): 6.47pmol /l low and triiodothyronine (T 3): 2.93pmol/l low, Blood electrolytes, renal and hepatic functions were normal. Pituitary magnetic resonance imaging revealed a 41 x 64 x 34 mm macroadenoma compressing the optic chiasm with subtentorial involvement. The visual field showed a tubular visual field in the right eye and a generalized agonal narrowing in the left eye. Trans-sphenoidal surgery was then performed. Immunohistochemical staining (Figure 1B) showed positive reactions to LH (70%). Postoperative pituitary MRI revealed a residual macroadenoma measuring 19mm x 18mm x 13mm and the patient was substituted for thyroid deficits with levothyrox50ug/d and corticotropic deficits: hydrocortisone 15mg/d

### 3. Observation 2

A 45-year-old patient was referred to our hospital for a bilateral visual acuity decrease evolving for 4 years. The medical history was unremarkable, with no headaches, no signs of deficient pituitary secretion and hypogonadism. On physical examination, he had a heart rate of 81 beats/minute and a blood pressure of 131/71 mmHg. Initial hormonal assessment: 8 h cortisol level low: 7.5ug/dl, follicle stimulating hormone (FSH) low: 6 mIU/ml; luteinizing hormone (LH) low: 1.9 mIU/ml; prolactin level: 8.1ng/ml; normal TSH: 2. 33 Uui/L; Thyroxine (T4) low limit: 11.36 pmol /l and triiodothyronine (T3): 3.4pmol/l normal; testosterone was not measured. Blood electrolytes, renal and liver functions were normal. Pituitary magnetic resonance imaging revealed a pituitary macroadenoma of 41 x 25 mm the 3 dimensions of measurements occupying the entire sella turcica with effacement of the optic chiasm, encompassing the carotid arteries and cavernous sinus. The visual field showed the right eye lost with narrowing of the isopters in the temporal field. Trans- sphenoidal surgery was then performed. Immunohistochemical staining (Figure1A) showed positive reactions to both FSH (30%). Postoperative pituitary magnetic resonance imaging (Figure 2) revealed a macro adenoma decrease in mass size by 20% (31 mm versus 41 mm), a visual field control still lost on the right and slight isopter narrowing in the temporal field on the left, and the patient was substituted for thyroid deficits by levothyrox50ug/d and corticotropic deficit: hydrocortisone 15mg/d;both patients are being followed up to evaluate residual tumor and gamma knife neurosurgery may be considered in this case



**Figure 1** (a) Immunohistochemical staining showed that the tumor cells were strongly reactive to follicle stimulating hormone (FSH) (30%) and reactive to luteinizing hormone (LH) (70%) (b)



**Figure 2** Sagittal slices in T1 A mass which is measured as 31 mm

#### 4. Discussion

The characterization of clinically silent adenomas or apparently non-secreting adenomas could be refined thanks to the progress of immunocytochemistry. During the 1980s, immunohistochemistry became the reference tool for classifying pituitary tumors and made it possible to completely revise the prevalence of the different histotypes. Gonadotropic adenomas were considered rare because their identification was based on plasma gonadotropin assays alone, which were often low [3]; series reported 2 to 5% of gonadotropic adenomas. In current series, 12 to 17% of operated adenomas are gonadotropic [4]; some studies even report figures as high as 30 to 37% [5]. Patients without hyperprolactinemia-related amenorrhea-galactorrhea syndrome, acromegaly, or Cushing's syndrome are considered to have 60-70% positive immunostaining for  $\beta$ FSH (Follicle-stimulating Hormone or follicle stimulating hormone),  $\beta$ LH (Luteinizing Hormone or luteinizing hormone), or for the  $\alpha$ -subunit of glycoproteins [4]. Silent gonadotrophs are defined as clinically nonfunctional adenomas despite FSH-LH immunopositivity. The pathophysiological mechanisms of these adenomas still remain, very mysterious, none of the numerous studies done on the subject allowing to retain an unequivocal mechanism at the origin of the development of these pituitary tumors. They are diagnosed incidentally or following neuro-ophthalmological symptoms: headache, bitemporal hemianopia and signs of hypogonadism: sexual impotence and amenorrhea [6]. In the study of our two cases, there is a constant decrease of gonadostimulines F.S.H, L. H, which in non-menopausal women in the presence of neuro-ophthalmologic signs, should draw attention [7]; Although clinically there was no evidence of ovarian or testicular gonadal hyperstimulation, focal staining with FSH and LH was detected by immunohistochemistry. The first-line treatment of gonadotropic adenomas is neurosurgery with good postoperative results in our two cases (improvement of neuro-ophthalmological signs), but complete excision of the tumor is rare because silent gonadotropic adenomas are diagnosed in case of enlarged macroadenomas. Only 1/3 of patients are cured by surgery. Other therapeutic options when surgery is incomplete or contraindicated are irradiation, somatostatin analogues and dopamine agonists. When the tumor residue or recurrence is small and located at a reasonable distance from the optic chiasm (> 5 mm), stereotactic radiosurgery, especially gamma-knife, can be proposed [8-9-10].

#### 5. Conclusion

Gonadotropic pituitary adenomas have become an important chapter in pituitary pathology due to advances in immunocytochemistry as described in this study. A comprehensive hormonal evaluation is important in patients with pituitary adenoma.

## Compliance with ethical standards

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### *Disclosure of conflict of interest*

The authors declare no conflict of interests.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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