

A rare case of silent pituitary macroadenoma with positive TSH and prolactin immunostaining

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Abstract

Silent thyroid stimulating hormone (TSH)-immunostaining pituitary adenomas are rare tumors, they can be either pure or immunoreactive to other pituitary hormones. We report a case of a silent macroadenoma with both TSH and prolactin immunostaining but with no clinical manifestations of hyperthyroidism or hyperprolactinemia. Pituitary magnetic resonance imaging revealed a macroadenoma. Transsphenoidal surgery was incomplete. The immunohistochemical staining showed that tumor cells were reactive to TSH (60%) and to prolactin (40%). Control pituitary imaging revealed a residual macroadenoma, and dopaminergic agonist treatment was administered. Mixed TSH and prolactin pituitary adenomas are rare and usually diagnosed incidentally or in the face of compression signs. Hormonal examinations for all patients who have a pituitary adenoma should be performed even in the absence of symptoms of hypersecretion. Pathological examination with immunostaining is key to diagnosis of clinically silent pituitary adenomas. Complementary therapies can be used when surgery is incomplete or contraindicated such as dopamine agonists and somatostatin analogs.

Keywords: Pituitary adenoma; Silent; Thyrotropin; Prolactin

1. Introduction

Silent pituitary adenomas are defined as clinically non-functioning adenomas with no hormonal hypersecretion. When they present in the form of macroadenomas they are diagnosed based on compressive symptoms such as headaches, visual impairment or pituitary hormone deficiencies [1]. Upon pathological examination these adenomas are immunoreactive for specific pituitary hormones, manifesting ultrastructural features for a particular pituitary cell type and/or expressing cell-specific transcription factors [2]. Depending on adenoma subtype, these tumors are called silent lactotroph, somatotroph, corticotroph, thyrotroph, and gonadotroph adenomas. We report a patient with a silent pituitary macroadenoma with positive thyrotropin stimulating hormone (TSH) and prolactin immunostaining, but with no signs of hyperthyroidism or hyperprolactinemia.

2. Case report

A 23-year-old male patient was referred to our hospital with a 1 year consultation delay for decreased visual acuity predominant on the right eye. The medical history was unremarkable. He had no headaches, no signs of deficient pituitary hormone secretion, no signs of thyrotoxicosis and no signs of hyperprolactinemia or hypogonadism. On physical examination he had a pulse rate of 80/minute, a blood pressure of 120/77 mmHg, thyroid gland examination was normal and no gynecomastia or galactorrhea were found.

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The initial hormonal assessment wasn't complete, it only included a normal thyroid stimulating hormone (TSH) of 2,3mUI/l [0,27-4,2], and a prolactin level of 31ng/ml [4,7-23] that was slightly elevated. Free thyroxine (T4) and triiodothyronine (T3) and the other pituitary hormones: follicle-stimulating hormone (FSH), lutenizing hormone (LH), testosterone, adrenocorticotrophic hormone (ACTH), cortisol and insulin-like growth factor 1 (IGF1) weren't measured. Blood electrolytes, renal and liver function were normal. The visual field test showed loss of vision in the right eye and a temporal hemianopia with partial nasal hemianopia in the left eye.

Pituitary magnetic resonance imaging revealed a 36 x 26 x 23 mm macroadenoma compressing the optic chiasm and invading carvenous sinuses. Transsphenoidal surgery was then performed. The immunohistochemical staining (figure 1) showed positive reactions to both TSH (60%) and prolactin (50%). The postoperative pituitary MRI control (figure 2) revealed a 31 x 21 x 19 mm residual macroadenoma and patient was put on dopamine agonists, Cabergoline 2mg/week. Due to the Covid 19 pandemic, the patient was evaluated after 8 months with a persistence of visual defect, a hormonal assessment showing no elevation of free T4 or T3 levels and a tumor shrinkage of 25% was obtained. Cabergoline was well tolerated so the weekly dose was elevated to 3,5 mg. Currently, the patient is followed up on medical treatment to evaluate residual tumor and a gamma knife neurosurgery way be considered in this case.

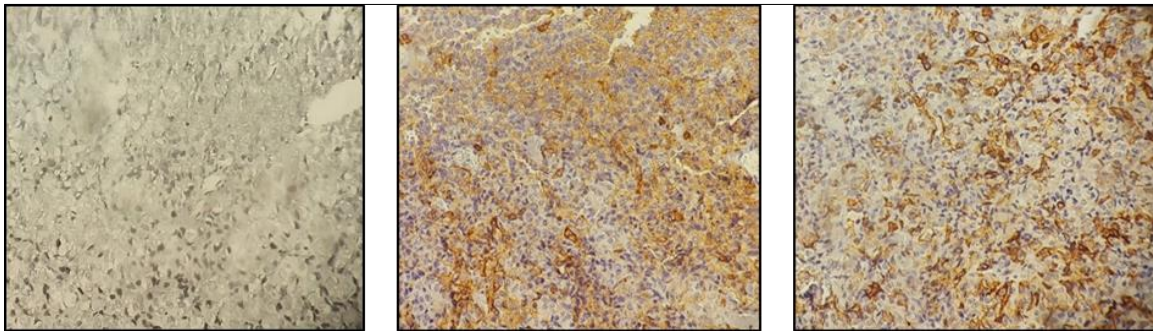


Figure 1 (a) Diffuse pattern of cellular proliferation suggesting a pituitary adenoma (HE ×200); (b) immunohistochemical staining showed that the tumor cells were strongly reactive to thyroid stimulating hormone (60%) and reactive to prolactin (50%) (c)

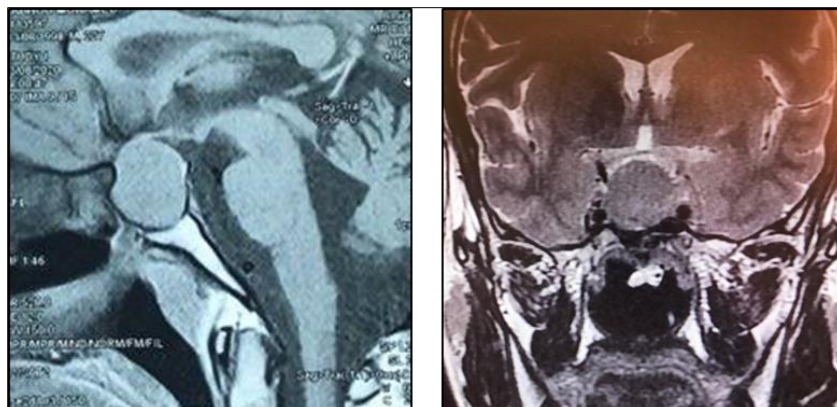


Figure 2 A mass which is measured as 31 mm × 21 mm × 19 mm in three dimensions, extended to suprasellar region and compressing internal carotid arteries

3. Discussion

Thyrotropin-secreting pituitary adenomas (TSHomas) are rare, accounting for approximately 1% of all pituitary adenomas [3]. In the last decades, TSH ultrasensitive measurements and physicians' awareness increased reported TSHoma cases [4].

They usually appear as macroadenomas and present clinically with mild thyrotoxicosis and a goiter due to inappropriate TSH secretion [5]. Silent TSHomas are defined as clinically non-functioning adenomas despite TSH

immunopositivity. They are diagnosed incidentally or as a result of compression symptoms. Pure TSHomas represent 75% of pituitary adenomas with TSH immunostaining. There are plurihormonal pituitary adenomas reported to secrete a combination of TSH and several other hormones such as growth hormone in 29 %, prolactin in 10 %, FSH and LH in 1,4 % of cases [6]. Macroadenomas cosecreting TSH and prolactin were rarely reported in literature [7,8].

In our case, peripheral thyroid hormones were not measured preoperatively, and patient was referred to endocrinology after surgery. Therefore, the presence of inappropriate TSH secretion in contrast with elevated T4 and T3 couldn't be established preoperatively. Although clinically, there were no signs of hyperthyroidism or hyperprolactinemia, focal staining with TSH and prolactin were detected with immunohistochemistry.

The first-line therapy of TSHomas is neurosurgery, but complete tumor excision is rare as silent TSHomas are diagnosed in case of enlarged macroadenomas. Only 1/3 of patients are cured with surgery. Other treatment options when surgery is incomplete or contraindicated are irradiation, somatostatin analogues and dopamine agonists. Therapeutic use of dopaminergic agents was established based on expression of dopamine receptors on the cell membranes of thyrotrophs but the best results of this therapy are seen with mixed TSH/prolactin adenomas like in our case [9,10].

4. Conclusion

Silent pituitary adenomas with positive TSH and prolactin immunostaining are a rare immunohistological finding. Diagnosis occurs incidentally or based on compression signs. A complete hormonal assessment is important in patients with pituitary adenoma. Somatostatin analogues and dopamine agonists are alternatives when surgery is incomplete.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest.

Statement of informed consent

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

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