

## The Silent Somatotropic Adenoma: When Immunohistochemistry Has the Last Word

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### Abstract

### Case Report

Silent somatotropic adenomas are pituitary adenomas with immunohistochemical expression of growth hormone (GH), but without clinical signs of acromegaly, and for which GH and insulin-like growth factor-1 (IGF1) levels are normal or slightly increased. For these adenomas, only histopathological examination reveals positive immunostaining for GH. However, their exact frequency is not known. We report the case of a patient who showed no signs of acromegaly with normal IGF1 levels and in whom only the anatomopathological study allowed the postoperative diagnosis of silent somatotropic adenoma.

**Keywords:** somatotropic, adenomas, pituitary, immunohistochemical, growth hormone, GH.

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### INTRODUCTION

Somatotroph adenomas are pituitary tumors with clinical and biochemical signs of hypersecretion of GH, confirmed by the immunohistochemical study, these adenomas are often identified because of the clinical consequences that they generate. Their diagnosis is generally suspected in the clinical aspect of the patient and is confirmed by the high dosage of GH and IGF1. Occasional cases of subclinical adenomas have been described in the literature. For these adenomas, only histopathological examination reveals positive immunostaining for GH. However, their exact frequency is not known [1].

A recent publication categorized somatotropic adenomas into four categories based on the presence or absence of acromegaly and plasma levels of IGF-1: classical (obvious acromegaly and high IGF-1), subtle (subtle acromegaly and IGF -1 high), clinically silent (no acromegaly, but high IGF-1) and silent (no acromegaly and normal IGF-1 level) [2]. The authors pointed out that one-third of GH adenomas are clinically non-functional and that plasma IGF-1 levels are slightly higher in almost all cases.

Very few studies have analyzed the characteristics of silent somatotropic adenoma with normal plasma levels of GH and IGF-1. However, it appears that compared to tumors associated with acromegaly, silent somatotropic adenomas are larger, more invasive and less differentiated, with different

histological characteristics (poorly granulated) [3-6]. Some silent tumors with GH-prolactin are aggressive, with multiple recurrence and resistance to treatment [7].

We report the case of a patient with pituitary adenoma that has immunohistochemical expression of GH, but without clinical signs of acromegaly, and with normal IGF1 levels.

### OBSERVATION

This is patient A.B, 56 years old, with no particular pathological history apart chronic cigarette smoking, admitted in our training for postoperative evaluation of a pituitary adenoma.

At anamnesis the onset of symptomatology seems to go back to 12 years by the installation of a decrease in visual acuity without notion of headache. The clinical examination notes the absence of acromegaloid features. A cerebral MRI was performed showing an intra and supra-sellar tumoral process compressing the optic chiasma leading first to a pituitary adenoma measured at 45 x 33. The patient was operated and the gesture consisted in a macroscopic removal of the tumor. Pathological study: Aspect of a pituitary adenoma with the immunohistochemical study: expression of the anti GH receptors antibody.

A postoperative hormonal assessment was made showing anterior pituitary insufficiency with a normal IGF1 level with pituitary MRI control:

persistence of a 2.6 cm tumor residue. The patient was referred for surgical revision.

## DISCUSSION

Somatotropic pituitary adenomas are benign tumors developed at the expense of the pituitary and, depending on their size and their functionality may be responsible for three major types of signs:

- A pituitary tumoral syndrome, revealed by visual disturbances or headaches.
- Acromegaly secondary to hypersecretion of growth hormone;

Or a syndrome of anterior pituitary insufficiency, generally covering all the pituitary hormones (panhypopituitarism).

Of course, these three major pathological frameworks are not mutually exclusive; they are even often associated [8]. In our patient, the pituitary adenoma was discovered in a context of visual disturbances. In some cases, hormonal evaluation may show elevated levels of GH and/or IGF-1, with no evidence of acromegaly [9,10]. In these cases, the first treatment option may be medical treatment with somatostatin analogues or surgery, depending on the clinical setting. In other cases, hormonal evaluation may show normal or slightly elevated levels of GH and / or IGF-1, without the presence of acromegaly, as in our case. In this situation, surgery is the first treatment option, mainly because these tumors are often bulky and invasive [7]. In addition, there are no data on the use of somatoline for the treatment of silent GH pituitary tumors. In most cases, tumor resection is subtotal, especially when the cavernous sinus is invaded. Several surgeries are necessary or complementary therapies are needed such as radiotherapy. Unfortunately, radiotherapy is associated with a risk of side effects [11]. In our case, the patient had a macroadenoma operated with a tumor residue requiring a second surgery.

Indeed, in case of acromegaly, the response to somatostatin analogues (SA) depends largely on the expression of the somatostatin receptor (SSTR), in particular SSTR2A and SSTR5 [12]. For silent GH tumors, a first therapeutic option is surgery. If surgical resection is not complete, additional therapy is required, including medical treatment or radiation therapy. No data is available to choose the optimal treatment for these tumors. Knowledge of positive immunostaining for the level of GH and SSTR expression in silent GH adenoma could guide management for patients with persistent disease after surgery [13].

## CONCLUSION

The relative frequency of silent somatotrophic adenomas is unknown. [14]. In such a context, preoperative determination of IGF1 and systematic

immunohistochemistry can detect this entity, correct preoperative diagnosis and ensure appropriate monitoring.

## REFERENCES

1. DeLellis RA, editor. Pathology and genetics of tumours of endocrine organs. IARC; 2004.
2. Wade AN, Baccon J, Grady MS, Judy KD, O'Rourke DM, Snyder PJ. Clinically silent somatotroph adenomas are common. *European journal of endocrinology*. 2011 Jul 1;165(1):39-44.
3. Kovacs K, Lloyd R, Horvath E, Asa SL, Stefaneanu L, Killinger DW, Smyth HS. Silent somatotroph adenomas of the human pituitary. A morphologic study of three cases including immunocytochemistry, electron microscopy, in vitro examination, and in situ hybridization. *The American journal of pathology*. 1989 Feb;134(2):345.
4. Trouillas J, Sassolas G, Loras B, Velkeniers B, Raccurt M, Chotard L, Berthezene F, Tourniaire J, Girod C. Somatotpic adenomas without acromegaly. *Pathology-Research and Practice*. 1991 Dec 1;187(8):943-9.
5. Yamada SH, Sano TO, Stefaneanu LU, Kovacs KA, Aiba TA, Sawano SH, Shishiba YO. Endocrine and morphological study of a clinically silent somatotroph adenoma of the human pituitary. *The Journal of Clinical Endocrinology & Metabolism*. 1993 Feb 1;76(2):352-6.
6. Naritaka H, Kameya T, Sato Y, Furuhashi S, Otani M, Kawase T. Morphological characterization and subtyping of silent somatotroph adenomas. *Pituitary*. 1999 May 1;1(3-4):233-41.
7. Batisse M, Raverot G, Maqdasy S, Durando X, Sturm N, Montoriol PF, Kemeny JL, Chazal J, Trouillas J, Tauveron I. Aggressive silent GH pituitary tumor resistant to multiple treatments, including temozolomide. *Cancer investigation*. 2013 Mar 19;31(3):190-6.
8. Trouillas J, Sassolas G, Loras B, Velkeniers B, Raccurt M, Chotard L, Berthezene F, Tourniaire J, Girod C. Somatotpic adenomas without acromegaly. *Pathology-Research and Practice*. 1991 Dec 1;187(8):943-9.
9. Sakharova AA, Dimaraki EV, Chandler WF, Barkan AL. Clinically silent somatotropinomas may be biochemically active. *The Journal of Clinical Endocrinology & Metabolism*. 2005 Apr 1;90(4):2117-21.
10. Sidhaye A, Burger P, Rigamonti D, Salvatori R. Giant somatotrophinoma without acromegalic features: more "quiet" than "silent": case report. *Neurosurgery*. 2005 May 1;56(5):E1154-.
11. Jenkins PJ, Bates P, Carson MN, Stewart PM, Wass JA, UK National Acromegaly Register Study Group. Conventional pituitary irradiation is effective in lowering serum growth hormone and insulin-like growth factor-I in patients with

- acromegaly. *The Journal of Clinical Endocrinology & Metabolism*. 2006 Apr 1;91(4):1239-45.
12. Colao A, Auriemma RS, Lombardi G, Pivonello R. Resistance to somatostatin analogs in acromegaly. *Endocrine Reviews*. 2010 Dec 1;32(2):247-71.
  13. Cooper O, Melmed S. Subclinical hyperfunctioning pituitary adenomas: the silent tumors. *Best practice & research Clinical endocrinology & metabolism*. 2012 Aug 1;26(4):447-60.
  14. Chinezu L, Jouanneau E, Vasiljevic A, Trouillas J, Raverot G. Silent GH pituitary tumor: diagnostic and therapeutic challenges. In *Annales d'endocrinologie* 2013 Dec 1 (Vol. 74, No. 5-6, pp. 491-495). Elsevier Masson.