Endocrinol Diabetes Nutr. 2018;65(4):237–243

Endocrinología, Diabetes y Nutrición

www.elsevier.es/endo

SCIENTIFIC LETTERS

A thyrotropin-secreting pituitary adenoma treated with radiosurgery: Long-term outcomes

Adenoma hipofisario secretor de tirotropina tratado con radiocirugía: resultados a largo plazo

Thyrotropin-secreting pituitary adenomas are rare, representing 0.5–3% of all pituitary adenomas (PA). Trans-sphenoidal surgery and somatostatin analogs are currently considered first and second-line treatment options respectively.[1] Radiotherapy, either pituitary fractionated stereotactic radiotherapy or radiosurgery, is considered a third-line treatment option; mainly due to lack of outcome data.[1] In a recent review of the literature, there were only 15 cases identified in the literature of patients with thyrotropin-secreting pituitary adenomas treated by gamma knife radiosurgery (GKRS).[2] We report here the case of a woman with a thyrotropin-secreting pituitary adenoma treated with GKRS in 2005, at age 50, as first-line treatment.

The patient was a smoker, had had tonsillectomy at age 16, breast augmentation surgery at age 19, and a simple hysterectomy for benign pathology at age 45. Her family history was unremarkable except for primary hypothyroidism in her mother.

At age 42 years old, she was first noted to have an elevated thyrotropin (TSH), during routine well-woman screening. She was commenced on treatment with levothyroxine, 50 μg daily. Because of failure to normalize her TSH, her dose of levothyroxine was progressively increased over a 3.5-year period, during which time she developed progressive headaches, fatigue, anxiety, palpitations and heat intolerance. In March 2005, she was noted to be clinically thyrotoxic, despite a mildly elevated TSH. Her levothyroxine treatment was withdrawn.

Off treatment, in October 2005, two thyroid function studies confirmed a profile consistent with mild central hyperthyroidism: TSH 2.5 μIU/mL and 6.8 μIU/mL (reference range [RR] 0.3–5 μIU/mL), FT4 2.1 ng/dl and 2.0 ng/dl (RR 0.8–1.8 ng/dL), FT3 3.1 pg/mL and 6.4 pg/mL (RR 2–3.5 pg/mL). Heterophilic antibody interference in the TSH immunoassay was excluded by polyethylene glycol precipitation. Anti-thyroglobulin (112 IU/mL; RR ≤ 2.3 IU/mL) and anti-thyroid peroxidase antibodies (372 IU/mL; RR ≤40 IU/mL) were positive. Thyroid stimulating immunoglobulins were negative. There was no evidence of co-secretion or deficit of other pituitary hormones. The α-subunit was 2.4 ng/mL (RR <1.2 ng/mL); and α-subunit/TSH molar ratio 9.6 (RR <1). The thyroid uptake in the I-131 nuclear scan was 51.5% at 6 hours (RR 3–16%); and the thyroid ultrasound demonstrated a hypervascular gland. A dedicated pituitary magnetic resonance imaging (MRI) revealed a left-sided, nonenhancing, 7 mm exophytic pituitary adenoma abutting the medial posterior aspect of the left cavernous sinus. No mutations were detected in exons 9 and 10 of the thyroid receptor beta gene by polymerase chain reaction and DNA sequencing, thus ruling out TSH resistance associated with a non-functioning pituitary adenoma. Inferior petrosal sinus sampling was performed without stimulation, to lateralize TSH secretion finding a central to peripheral gradient of 9:1, and left to right gradient of 8:1.

After a discussion of treatment options, the patient declined trans-sphenoidal surgery and elected to receive treatment with GKRS on December 2005. One 8-mm isocenter and three 4-mm isocenters of radiations were used to cover a tumor volume of 879 mm^3. The maximum dose received was 60 Gy, with the margins receiving 30 Gy. Propylthyouracil was initiated in December 2005, following the GKRS (TSH 24 μIU/mL [RR 0.3–5 μIU/mL], FT4 4.4 ng/dL [RR 0.8–1.8 ng/dL]) and maintained through June 2006, when it was voluntarily interrupted (TSH 7.1 μIU/mL [RR 0.3–5 μIU/mL], FT4 1.3 ng/dL [RR 0.8–1.8 ng/dL], FT3 3.1 pg/mL [RR 2–3.5 pg/mL], α-subunit 1.2 ng/mL [RR <1.2 ng/mL]; and α-subunit/TSH molar ratio 3 [RR <1]). A MRI in February 2007 showed a decrease in the size of the tumor and persistence of mild hyperthyroidism (TSH 3.7 μIU/mL [RR 0.3–5 μIU/mL], FT4 1.8 ng/dL [RR 0.8–1.8 ng/dL], FT3 4.1 pg/mL [RR 2–3.5 pg/mL]). Subsequent follow-up was performed intermittently at a different center without developing new signs or symptoms suggestive of thyroxicosis or hypopituitarism, and without receiving any further treatment.

A pituitary MRI in December 2016, 10 years after GKRS treatment, revealed no evidence of a pituitary adenoma. In March 2017, the patient was clinically asymptomatic and was not receiving any treatment. TSH was 5.66 (RR 0.27–4.2 μIU/mL), FT4 1.26 ng/dL (RR 0.93–1.7 ng/dL). A suppression test with triiodothyronine was performed demonstrating adequate TSH suppressibility (TSH 0.06 μIU/mL, 99% reduction from baseline) ruling

out autonomous TSH secretion. There was no evidence of pituitary dysfunction on the time of this evaluation.

As for other pituitary adenomas, transsphenoidal surgery is the preferred initial treatment option.[1] However, unlike other pituitary adenomas, thyrotropin-secreting pituitary adenomas are generally invasive and often fibrous. For this reason, surgery is associated with higher rates of persistent or recurrent disease (47%-78%) than in other pituitary adenomas; and with higher rates of post-surgical complications (30–60%).[3–6] Nonetheless, trans-sphenoidal surgery is the preferred initial treatment because it can achieve complete resection while preserving the pituitary function.[1] Somatostatin analogs are second-line treatment, achieving biochemical and structural control in most patients.[1] However, cure is anecdotal with somatostatin analogs for which chronic treatment is often necessary, and expensive.[7] Radiotherapy is usually reserved for patients in whom surgical and medical treatments fail, are contraindicated or, as in this case, declined by the patient.[1] Nevertheless, GKRS appears to be safe and efficacious, at least in the short-term, for the treatment of thyrotropin-secreting pituitary adenomas.[2] This case demonstrates that long-term outcomes of GKRS for thyrotropin-secreting pituitary adenomas can be favorable, as is the case for other types of pituitary adenoma.[8] To our knowledge, this is only the second case to be described in the literature of a patient with a thyrotropin-secreting pituitary adenoma treated by GKRS as first-line treatment[9]; and represents the longest reported follow-up of such a case.[2] In this case, GKRS was well tolerated, achieved biochemical control and complete resolution of the pituitary mass while preserving the pituitary function for more than 10 years of follow-up. Further reports assessing GKRS efficacy and long-term outcomes are needed to clarify its role in the management of these challenging tumors.

Conflict of interests

The authors declare that there is no conflict of interest.

References

1. Beck-Peccoz P, Lania A, Beckers A, Chatterjee K, Wemeau JL. 2013 European thyroid association guidelines for the diagnosis and treatment of thyrotropin-secreting pituitary tumors. Eur Thyroid J. 2013;2:76–82.
2. Mouslech Z, Somali M, Sakali AK, Savopoulos C, Mastorakos G, Hatzitolios AI. TSH-secreting pituitary adenomas treated by gamma knife radiosurgery: our case experience and a review of the literature. Hormones (Athens, Greece). 2016;15:122–8.
3. Gatto F, Grasso LF, Nazzari E, Cuny T, Anania P, Di Somma C, et al. Clinical outcome and evidence of high rate post-surgical anterior hypopituitarism in a cohort of TSH-secreting adenoma patients: might somatostatin analogs have a role as first-line therapy? Pituitary. 2015;18:583–91.
4. Losa M, Mortini P, Franzin A, Barzaghi R, Mandelli C, Giovanelli M. Surgical management of thyrotropin-secreting pituitary adenomas. Pituitary. 1999;2:127–31.
5. Brucker-Davis F, Oldfield EH, Skarulis MC, Doppman JL, Weintraub BD. Thyrotropin-secreting pituitary tumors: diagnostic criteria, thyroid hormone sensitivity, and treatment outcome in 25 patients followed at the National Institutes of Health. J Clin Endocrinol Metabol. 1999;84:476–86.
6. Valdes Socin H, Chanson P, Delemer B, Tabarin A, Rohmer V, Mockel J, et al. The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. Eur J Endocrinol/Eur Feder Endocr Soc. 2003;148:433–42.
7. Fliers E, van Furth WR, Bisschop PH. Cure of a thyrotrophin (TSH)-secreting pituitary adenoma by medical therapy. Clin Endocrinol. 2012;77:788–90.
8. Minniti G, Clarke E, Scaringi C, Enrici RM. Stereotactic radiotherapy and radiosurgery for non-functioning and secreting pituitary adenomas Reports of practical oncology and radiotherapy. J Greatpoland Cancer Center Poznan Pol Soc Radiat Oncol. 2016;21:370–8.
9. Zhao W, Ye H, Li Y, Zhou L, Lu B, Zhang S, et al. Thyrotropin-secreting pituitary adenomas: diagnosis and management of patients from one Chinese center. Wien Klin Wochensch. 2012;124:678–84.

Marta Araujo Castro[a,*], Bryan McIver[b], Pablo Valderrabano[b]

[a] *Department of Endocrinology and Nutrition, Hospital Universitario de la Princesa, Calle de Diego de León, 62, Madrid, Spain*
[b] *Department of Head and Neck-Endocrine Oncology, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, FL 33612, USA*

* Corresponding author.
E-mail address: martaazul.2a@hotmail.com
(M. Araujo Castro).

https://doi.org/10.1016/j.endinu.2017.12.007
2530-0164/