LETTER TO THE EDITOR

Long-term treatment of thyrotropin-secreting microadenoma with lanreotide and cabergoline

Robert Pichler and Wilhelmine Maschek

Institute for Nuclear Medicine and Endocrinology, General Hospital Linz, Austria

(Correspondence should be addressed to Robert Pichler; Email: Robert.Pichler@akh.linz.at)

Thyrotropin (TSH)-secreting adenoma is a rare entity and may be overlooked as a cause of clinical hyperthyroidism. Since the introduction of ultrasensitive assays for TSH and direct methods for free thyroid hormone measurements as first-line tests of thyroid function, thyrotropinomas have been recognized with increasing frequency (1). Somatostatin analogues have been proposed for the treatment of thyrotropinomas. The dopamine agonist bromocriptine has been reported to be ineffective in more than 75% of those adenomas (2).

We present the case of a 44-year-old woman with TSH-producing microadenoma who has been treated successfully with lanreotide and subsequently cabergoline for 3 years. The then 40-year-old nurse presented in October 1996 in our outpatient clinic with a clinical pattern consisting of restlessness, paroxysmal tachycardia, loss of weight, tremor and depression. The symptoms had started 2 months previously. Laboratory findings showed elevated levels of circulating thyroid hormones despite inadequately high levels of TSH (Table 1). A stimulation test with TRH doubled the basal level of TSH. Sonography of the thyroid demonstrated normal volume (16 ml). Scintiscan with Tc99m detected an elevated uptake of 2.6% (normal range: 0.5–1.5%) and a homogeneous picture of the thyroid.

Antibodies for thyroglobulin, thyroid peroxidase and thyrotropin receptor were measured repeatedly in the

following months – always with negative result. TSH was not suppressed at any time when observed. Various controls always showed normal values of α -subunits. MRI of the pituitary demonstrated a 5 mm microadenoma, which was not enhanced after gadolinium administration.

There was no evidence for familiar protein binding anomaly, the existence of T3- and T4-autoantibodies was excluded. Therefore the diagnosis of the microthyrotropinoma was established. In August 1997 endocrine screening of anterior pituitary hormones (LH, FSH, PRL, ACTH and HGH), estradiol, cortisol and IGF-1 revealed normal physiological levels. Symptomatic treatment with atenolol (20 mg every 8 h) was started as an intermediate therapeutic approach. Pituitary surgery was recommended but the patient refused and insisted on conservative treatment. Lanreotide (30 mg i.m.) therapy was started in August 1997 initially with a 2 week interval between injections, which was later extended because the patient remained free of thyrotoxic symptoms for longer. For 3 weeks after medication thyroid hormone levels remained within the normal physiological range. Diarrhea and abdominal discomfort for 2–3 days after injection of lanreotide were reported by the patient. These side effects were tolerated well at first, but after a while the patient decided to discontinue the treatment because of colics, which appeared more frequently.

Table 1 Thyroid hormone levels before and during therapy.

Date	fT4	fT3	TSH	TSH after TRH	Treatment	Time since last application
10/96	30.9	7.1	0.47	1.48	–	–
6/97	35.6	8.6	0.90	–	–	–
8/97	23.2	4.4	0.04	–	lanreotide	1 week
9/97	21.5	5.0	0.79	–	lanreotide	2 weeks
10/97	22.7	5.5	0.82	–	lanreotide	3 weeks
11/97	27.3	6.0	0.76	–	lanreotide	25 days
3/98	31.8	7.4	1.10	–	lanreotide	4 weeks
7/98	35.3	7.2	0.80	–	lanreotide	5 weeks
10/98	42.0	10.5	1.08	–	lanreotide	8 weeks
2/99	22.9	6.6	0.78	–	cabergoline	1 day
6/99	23.2	6.9	0.98	2.63	cabergoline	4 day
7/00	26.7	7.9	1.02	–	¹ / ₂ cabergoline	6 hours
Normal range	9.6–24.5 pmol/l	3.1–6.9 pmol/l	0.1–4.0 μ U/ml	4.0–25.0 μ U/ml		

Cabergoline was introduced in January 1999 as a second therapeutic option and proved successful (Table 1). Normal physiological levels of thyroid hormones and absence of clinical symptoms were achieved with a dose of 5 mg cabergoline twice a week (Table 1). As a skilled nurse, the patient decided voluntarily to reduce medical treatment because at half the dose she still did not present any clinical symptoms but simply felt better and her mood was improved.

The latest control MRI of the pituitary was performed in January 2000 and showed no change from the previous scan. It was decided to continue with 2.5 mg cabergoline twice a week and accept slightly elevated fT4 laboratory parameters considering the clinical situation. Control scans are scheduled every 3 months and we expect that pituitary surgery will no longer be necessary. Whether treatment with cabergoline can be continued for the rest of the patient's life remains to be seen. Thus far the patient has not reported any side effects.

We recommend long-term medical treatment of TSH-secreting adenomas. Medical treatment should be encouraged before pituitary surgery to avoid the risk of thyrotoxicosis at the time of operation. Somatostatin analogs with longer biological half-lives have been shown to normalize fT4 and fT3 levels on day 2 following injection, these remain in the normal range

for up to 3 weeks (3). Long-term medical management could be worthwhile in many cases, because pituitary surgery often leads to (partial) hypophyseal hormone deficiency. In a minority of TSH-secreting adenomas dopamine agonists appear to be a successful therapeutic alternative (4). As side effects can be a limiting factor for the use of lanreotide – as for our patient – cabergoline should be tested as an alternative means of TSH and fT4/fT3 suppression.

References

- 1 Beck-Peccoz P, Brucker-Davis F, Persani L, Smallridge RC & Weintraub BD. Thyrotropin-secreting pituitary tumors. *Endocrine Reviews* 1996 **17** 610–638.
- 2 Shimon I & Melmed S. Management of pituitary tumors. *Annals of Internal Medicine* 1998 **129** 472–483.
- 3 Gancel A, Vuillermet P, Legrand A, Catus F, Thomas F & Kuhn JM. Effects of a slow-release formulation of the new somatostatin analogue in TSH-secreting pituitary adenomas. *Clinical Endocrinology* 1994 **40** 421–428.
- 4 Bevan JS, Webster J, Burke CW & Scanlon MF. Dopamine agonists and pituitary tumor shrinkage. *Endocrine Reviews* 1992 **13** 220–240.

Received 15 September 2000

Accepted 11 October 2000