

Transient Headache and Impaired Vision after Intravenous Thyrotropin-Releasing Hormone in a Patient with Pituitary Macroadenoma

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Abstract

We report a case of transient headache and impaired vision following administration of intravenous thyrotropin-releasing hormone (TRH) to a woman with a non-functioning pituitary macroadenoma, visual field defect, and elevated thyroid-stimulating hormone (TSH). The symptoms lasted for two hours and then resolved without known sequelae. There are a few other reported cases of similar adverse reactions to neuroendocrine manipulation in patients with pituitary macroadenomas. This is the second reported case of such adverse reactions to TRH alone and the first in which the patient had prior elevation of TSH. **Key Words:** Thyrotropin-releasing hormone, pituitary macroadenoma, headache, primary hypothyroidism, impaired vision.

Introduction

PITUITARY FUNCTION TESTS are often performed in the evaluation of a macroadenoma, usually to assess pituitary reserve. Stimulation testing with synthetic releasing factors is generally well tolerated, except for the mild side effects associated with each agent (1–4).

There have been a number of reports of pituitary apoplexy, frontal headaches and amaurosis following administration of gonadotropin-releasing hormone (GnRH), thyrotropin-releasing hormone (TRH), or insulin-tolerance test (ITT) alone or in combination (5–9). We report the onset of severe headache and impaired vision 5 minutes

after pituitary testing with TRH, in a patient with a non-functioning pituitary macroadenoma and coexistent primary hypothyroidism.

Case Report

A 67-year-old woman presented to her ophthalmologist for visual difficulties. Formal visual field testing revealed a right temporal hemianopia and left lower temporal quadrantanopia. An MRI disclosed a 4.1 x 2.3 cm pituitary macroadenoma with suprasellar extension (Figure). She was referred to a neurosurgeon for a transsphenoidal resection of the tumor. Endocrine evaluation was requested prior to her surgery.

Her medical history was noncontributory. There was no history of hypertension or any known thyroid disease. She denied seizures, diplopia, or anosmia. Prior to an uneventful menopause at age 45, the patient had normal menstrual cycles. Family history for endocrine or autoimmune diseases was negative.

On physical examination, her blood pressure was recorded at 138/78 mm Hg, with a regular

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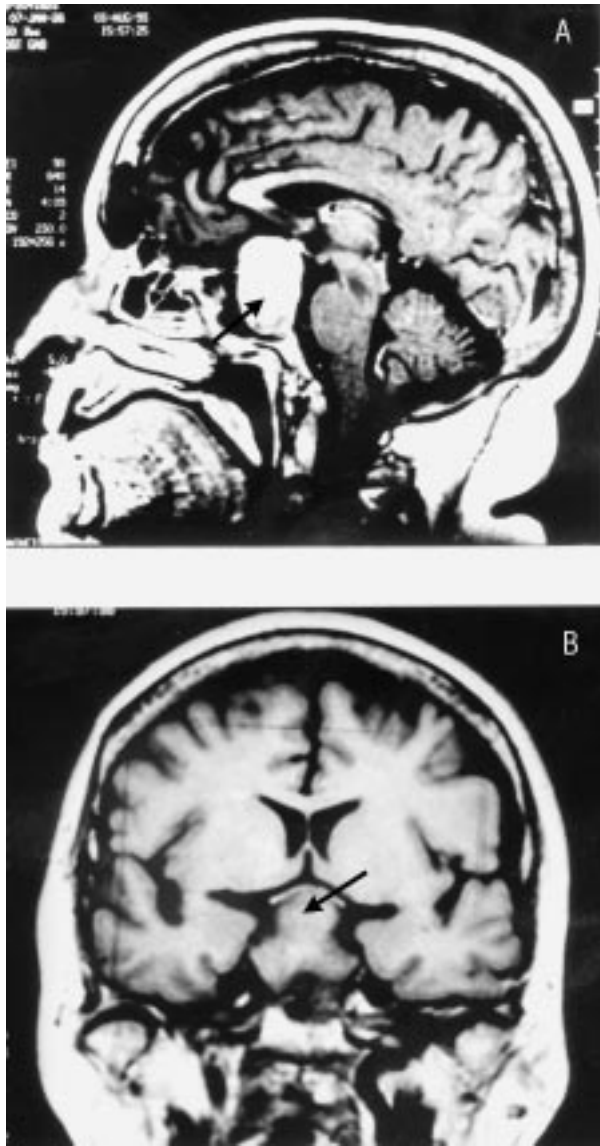


Figure. A magnetic resonance imaging of pituitary fossa showing 4.1 x 2.3 cm pituitary macroadenoma with suprasellar extension (arrow).

pulse of 72 beats per minute. There was no proptosis, and her extraocular movements were normal. The optic discs were flat. The right temporal visual field was cut. The thyroid was normal in size and without nodularity.

The rest of her examination was unremarkable. However, her pituitary function tests included the following results: TSH 33 IU/L (normal range 0.3–5.0), T_4 47.73 nmol/L (normal range 58.05–161.25), free T_4 11.09 pmol/L (normal range 18.06–38.7), prolactin 1.91 nmol/L (normal <0.91), follicular stimulating hormone 9 IU/L (normal range postmenopausal 34.3–95.8), luteinizing hormone 11 IU/L (normal range postmenopausal >20), AM cortisol 0.22 pmol/L (nor-

mal range 0.14–0.63), estradiol 73.4 pmol/L (normal range postmenopausal <216.53).

Our differential diagnosis considered the following possibilities: (1) a large pituitary adenoma associated with elevated TSH and low circulating thyroid hormone levels characteristic of primary hypothyroidism with marked thyrotroph hyperplasia; (2) chromophobe adenoma with secondary hypothyroidism with elevated levels of bio-inactive TSH (10); (3) coexisting chromophobe adenoma and primary hypothyroidism. The diagnosis of a TSH secreting tumor was not considered because of the low circulating thyroid hormone levels. Antithyroid antibodies were ordered. A TRH stimulation test was performed in an attempt to assess its usefulness in differentiating between the above possibilities.

Five minutes after the intravenous injection of TRH (200 μ g TRH, Relefact Ferring Lab, Suffern, NY), the patient developed severe bifrontal headaches and blurring of vision. Her blood pressure remained unchanged. Visual acuity improved after 30 minutes and the blurring disappeared after 2 hours. One hour after TRH injection, examination of her visual fields was unchanged from baseline. However, since she continued to complain of headaches, a repeat MRI of sella turcica was ordered but, unfortunately, could not be obtained because of a mechanical problem with the machine.

Due to the persistent headache and concern about hemorrhage into the tumor, transsphenoidal surgery was performed eight hours after the TRH test. Pathology revealed a chromophobe adenoma without evidence of hemorrhage or infarction. Immunohistochemical staining of the tumor was negative for TSH, prolactin, and ACTH. On the third postoperative day, results of antithyroid antibodies were reported to be greater than 1200 IU/mL (normal <1.0). The alpha subunit was 1.6 mg/L (<1.2). The serum TSH levels after the TRH test were: 40.2, 71.8, 93.7, 95.8, 114.1, 93.9 (IU/L) at time 0', 15, 30, 60, 90, 120 minutes respectively.

The patient's visual fields recovered to nearly normal one week following surgery. She refused to consider a repeat TRH stimulation test.

Discussion

Side effects from intravenous TRH are usually mild. These have mainly included dryness of the mouth, flushing, a sensation of urinary urgency, abdominal and chest discomfort (2, 11) and transient elevation of blood pressure (1, 12). There are only a few case reports of transient

amaurosis and headache after injection of TRH (5, 6, 8, 9). Except for one patient, all reported cases received other releasing factors and/or insulin, in addition to TRH. In our patient, the only administered releasing factor was TRH.

The results of TRH suggested primary hypothyroidism (high baseline TSH with brisk rise). The fact that the TSH levels remained elevated at two hours suggested a possible central component. Although most patients with pituitary lesions and hypothyroidism fail to respond to TRH, some may have a normal, delayed, or even exaggerated response in their levels of serum thyrotropin (13).

Autoimmune thyroid disease was confirmed during the immediate postoperative period when the preoperative laboratory test revealed the presence of markedly elevated antimicrosomal antibodies. Histological examination of the tumor did not reveal any TSH staining. Pituitary function testing revealed secondary hypogonadism.

A pituitary macroadenoma in a patient with an elevated TSH and positive thyroid autoantibodies can be seen in unusual cases of primary hypothyroidism with marked thyrotroph hyperplasia. This can masquerade as a prolactinoma because of the occasional associated hyperprolactinemia (14–20). Pituitary enlargement with suprasellar extension up to 8 mm has been reported with TSH levels of 50–100 IU/mL (15, 17). Interestingly, a brain scan revealed a 2x2 cm area of increased uptake of ^{99m}technetium in the area of sella turcica in a patient reported by Vagenakis et al. (18). Treatment consisted of exogenous thyroid hormone with radiologic documentation of shrinkage of the pituitary mass. Indeed, if surgery had not been deemed urgently necessary, a trial of thyroid hormone therapy would have been started to see if the pituitary mass decreased in size as TSH returned to normal.

It is of interest that all reported cases of adverse effect to TRH, or combined pituitary testing, were in patients with non-functioning pituitary macroadenomas. The one exception (9) was a growth-hormone-secreting microadenoma.

The fact that the acute onset of headache and impaired vision occurred 5 minutes after injection of TRH suggests that these symptoms were precipitated by the TRH itself. Such reactions to TRH are infrequent, occurring in 1:1000 patients tested (9). Possible explanations are: (1) vasospasm induced by TRH (TRH elevates levels of serum norepinephrine [11]) or (2) acute swelling of the pituitary following TRH, causing stretching of the dura and further pressure on the

optic chiasm. The role of prior elevation of TSH in producing these unusual reactions to exogenous TRH is uncertain.

In retrospect, the TRH test did not add any important information in the differential diagnosis of our case. Due to the potential risk of TRH stimulation testing in patients with pituitary macroadenoma, it should be performed only if the benefit clearly outweighs the risk.

Conclusion

Intravenous TRH stimulation testing in a patient with a pituitary macroadenoma can, on rare occasions, result in serious side effects, including amaurosis and even pituitary apoplexy. This risk must be considered prior to such neuroendocrine testing in patients who might have pituitary macroadenomas.

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