Serum prolactin levels in hypothyroidism

Leslie R. Sheeler, M.D.
Department of Endocrinology

Manjula S. Kumar, Ph.D.
Department of Immunopathology

O. Peter Schumacher, M.D., Ph.D.
Department of Endocrinology

The association of amenorrhea, galactorrhea, and an elevated serum prolactin level with primary thyroid failure has been reported by several investigators.[1-6] We report a case with these findings as well as the serum prolactin levels in 47 additional patients with elevated thyrotrophin concentrations.

Case report

A 24-year-old white woman was examined at the Cleveland Clinic for evaluation of amenorrhea in August 1976. She had cessation of menses 4 years earlier. Following delivery of her only child in 1968, galactorrhea developed and persisted until the time of her evaluation. Facial puffiness, dry skin, and delayed return of deep tendon reflexes were noted. The thyroid gland was not enlarged. Laboratory values are reported in the *Table.* The galactorrhea ceased and menses resumed within 4 weeks after thyroid replacement therapy with 0.2 mg of L-thyroxine was begun.

Patients

Serum prolactin levels were measured in 48 consecutive patients with elevated thyroid-stimulating hormone (TSH) levels. The age range of the 12 male subjects was 7 to 77 years (mean, 53 years) and the age range of the 36 female subjects was 37 to 84 years (mean, 54 years). Primary thyroid failure was classified into four categories: primary hypo-

Table. Laboratory results in the reported case

	T_4, μg/dl	TSH, μU/ml	Prolactin, ng/ml	^{131}I uptake, 5 hr	Post-TSH, 5 hr
Before treatment	1.6	360	62	2%	1.5%
After 0.2 mg LT_4 for 4 weeks	...	<2	52	...	...
After 0.2 mg LT_4 for 8 weeks	...	<2	17	...	...

thyroidism without goiter (16 patients), Hashimoto's thyroiditis (22 patients), post ^{131}I therapy (1 patient) and post-thyroidectomy (8 patients). The results shown in *Figures 1 and 2* include those of the case reported here in addition to the 47 patients.

Materials and methods

Assays. Serum specimens were assayed in duplicate for prolactin and TSH levels using double antibody radioimmunoassay techniques. Methods previously described[7-9] were used with slight modifications. Rabbit antiserum to human prolactin, human TSH, and also purified human TSH for radioiodination were obtained from National Institute of Arthritis, Metabolism, and Digestive Diseases. Human prolactin standard A and TSH research standard B were received from the Medical Research Council, National Institute for Medical Research, Mill Hill, London. Labeled prolactin ^{125}I was purchased from Serono Laboratories, Inc., Boston, Massachusetts 02116. Human TSH was labeled with chloramine-T method as described by Greenwood et al[9] with some modifications. The sensitivity limit for the prolactin assay was 1.0 ng/ml and for TSH it was 1.5 μU/ml. Interassay variation for prolactin at the level of 7 ng/ml was 6.6%, and for TSH at the level of 3 μU/ml was 8%. The mean serum prolactin level in 21 normal men (age range, 23 to 55 years) was 5.8 ± 2 ng/ml and in 27 normal women (age range, 20 to 60 years) was 8.9 ± 2.3 ng/ml (SD). The mean serum TSH in 45 normal subjects was 2.8 ± 1.0 μU/ml (SD).

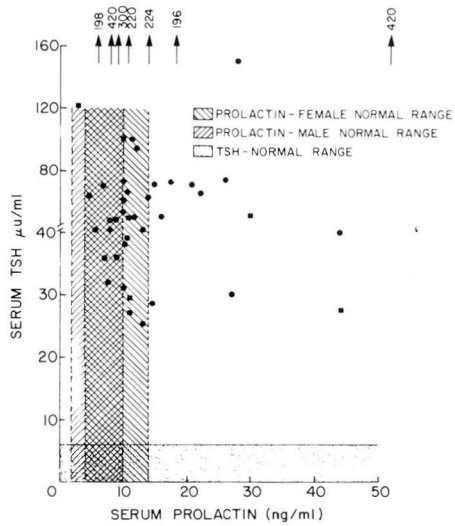

Fig. 1. Prolactin and TSH levels in 48 hypothyroid patients (● = female and ■ = male).

Laboratory findings

The mean TSH level in 48 patients with primary thyroid failure was 88.8 ± 92 μU/ml (range 25 to 420 μU/ml). The mean prolactin level in these patients, 14.3 ± 10.3 ng/ml (SD) (range 2.8 to 52 ng/ml), was significantly higher than in the control group which had a mean of 7.6 ± 2.6 ng/ml (SD). When these patients were grouped according to sex, the mean prolactin level in 12 hypothyroid men was 14 ± 11 ng/ml; in 36 women, the mean value was 14.5 ± 10 ng/ml (SD). These mean values for both men and women pa-

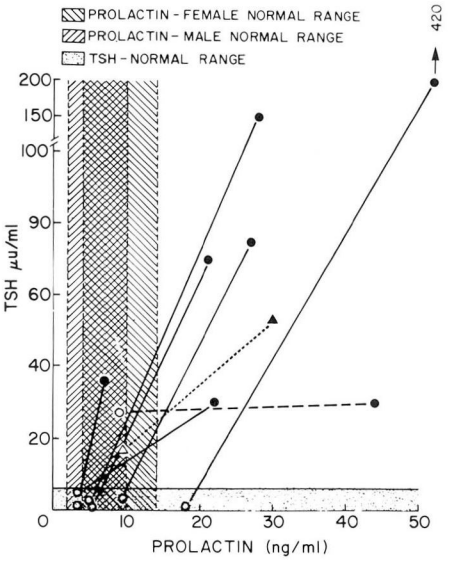

Fig. 2. Serum prolactin and TSH levels in eight patients before (●) and after (○) thyroid hormone treatment (▲ = male and ● = female). The patient whose level is indicated with the broken line had second TSH and prolactin levels (○) measured after the patient stopped taking the medication.

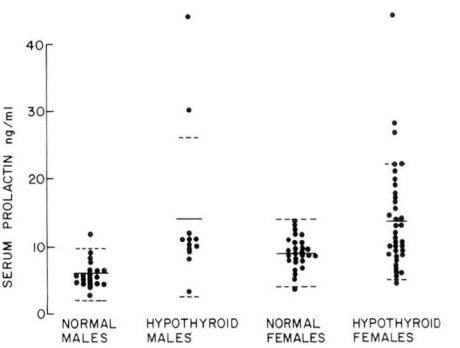

Fig. 3. Serum prolactin levels in normal and hypothyroid subjects. The mean levels are represented by solid horizontal lines and the two standard deviation ranges by the broken line.

tients were significantly higher when compared to the respective controls ($p < 0.01$) (*Fig. 3*).

Although the mean prolactin and the mean TSH levels were higher in this group of hypothyroid patients, no statistical relationship was observed between the two parameters (*Fig. 1*). Of 12 men, 6 (50%) had prolactin levels above the normal range, but only 14 of 36 women (39%) had elevated serum prolactin levels.

Six of the seven patients who had prolactin levels higher than 20 ng/ml were studied again after thyroid hormone treatment (*Fig. 2*). In all six, the prolactin levels returned to normal. One patient was unable to tolerate more than 0.05 mg a day of L-thyroxine due to angina pectoris. His prolactin level decreased from 30 ng/ml to 9 ng/ml and the TSH level decreased from 50 μU/ml to 15.6 μU/ml. Another patient had taken thyroid hormone for 4 months. However, she had discontinued therapy 2 months before she was recalled. Her TSH level was 34.5 μU/ml, but the prolactin level had decreased from 44 to 6.8 ng/ml. In 2 of the 19 patients with elevated prolactin levels, other factors were present which conceivably might have caused the elevation, i.e., metastatic cancer in one and reserpine therapy in the other. The patient on a regimen of reserpine therapy was among the patients recalled. Despite continuing therapy with reserpine, the prolactin level decreased from 21 to 5 ng/ml after 6 months of replacement.

Discussion

Hormonal overlap that occurs in children, analogous to that noted by Van Wyk and Grumbach[10] and later by Costin et al,[11] may occur in adults with primary hypothyroidism. Nineteen of 47 consecutive patients with primary hypothyroidism had elevated serum prolactin levels. Expected sequelae (amenorrhea, galactorrhea, gynecomastia, or impotence) associated with this elevation of prolactin were reported in only one case.

Possibly the duration and severity of the hypothyroidism contribute to the development of clinical sequelae. In the one patient in whom amenorrhea with galactorrhea developed, the TSH was extremely high for an adult with hypothyroidism. Since the galactorrhea persisted after delivery, she may well have been hypothyroid for at least 7 years. In other cases reported, the galactorrhea usually began postpartum.[2, 4, 6]

No problem with thyroid replacement occurred in our patient or in most patients with this syndrome reported by others. However, pituitary enlargement with visual field impairment after thyroid replacement has been recorded.[12]

Our findings are comparable to those of Yamaji[13] who found high basal prolactin levels in two of eight patients with primary hypothyroidism. Seven of the eight patients in his series had an augmented prolactin response to thyrotrophin-releasing hormone infusion. Onishi and co-workers[6] found elevated prolactin levels in 10 of 16 hypothyroid women. Negative results in 14 hypothyroid patients were reported by Fossati et al.[14]

Honbo et al[15] reported findings similar to ours. They found elevated prolactin levels in 19 of 49 hypothyroid patients.

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