Pituitary Hyperplasia Secondary to Thyroid Failure: CT Appearance

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Pituitary hyperplasia in response to primary end-organ failure is well established in the medical literature [1-5]. However, the role of radiology in the evaluation of this phenomenon has been explored only recently. To date, descriptions of radiographic abnormalities associated with this entity have included plain-film, tomographic, angiographic, and pneumoencephalographic findings [2-6]. Five patients evaluated with computed tomography (CT) have been reported [7-9]. In these cases, older-generation scanners and relatively thick sections were used; thus, scant data were obtained about the nature of the enhancing masses. We report two patients with pituitary hyperplasia secondary to primary hypothyroidism in whom direct coronal, enhanced CT scans demonstrated the nature of the enhancing masses initially and on follow-up.

Case Reports

Case 1

A 37-year-old woman was admitted to the Wilford Hall USAF Medical Center Thyroid Clinic with a recent history of headaches, generalized fatigue, myalgias, scalp hair loss, a 12.3 kg weight gain, and galactorrhea. She had been amenorrheic since discontinuing use of oral contraceptives about 16 months earlier. Physical examination revealed hypothyroid facies, dry skin, and periorbital edema. Her visual fields were normal and no goiter was palpable. Milky fluid was expressible from both breasts. The return phase of her Achilles reflex was prolonged.

Initial laboratory testing revealed thyroxine (T4) of less than 1.0 µg/dl (normal, 4.1–11.2), thyroid-stimulating hormone (TSH) of greater than 50 µU/ml (normal, 0–5.2), and serum prolactin of 28.4 ng/ml (normal, <25). After administration of thyrotropin-releasing hormone (TRH), TSH remained tonically elevated whereas prolactin increased slightly. An insulin tolerance test showed intact serum cortisol and growth hormone responses. Radiographs of the sella were normal, but direct coronal CT demonstrated a homogeneously enhancing pituitary mass with its superior margin extending convexly upward well above the sella (fig. 1A). Replacement therapy was begun with levothyroxine 200 µg daily; 6 weeks later, serum T4 and TSH were normal. A follow-up CT scan after 9 weeks of therapy showed a marked decrease in tumor size (fig. 1B). At that time, the patient was euthyroid, her galactorrhea had resolved, and regular cyclic menses returned. On reevaluation 28 months after institution of therapy, she was clinically well, and repeat follow-up CT confirmed continued reduction in pituitary size (fig. 1C).

Case 2

A prepubertal 14-year-old girl was referred to the National Institutes of Health Clinical Center for evaluation of short stature (below the first percentile). Her development milestones were normal, but for the past several years she had slept with many blankets and had only weekly bowel movements. Physical examination revealed a deep voice, slow speech, delayed reflexes, and dry skin. The thyroid gland was not palpable.

Serum T4 was low (1.4 µg/dl) and TSH elevated (820 µU/ml). ACTH test showed an adequate cortisol reserve. No antithyroid or antimitochondrial antibodies were identified. Her visual fields and chromosomes were normal. Radiouclide thyroid scanning showed no technetium uptake in the cervical region, but there was uptake at the base of the tongue consistent with a lingual thyroid. Skull films showed marked enlargement of the sella turcica with some erosion of the dorsum sellae (fig. 2A). Coronal CT revealed an enlarged, homogeneously enhancing pituitary gland with an upwardly convex upper margin (fig. 2B). She was treated with levothyroxine; after 4 months of therapy, she was thinner and had more active reflexes and regular bowel movements. Her height increased 5 cm. Repeat CT demonstrated a reduction in size of the pituitary gland (fig. 2C).

Discussion

The effect of thyroid hormones (T3 and T4), TSH, and TRH on the pituitary gland is complex, and the interhormonal relations are not fully understood. It is known that the fall in T3 and T4 in primary thyroid failure engenders a response from the hypothalamic-pituitary feedback loop in a futile attempt to stimulate thyroid hormone production. There is an accelerated delivery of TRH from the hypothalamus through the infundibulum and an outpouring of TSH from the pituitary thyrotrophs [10]. In addition to stimulating TSH release, there is now clinical and experimental in vivo and in vitro evidence...
that TRH also accelerates the delivery of prolactin by the pituitary lactotropes [11, 12]. Galactorrhea and amenorrhea may first bring the patient to medical attention. This "hormonal overlap" may possibly involve gonadotropins and growth hormone as well [3].

The morphologic response of the pituitary to hypothyroidism has been studied extensively in mice [1, 13] and in man [2]. Initially there is degranulation of the thyrotrophs and hyperplasia of the adenohypophysis. The hyperplastic pituitary at this stage can be successfully transplanted only to thyroidectomized mice; it will not grow in a normal host [13]. Through transplantation of cell suspensions of hyperplastic pituitary cells into thigh muscles of succeeding generations of hypothyroid mice, autonomous tumors have been produced [1]. Whether pituitary hyperplasia secondary to end-organ endocrine failure may undergo transformation to an autonomously functioning tumor in man is debatable; such a case has not been documented at this time.

The CT appearance of the adult pituitary has been described [14, 15]. Normally, it is 7–8 mm in maximum height and is completely confined within the sella; it is generally somewhat larger in women. Its upper surface is usually concave downward or flat, but may be convex upward, particularly in adolescent girls, in whom the pituitary also may be somewhat larger than in adults [16]. The normal pituitary gland is heterogeneous on CT, containing small (<3 mm) luencies on contrast-enhanced scans; these areas correspond to "loose" tissue containing cells of decreased or absent granularity [17].

The initial appearance of the pituitary was similar in our two cases. There was upward convexity of the superior margin of the gland and substantial suprasellar extension. Contrast enhancement was relatively uniform throughout the gland. This appearance (a homogeneously enhancing, enlarged pituitary on thin-section coronal CT) and a clinical picture compatible with hypothyroidism suggests pituitary hyperplasia. Pituitary adenomas are typically heterogeneous, with areas of low density mixed with areas of enhancement [14, 15]. Lymphoid adenohypophysitis is a rare autoimmune disorder that results in pituitary insufficiency and may present as an enhancing mass and be associated with hypothyroidism [18].

The CT findings in our patients lend support to previous reports that pituitary hyperplasia secondary to longstanding primary thyroid failure can be reversed with oral thyroid hormone replacement [2, 5, 7–9]. We also describe the CT appearance of pituitary hyperplasia on thin-section (1.5 mm), direct coronal, enhanced scans. It is imperative that radiologists be familiar with this phenomenon since proper treatment is thyroid hormone replacement rather than surgery or radiotherapy.

REFERENCES

1. Halmi NS, Gude WD. The morphogenesis of pituitary tumors induced by radiothyroidectomy in the mouse and the effects of their transplantation on the pituitary body of the host. Am J
Addendum

Since this article was submitted for publication, we have seen another patient with similar clinical and radiographic findings, substantiating the conclusions of the foregoing report:

Case 3

After a normal pregnancy and delivery, a 25-year-old physician failed to resume normal menses and had persistent galactorrhea although she was not breast-feeding. She had been easily fatigued but attributed this to the demands of her work and the new child. Endocrinologic evaluation demonstrated no significant physical abnormalities other than galactorrhea. Serum prolactin was elevated (43.2 ng/ml), thyroid hormone levels were in the hypothyroid range, and serum TSH was 20 times the normal upper limit for our laboratory. Thin-section axial CT of the sella with sagittal and coronal reconstruction demonstrated suprasellar upward bowing of the superior margin of the enlarged pituitary (figs. 3A and 3B). She was treated with levothyroxine, 200 μg/day. Six months after institution of therapy, her clinical and laboratory abnormalities had resolved; repeat CT of the sella demonstrated a pituitary of normal size and configuration (figs. 3C and 3D).