The Rapid Progression of Pituitary Hyperplasia in Primary Hypothyroidism Demonstrated by MR Imaging

Department of Nuclear Medicine and Radiology, Faculty of Medicine, Kyoto University, Kyoto, Japan
*Department of Radiology, Beth Israel Deaconess Medical Center, Boston, USA

Introduction
Pituitary enlargement in patients with long-standing primary hypothyroidism is well established. However, the time course of the progression of thyrotrhop hyperplasia in humans has not been studied [1]. We hypothesized that MR imaging can demonstrate the temporal change of pituitary hyperplasia in vivo in patients who rapidly develop hypothyroidism in a short period. One such group of patients are thyroidecomized patients prepared for radioactive iodine-131 (I-131) treatment, which has been widely used to treat metastases of differentiated thyroid carcinoma. These patients are rendered euthyroid by thyroid hormone replacement therapy after total thyroidectomy. To prepare for I-131 therapy, however, the administration of thyroid hormones should be discontinued for 2 - 3 weeks. During this interval, primary hypothyroidism was induced iatrogenically. Our aim is to evaluate the morphological changes of the pituitary gland during development of hypothyroidism in the thyroidectomized patients preparing for I-131 therapy using MR imaging.

Material and Methods
Fourteen thyroidecomized patients before I-131 therapy were evaluated. In each patient, MR scans and serum hormone measurements were performed twice; five weeks before I-131 treatment as the "euthyroid-state" with thyroid hormone supplement; and on the day of I-131 treatment as the "hypothyroid-state" after three-week depletion of thyroid hormone supplement. Nine normal volunteers also underwent MR scans twice at an interval of five weeks. T1- and T2 (and proton)-weighted images were acquired using a multisection 2D Fourier transform conventional SE technique. Pituitary volume and relative signal intensity ratio of the anterior pituitary compared with the pons were measured. Pituitary volume (mm3) was estimated in two ways: 1) by the formula Volume 1 = 1/2 x length x width x height, as reported by DiChiro et al [2]; and 2) Volume 2 = cross-sectional area x width, as reported by Lurie et al [3]. The shape and signal intensity of pituitary glands were also visually assessed by two experienced radiologists. The paired t-test was used to evaluate the significance of difference of the pituitary volumes and the relative signal intensity ratio in each subject between the euthyroid-state and the hypothyroid-state, and in each normal volunteer between the two MR scans at an interval of five weeks. In each analysis, a p-value of 0.05 was considered significant.

Results
The volume of the pituitary gland increased significantly by the depletion of thyroid hormone supplement; 331 ± 67.5 mm3 vs. 453 ± 109 mm3 in Volume 1 (p=0.000004); and 453 ± 107 mm3 vs. 626 ± 173 mm3 in Volume 2 (p=0.000003). Figure 1 shows the comparison of pituitary gland volumes between euthyroid and hypothyroid states (Figure 1). There were no significant differences in the relative signal intensity ratios of the anterior lobe to the pons on T1-weighted images before and after the depletion of thyroid hormone supplement. On visual evaluation of the gland shape, enlarging trends were noted. Visual examination of the signal intensity of the glands revealed no differences on both T1- and T2 (and proton)-weighted images. In normal volunteers, no significant differences in pituitary volumes and intensity were found between the two MR images.

Discussion
Circulating thyroid hormones normally act as a negative feedback on the hypothalamic secretion of thyrotropin-releasing hormone (TRH). If the thyroid gland secretes an insufficient quantity of thyroid hormones, serum level of TRH will increase. This, eventually, results in hyperplasia of thyrotrhops and subsequent enlargement of the pituitary gland [4]. Though pituitary hyperplasia with primary hypothyroidism is well established, the kinetics of the progression and regression of pituitary thyrotrhop hyperplasia has not been studied in detail in humans. Our study demonstrated that the pituitary gland volumes significantly increased quantitatively in only three weeks of development of hypothyroidism, and also shows that physiologic changes of pituitary gland of normal volunteers cannot occur during five weeks. Supporting our data in humans are animal experiments performed by DeFesi et al [5] to assess the kinetics of changes in thyrotrhop populations in the rat anterior pituitary after thyroidectomy.

Conclusion
Rapid progression of hyperplasia of pituitary gland following hypothyroidism in humans is demonstrated for the first time using a MR volumetric technique; while pituitary hyperplasia in patients with hypothyroidism has been reported in only chronic conditions.

References

Figure 1. Pituitary gland volume in fourteen patients. The hypothyroid-state had significantly larger pituitary gland volumes than the euthyroid-state in both two ways. Two of the fourteen patients had same values (385 mm3 at euthyroid and 539 mm3 at hypothyroid) in Volume 1.