Central Hypothyroidism in Acromegaly

Takamizawa et al., investigated serum thyroid levels and GH/IGF-1 in Central Hypothyroidism (CH) in untreated patients with nonfunctioning pituitary neuroendocrine tumor (NFPA) and Somatotroph adenomas.

This was a retrospective cross-sectional study of cases collected from Gunma University Maebashi and Toranomon Hospitals between 2007 and 2010.

One-hundred thirty-nine cases of non-functioning (NFPA) and 150 cases of GH secreting pituitary neuroendocrine tumor (GHPA) were analyzed.

The correlations between thyroid levels, several clinicopathological parameters, and GH/IGF-1 were examined.

Twenty-four percent of NFPA patients had Central Hypothyroidism (CeH). The severity did not correlate with tumor size, age, or sex, and all cases had normal TSH levels. In contrast, only 8.7% of GHPA patients had CeH; about half had normal TSH levels and about half had low TSH levels. Serum TSH levels in GHPA patients were significantly lower and free T4 (FT4) and free T3 levels were higher than those in patients with NFPA. Furthermore, about one-fourth of GHPA patients had normal FT4 and low TSH levels. In addition, serum FT4 levels and serum TSH levels were positively and negatively correlated, respectively, with serum IGF-1 levels. Furthermore, IGF-1 levels in patients with GHPA decreased with age.

1) NFPA patients with CeH had TSH levels within a normal range. 2) GHPA patients had a low incidence of CeH, which may be a result of stimulated thyroid function by GH/IGF-1. 3) They found an age-dependent decrease in serum IGF-1 levels in patients with GHPA [1)].

The pituitary-thyroid axis of 12 acromegalic patients was evaluated by measurement of the serum concentrations (total and free) of thyroxine (T4), triiodothyronine (T3) and reverse T3 (rT3) and thyrotropin (TSH), growth hormone (GH) and prolactin (PRL) before and after iv stimulation with Thyrotropin-releasing hormone. (TRH). Using an ultrasensitive method of TSH measurement (IRMA) basal serum TSH levels of the patients (0.76, 0.07-1.90 mIU/l) were found slightly, but significantly (P less than 0.01), lower than in 40 healthy controls (1.40, 0.41-2.50 mIU/l). The total T4 levels (TT4) were also reduced (84, 69-106 nmol/l vs 100, 72-156 nmol/l, P less than 0.01) and significantly correlated (P less than 0.02, R = 0.69) to the TSH response to TRH, suggesting a slight central hypothyroidism. The acromegalics had, however, normal serum levels of TT3 (1.79, 1.23-2.52 nmol/l vs 1.74, 0.78-2.84 nmol/l, P greater than 0.10), but significantly decreased levels of TrT3 (0.173, 0.077-0.430 nmol/l vs 0.368, 0.154-0.584 nmol/l, P less than 0.01) compared to the controls. The serum concentration of the free iodothyronines (FT4, FT3, FrT3) showed similar differences between acromegalics and normal controls. All the acromegalics showed a rise of serum TSH, GH and PRL after TRH. Positive correlation (P less than 0.05, R = 0.59) was found between the TSH and GH responses, but not between these two parameters and the PRL response to TRH. These findings may be explained by the existence of a central suppression of the TSH and GH secretion in acromegalic subjects, possibly exerted by somatostatin. Euthyroidism might be maintained by an increased extrathyroidal conversion of T4 to T3 [2)].

1)

Takamizawa T, Horiguchi K, Nakajima Y, Okamura T, Ishida E, Matsumoto S, Yoshino S, Yamada E, Saitoh T, Ozawa A, Tosaka M, Yamada S, Yamada M. Central Hypothyroidism related to pituitary neuroendocrine tumors: Low incidence of Central Hypothyroidism in patients with Acromegaly. J Clin Endocrinol Metab. 2019 Jun 12. pii: jc.2019-00466. doi: 10.1210/jc.2019-00466. [Epub ahead of print] PubMed PMID: 31188431.

2)

Eskildsen PC, Kruse A, Kirkegaard C. The pituitary-thyroid axis in acromegaly. Horm Metab Res. 1988 Dec;20(12):755-7. PubMed PMID: 3146541.