



Central or primary hypothyroidism?: How to differentiate in patients with low T4 but mildly elevated TSH levels

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Background

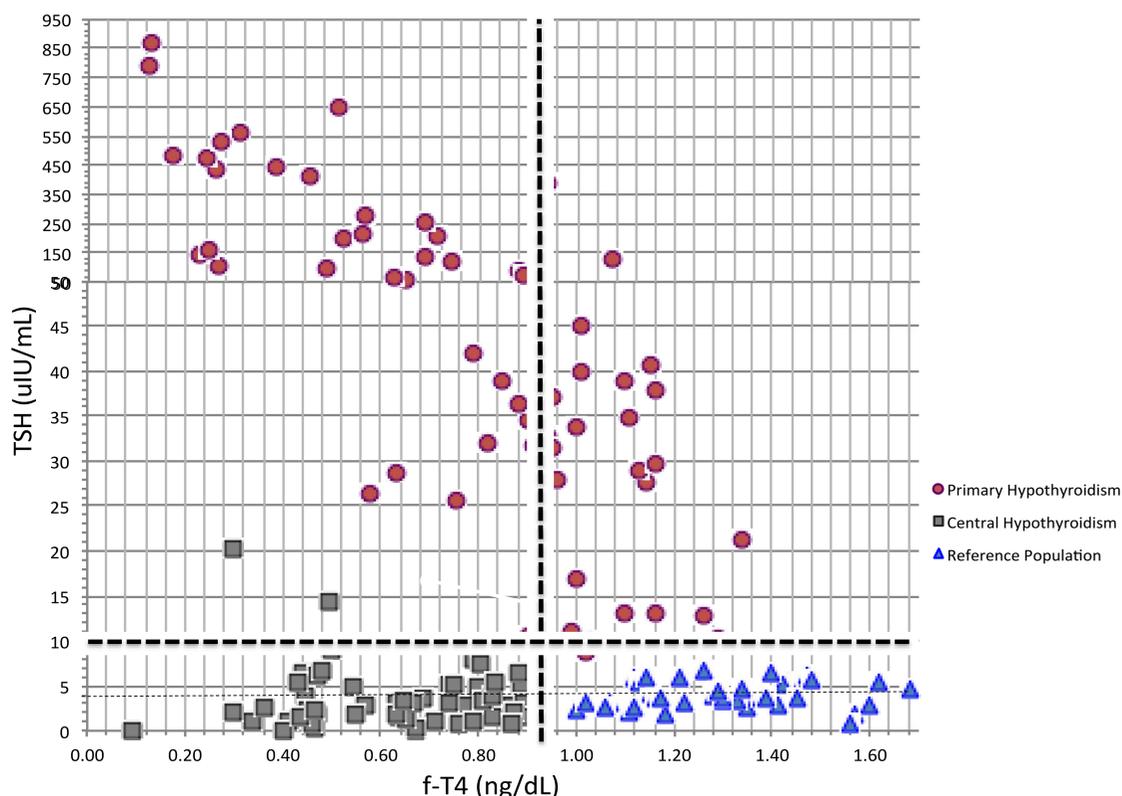
Central hypothyroidism (CH) is caused by TSH and/or TRH deficiency leading to hypothyroxinemia with low, normal or mildly elevated TSH levels. Differentiation of CH with mildly elevated TSH levels from primary hypothyroidism (PH) can be difficult. However, this differentiation has important clinical implications (i.e. cortisol replacement before L-T4).

In this study, we constructed a nomogram allowing us evaluating TSH levels relative to f-T4 levels in CH and PH, thus providing more objective criteria for the diagnosis

Methods

Sixty-three patients with congenital PH (24 thyroid dysgenesis, 39 with eutopic thyroid) and 55 patients with CH having multiple pituitary hormone deficiencies (33 congenital hypopituitarism, 22 hypopituitarism secondary to hypothalamo-pituitary tumor and/or cranial radiation) and 63 healthy controls included in the study. TSH and f-T4 levels before initiation of L-thyroxine treatment were evaluated in the patients.

Figure. TSH and f-T4 levels in reference population, patients with primary and central hypothyroidism. Vertical dashed line indicates lower limit of f-T4 in the assay used (0.93 ng/ml).



Reference ranges (fT4: 0.93 to 1.7 ng/dL) TSH: (0.27 to 4.2 uIU/mL), by ECLIA method .

Results

In CH, the mean TSH was 3.6 ± 3.5 uIU/mL (median: 2.8, range: 0.006-20.3) with a mean f-T4 of 0.61 ± 0.2 ng/dL (median: 0.66, range: 0.009-0.91).

In PH group, mean TSH was 148 ± 205 uIU/mL (median: 40, range: 8.65-867) with a mean f-T4 of 0.78 ± 0.3 ng/dL (median: 0.89, range: 0.12-1.34).

TSH versus f-T4 nomogram is shown in Figure.

Analyses revealed that in a patient with hypothyroxinemia, a TSH cut off of <10 uIU/mL is discriminatory for CH with a sensitivity and specificity of 96% (95% CI: 86%-99%) and 100% (95% CI: 88%-100%) respectively.

Similarly, a TSH cut off of >25 uIU/mL is discriminatory for PH with a sensitivity and specificity of 97% (95% CI: 84%-99%) and 100% (95% CI: 91%-100%) respectively.

There were two patients in CH group with TSH levels 20.3 and 14.3 uIU/mL who also had ACTH and GH deficiencies and, pituitary hypoplasia and pituitary hypoplasia with ectopic neurohypophysis on MRI, respectively. There was one patient with PH with $TSH < 25$ uIU/mL.

Conclusion:

When f-T4 is low, TSH cut-off <10 uIU/mL is highly sensitive for diagnosis of CH, however TSH levels could be up to 20 uIU/mL in proven CH cases. Nomogram provided in this study could be useful for discrimination in uncertain cases.

