TBG deficiency and Central Congenital Hypothyroidism (CH-C): Our experience in neonatal screening with TSH and T4

Analyze CCH detection program results from 3 Autonomous Communities (AC) of Spain, at our Public Health Regulatory Laboratory (LNSP):

- TSH and total T4 (T4T) in dried blood spot (DBS) at initial screening (48 hours of life) and at retesting.
- Describe the characteristics of neonates with screening compatible with CCH.
- Consider whether TBG deficiency (TBGD) is an added difficulty in said study.

Material and methods

Retrospective study (May 2016-May 2020) of all neonates ≥33 weeks and/or ≥1500 grams referred to the Child Endocrinology services of 3 AC from the LNSP due to low T4 (<6 µg/dL), out of a total of 105,858 CH screenings.
The positives for low T4 (<6 µg/dL) in the retesting compatible with CCH (low T4 and low/normal TSH) were analyzed. After determination in serum, the diagnoses were:

1. CCH: low free T4 (FT4) and low/normal TSH
2. TBG deficiency (TBGD): normal FT4 and elevated TSH
3. Hyperthyrotropinemia: normal FT4 and elevated TSH
4. Euthyroid sick syndrome.

Clinical and laboratory variables were compared between CCH and TBGD. The evolution of the cases considered CCH was assessed.

Results

Forty-four neonates were referred due to low T4T, 15 corresponding to primary CH and 29 cases were compatible with CCH.

The final diagnosis of the positives with initial suspicion of CCH was: 15 TBGD, 8 CCH, 5 hyperthyrotropinemia and 1 euthyroid sick syndrome. CCH prevalence in this period was 1/13,333 screenings.

Evolution of patients with CCH

Statistically significant differences were found in FT4 values when comparing CCH and TBGD.

All CCH started treatment with levothyroxine with a median age of 9.5 days (7-155). 1 patient with multiple hormonal deficiency and 7 patients with isolated CCHs have been diagnosed (according to evolution data and/or genetic results). 6 out of 8 patients with CCH also had TBGD.

Conclusions

- The determination of T4T in neonatal screening has diagnosed 8 patients with CCH.
- TBG defect is very common in the population; TBGD diagnosis does not exclude a CCH, since they can coexist.
- Genetic studies would help to confirm CCH diagnosis.

Contact information: mchueca@cn.navarra.es