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ONLY A FEW PEDIATRIC PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM PROGRESS TO OVERT DISEASE WITHIN 3 YEARS

Radetti G, Maselli M, Buzi F, Corrias A, Mussa A, Cambiaso P, Salerno M, Cappa M, Baiocchi M, Gastaldi R, Minerba L, Loche S. **The natural history** of the normal/mild elevated **TSH serum levels in children** and adolescents with Hashimoto's thyroiditis and isolated hyperthyrotropinaemia: a three year follow-up. Clin Endocrinol (Oxf). October 10, 2011. [Epub ahead of print]. doi: 10.1111/j.1365-2265.2011.04251.x.

BACKGROUND

To treat or not to treat, that is the question. Should a pediatric patient with an isolated increase of serum thyrotropin (TSH) or with positive thyroid autoantibodies but with normal free thyroxine (T_4) and free triiodothyronine (T_3) levels be treated? Most endocrinologists agree that patients with a serum TSH above 10 mU/L would benefit from thyroxine treatment. In fact, in this situation, serum thyroid hormone levels are mostly at the lower limit of normal or are decreased. In patients, who present with a serum TSH below 10 mU/L with or without thyroid antibodies, there is still no clear agreement on how to proceed. In the present study, the authors followed the evolution of thyroid function over three years in a large cohort of children collected in seven pediatric endocrinology centers in Italy.

METHODS AND RESULTS

The study included 382 children, with a mean age at the entry of 10.5 years. The study lasted 3 years; the mean age at the end of the study was 13.8 years. The patients were separated into subgroups with either an isolated increase of serum TSH (59 children) or with thyroid autoantibodies (323). Ultrasound evaluation of thyroid morphology was done in all patients. Additional subgroups were formed depending on the degree of alterations of serum TSH and of thyroid antibodies (serum TSH: grade 0, normal; grade 1, <8 to 10 mU/L; grade 2, > 8 to 10 mU/L; antibody titer: grade 1,<10 times normal; grade 2, >10 times normal). The family histories revealed a strong prevalence of autoimmune diseases.

Patients with initial grade 2 serum TSH levels and/or grade 2 thyroid antibodies were excluded from the study. Among the patients with autoimmune thyroid *continued on next page*

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antibodies, 236 had normal serum TSH, while 86 had a serum TSH level of grade 1; 72% of these patients remained stable. Only 13% moved from normal to grade 1 TSH levels and a similar percentage became hypothyroid (grade 2), 39% who initially had a moderate TSH increase (<8 to 10 mU/L) had their serum TSH spontaneously normalize, while 39% remained stable and another 14% progressed to overt disease.

The changes in thyroid antibody levels over time were not significant. The percentage of children with moderate or marked increases of thyroid antibodies did not change. In both groups (isolated TSH increase or Hashimoto's thyroiditis), progression toward hypothyroidism occurred in a similar percentage of cases (21% vs. 14%). In search of predictors indicating future hypothyroidism, only the association of celiac disease with thyroid antibodies was found to increase this risk—by a factor of 4. This association was not present in patients with only an increased serum TSH.

In most patients with an isolated TSH increase, the thyroid volume was normal and did not change. In patients with autoimmune antibodies, thyroid volume tended to be initially slightly increased, and this tendency persisted to a moderate degree during the observation period.

CONCLUSIONS

Pediatric patients with either increased serum TSH or thyroid autoantibodies need careful monitoring because no criteria exist to predict the development of frank hypothyroidism. It was only the association of celiac disease with thyroid autoantibodies that increased the risk of hypothyroidism by a factor of 4. It is reassuring that in a large proportion of patients, serum TSH or thyroid antibody levels returned to normal. Overt hypothyroidism developed in less than one fifth of patients with moderate TSH elevations or euthyroid Hashimoto's thyroiditis.

This study confirms the widely held opinion that patients with an isolated TSH increase or with thyroid autoantibodies need thorough and similar careful follow-up. The percentage of patients in whom hypothyroidism developed is not large and is quite similar in both groups. The findings of the present study may be compared with the results of the famous Whickham study, in which over a much longer observation period (20 years) approximately 30% of patients needed treatment (1). Both studies stress the point that hypothyroidism develops in only a minority of patients and, if the thyroid abnormalities persist, it is advisable to follow thyroid function at yearly intervals for the next 10 to 20 years.

The authors also raise the question of how to define

REFERENCE

1. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, Grimley Evans J, Hasan DM, Rodgers H, Tunbridge F, et al. The tissue hypothyroidism, since elevated serum TSH is clearly a poorly sensitive indicator that points only to the need to recruit the remaining capacities of a failing thyroid. Thus, thyroid hormone levels remain within the normal range for a long time. There is, however, no doubt that in each affected individual there is a moderate decrease of thyroid hormone levels as compared with the disease-free state. Do peripheral tissues recognize these changes? At present, we have no unequivocal way to answer this question; therefore, some clinicians start treatment early and others do not. It needs to be stressed that serum TSH levels or thyroid hormone antibodies normalize in a considerable percentage of subjects over time In my view, this is a strong argument in favor of an initial follow-up of these patients without treatment.

— Albert G. Burger, MD

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