Dyshormonogenetic goiter of the thyroid gland

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Dyshormonogenetic goiter is the name given to a family of inborn errors of metabolism that lead to defects in the synthesis of thyroid hormone. The prevalence of this disease is 1 in 30,000 to 50,000 live births, and it is the second most common cause (10 to 15%) of permanent congenital hypothyroidism.

Many biochemical defects can cause dyshormonogenetic goiter. The impaired synthesis of thyroid hormone leads to a loss of the negative feedback to the pituitary gland, which results in an overproduction of thyroid-stimulating hormone (TSH). The overproduction of TSH results in constant stimulation of the thyroid follicular cells. The clinical presentation depends on the severity of the inborn error. A severe defect will lead to neonatal or congenital hypothyroidism, goiter, mental retardation, and growth abnormalities (cretinism). Milder defects will present later in life (adolescence or young adulthood) as goiter and minimal (if any) thyroid dysfunction. Laboratory evaluation for inborn errors of thyroid metabolism is complex and extensive.

Macroscopically, the thyroid gland is enlarged and multinodular, and fibrous bands encapsulate individual nodules. Histologically, the process is diffuse, without normal thyroid tissue. There is marked follicular hyperplasia, hypercellularity, simple papillary formations, and decreased to absent colloid (figure, A). The follicular cells typically exhibit severe cytologic atypia, including bizarre and markedly enlarged, hyperchromatic nuclei (figure, B). These nuclear changes are most common in the internodular areas. The fibrosis entraps abnormal follicles, which can simulate a malignancy. Dyshormonogenetic goiter can mimic follicular carcinoma, papillary carcinoma, and Graves’ disease, but strict histologic criteria will help separate these lesions.

Treatment can be medical (thyroid hormone replacement) or surgical if there is symptomatic enlargement. Early treatment is particularly important in severe cases to avoid or diminish mental retardation and growth abnormalities. The prognosis is excellent with treatment.

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