Dyshormonogenetic Goiter: A Clinicopathologic Study of 56 Cases

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Abstract

Dyshormonogenetic goiters (DG) are genetically determined thyroid hyperplasias due to enzyme defects in thyroid-hormone synthesis. We report 56 cases of DG occurring in 34 females and 22 males. The patients age ranged from newborn to 52 yr (median 16), 75% of the cases occurring before the age of 24. All patients presented with clinically evidence of goiter except for two patients that were diagnosed at autopsy. Hypothyroidism was documented before the histological diagnosis was made in 36 patients (64%). The thyroid gland was enlarged and multinodular in all cases, weighing up to 600g. Microscopically, the most common alteration consisted of markedly cellular nodules exhibiting a variety of architectural appearances, the solid and/or microfollicular patterns predominating. Papillary proliferations and an insular growth pattern were also present. Fibrosis was a common finding; in some instances it was very conspicuous, resulting in irregularities at the edge of the nodules simulating capsular invasion. Other constant features included marked nuclear atypia and minimal amount of colloid.

In 18% of the cases, the degree of hyperplasia and atypia were such as to result in a mistaken diagnosis of follicular, papillary, medullary, or undifferentiated carcinoma. Three of the glands contained incidental small neoplasms fulfilling the criteria of papillary microcarcinoma; one of them was multicentric.

The presence in a thyroid gland of the combination of these morphologic features should suggest the diagnosis of dyshormonogenetic goiter. The only other condition we are aware of that can result in a similar microscopic picture is iatrogenic goiter resulting from the administration of antithyroidal agents.

Key Words: Thyroid; goiter; dyshormonogenesis; thyroid tumors; hyperplasia.

Introduction

Dyshormonogenetic goiter (DG) is the generic term given to a group of familial goiters owing to an inherited error in the metabolism of thyroid hormones [1]. The prevalence of the disease is 1 in 30,000–50,000 live births in Europe and North America [2]. DG is the second most frequent cause of permanent congenital hypothyroidism [2] following thyroid dysgenesis (i.e., aplastic, hypoplastic, or ectopic thyroid), because it accounts for 10–15% of patients with this disorder. Five major biochemical defects have been recognized, all of them leading to a defect in thyroid hormone synthesis, which in turn results in prolonged thyroid-stimulating hormone (TSH) stimulation and compensatory goiter [1]. Morphologic studies of DG have been scarce. We conducted a clinico-pathologic evaluation of 56 cases of DG in order to better characterize the pathologic features of the disease and define criteria that will distinguish these exuberant hyperplastic benign nodules from true neoplastic processes.
Material and Methods

The files of the Armed Forces Institute of Pathology (A.F.I.P.) and the personal consultation files of one of the authors (J.R.) were searched for all thyroid lesions coded as congenital goiter, sporadic goitrous cretinism, and dyshormonogenetic goiter. In all 56 retrieved cases, the presumptive diagnosis of DG was based on a combination of clinical and pathologic findings. Confirmatory biochemical data was available in only four cases. Clinically, a goiter was regarded as of probable dyshormonogenetic origin if: familial in a nonendemic area, associated with deafness (Pendred syndrome), congenital, presenting in infancy, or childhood in association with hypothyroidism/cretinism, or recurrent after thyroideectomy [3]. Patients taking goitrogen medications were excluded from the study. Clinical information was provided by the referring pathologist and the clinician. Four patients had elevated TSH values. The gross features of the thyroidectomy specimens were recorded in the 24 cases in which adequate description was available.

Hematoxylin and eosin stained slides were assessed for the following features: cellularity, nodularity, growth pattern (e.g., papillary, solid, trabecular, insular), amount of fibrosis, amount and staining quality of colloid, mitoses, presence and distribution of cellular atypia, soft-tissue extension of the hyperplastic process, and presence of capsular/vascular invasion. Immunohistochemical stains for thyroglobulin and calcitonin were performed in five cases. One case was studied ultrastructurally. Twenty-four cases of endemic goiter from Salta, Argentina were reviewed for comparison purposes.

Results

Clinical and Biochemical Features

The patients included 34 females and 22 males. The median age at histological diagnosis was 16 yr (range: newborn–52 yr), with 75% of cases being diagnosed before the age of 24. In 42 cases (75%), goiter and/or hypothyroidism appeared years before the histological diagnosis was established. The time interval between the onset of goiter and the diagnosis of DG in these cases ranged from 1–33 yr. The median age at onset of goiter and/or clinical hypothyroidism was 6 mo (range: newborn–36 yr) in the 50 patients whose exact date of onset of symptoms was recorded. Of the 25 patients whose race was known, 19 were White, 5 were Black, and 1 was Asian.

All patients presented with clinically evident goiter except for two patients whose DG was discovered at autopsy. Clinical and/or laboratory evidence of hypothyroidism was documented before the histologic diagnosis in 36 patients (64%). A family history of goiter or hypothyroidism was present in 11 cases. Eight patients (14%) underwent multiple thyroidectomies (up to three operations) in the course of their disease. Three patients (5%) developed airway obstruction and one patient had Pendred syndrome. In one case, death occurred in a 2-mo-old infant owing to asphyxia. Detailed biochemical data was available only in four cases. The abnormalities of thyroid function were owing to a partial coupling defect of moniodotyrosine to diiodotyrosine (one case), and to defective organification of iodide (three cases). One of the latter was found to be specifically owing to a defective thyroid peroxidase.

Pathologic Features

Grossly, the thyroid gland was asymmetric, multinodular, and enlarged (up to 600 g). Foci of cystic degeneration, hemorrhage, and fibrosis were common. Histological examination revealed a striking similarity of altered thyroid architecture in