Single Lobe Disease in Cases of Advanced Endemic Goiter: A New Phenotype

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Key Words

Endemic goiter · Unilateral goiter · Monolobar goiter

Abstract

Objectives: To report a new phenotype of advanced endemic goiter that affects only one lobe of the thyroid gland. **Patients and Methods:** This study included 60 patients from the west of Sudan with long-standing unilateral simple endemic goiter that required lobectomy, with emphasis on the gross appearance, measurements and cytological features of the contralateral lobe. **Results:** Out of 60 patients with unilateral goiter, 50 (83%) were found to have the disease on the ipsilateral lobe only (monolobar goiter). The contralateral lobe in these 50 patients showed no nodularity, and its volume was within the normal limits. All patients with monolobar disease had total lobectomy on the affected side, and postoperatively they continued to have normal blood levels of T₃, T₄ and TSH. **Conclusion:** We report a new phenotype of advanced endemic goiter that affects only one lobe of the thyroid gland, and in the presence of a structurally and functionally normal contralateral lobe.

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Introduction

Iodine deficiency disorders constitute a severe public health problem in Sudan. It affects children and women throughout life. More than 2 out of 10 school age children have goiter [1]. Dietary iodine intake was reported to be low in the west of Sudan. The prevalence of endemic goiter may reach 86% in some regions [2]. The inhabitants subsist on local crops and use local mountain salt. Through his experiments, Osman [3] investigated the effect of pearl millet on rat thyroid gland size and structure and suggested that this type of food, which is widely consumed in the west of Sudan, contains thiocyanate, a goitrogen which could be a major factor responsible for endemicity in addition to iodine deficiency [4].

The usual presentation of this disease is the affection of the two lobes of the thyroid gland, often in an asymmetrical pattern [5]. In our hospital, we have noticed some patients from endemic goiter areas in the west of Sudan to present with advanced forms of unilateral simple goiter that needed surgery and intraoperatively proved to express the disease on the ipsilateral lobe only (fig. 1a–c). The contralateral lobe in these patients was found to be disease-free. This is in contrast to the bilateral nodularity that characterizes endemic goiter (fig. 1d).

Our search in the literature had revealed deficiency both in the description of such an unusual type of en-

Fig. 1. **a** Preoperative photograph of a patient with left-sided monolobar multinodular goiter causing tracheal compression. **b** A patient with monolobar endemic goiter and severe cosmetic deformity. **c** Huge monolobar multinodular goiter. **d** Bilateral multinodular goiter for comparison.

demetic goiter and the possible causes underlying its development. The primary aim of our study is to report this unusual form of the disease based on clinical, volumetric and cytological findings of the contralateral lobe.

Patients and Methods

This is a case series study which was done during the period 2003–2007. The study included 60 patients from endemic goiter areas who presented with a long-standing (6 years on average) unilateral goiter that required surgery, either because of compressive symptoms or the presence of a significant cosmetic deformity (fig. 1a–c). This group of patients represents 9% of a total number of 648 patients operated for advanced multinodular goiter (620 patients with endemic goiter and 28 with sporadic goiter). Clinical examination of the neck of these patients had shown that the goiter was obviously lying to one side of the midline. No goiter was detected either by inspection or by palpation on the contralateral side (goiter grade 0 by WHO classification system) [6].

All patients were interviewed using a questionnaire. This included age, sex, tribe, and residence, as well as the duration of goiter, symptoms indicative of hypo- or hyperthyroidism, compressive symptoms, and previous treatment for the goiter. The function of the gland was assessed by measuring serum T_3 , T_4 and TSH.

The surgical procedure carried out for the affected lobe was total lobectomy. Regarding the contralateral lobe, the plane between its anterior surface and the strap muscles was entered, the

pretracheal fascia overlying its surface was carefully dissected, and the lobe was fully mobilized and examined for nodularity. If the contralateral lobe was found to be normal in the general appearance and texture and without nodularity, then its three linear dimensions were measured in millimeters using a measuring caliper (fig. 2).

Those patients whose contralateral lobes were found to be nodular – regardless of their volumes – or to show the mildest degrees of enlargement as compared to reference volumes were considered to have bilateral disease. For more accurate assessment of the contralateral lobe, intraoperative fine-needle aspiration cytology (FNAC) was performed. This was done on 20 patients. The test was done by repeated passages through the glandular tissue using a 24-gauge needle. The aspirate was spread on a glass slide, fixed with alcohol and sent for cytology.

The volume of each lobe was calculated in milliliters using an ellipsoid formula as follows:

$$\text{Volume} = c (CC \times LM \times AP)$$

where CC is the craniocaudal dimension, LM is the lateromedial dimension, and AP is the anteroposterior dimension. C represents a constant which equals 0.52 (or $\pi/6$). The lobe volumes obtained were analyzed using the SPSS version 10 computer program to produce frequency distribution of these volumes.

The above formula is used by radiologists to calculate the volume of thyroid gland. It gives volumes correlating well with the actual lobe volume [7]. All resected lobes were subjected for histopathological examination. Serum T_3 , T_4 and TSH levels were measured postoperatively at 3-month intervals for a period of 18 months.

Fig. 2. Photographs showing the cranio-caudal (a) and lateromedial (b) diameters of a normal lobe.

Results

Out of the 60 patients, 57 were female and 3 were male (ratio 19:1), with an average age of 40 years (range 20–86). This female predominance is in keeping with the fact that simple goiter is far more common in the female than in the male [8]. The mean duration of the goiter was 6 years. All patients studied were clinically euthyroid and their thyroid function tests were within the normal limits. 60% of patients had surgery because of the presence of pressure symptoms (tracheal compression), 27% because of the presence of significant cosmetic deformities, and 13% because of both symptoms.

From a total of 60 patients with unilateral goiter, 50 patients (83%) were found to have multinodular goiter that is confined to the enlarged lobe only (monolobar goiter) and these formed the group of our study. The remaining 10 patients did not meet the criteria of monolobar affection because 8 (13%) were found to have bilateral disease and 2 (4%) to have huge benign adenoma. It is worth mentioning that those patients who were found to have small and/or solitary nodules on the contralateral lobe that do not characterize endemic multinodular goiter, for example simple cysts, were considered as patients with bilateral nodularity [9]. Of the 20 patients who had FNAC intraoperatively, 16 showed uniform follicular cells and a colloid background consistent with normal thyroid tissue, two aspirates were unsatisfactory, one aspirate showed abundant colloid with scanty follicular cells consistent with colloidal goiter and one aspirate showed degenerative follicular cells with hemosiderin deposition consistent with a cystic lesion, most properly a tiny simple goiterous cyst. The majority of patients with monolobar affection (92%) were found to have a contralateral lobe volume in the range of 4–12 ml (fig. 3), corresponding to a whole thyroid volume of 10–26 ml. The contralateral lobe in all 50 patients was nodule-free and appeared nor-

Fig. 3. Graph showing the volume of the contralateral lobe in 50 patients with monolobar goiter.

mal in texture and consistency (fig. 4a, b). The mean lobe volume was found to be 9 ml (corresponding to a whole thyroid volume of 20 ml). There was no apparent correlation between the volumes of the contralateral lobe, the age of the patient, his or her sex or the duration of the goiter.

An interesting intraoperative finding was the presence of a normal-looking and well-defined pretracheal fascia and loose aerolar tissue over the surface of these normal lobes. In other words, the whole contralateral hemithyroid compartment appeared normal. Another important intraoperative finding seen in some patients with the monolobar disease and may also indicate that the two lobes have different growth characteristics, was the presence of a distinct and a well-defined plane between the

Fig. 4. **a** Preoperative photograph of a patient with left-sided monolobar endemic goiter. **b** The same patient with both lobes shown during surgery. The forceps point to the normal lobe. The enlarged lobe is held between the fingers and taken to the left of the patient.

Color version available online

normal lobe and the isthmus when the latter was found to be affected by the disease as well (fig. 5).

Histopathological examination of the resected lobes had confirmed benign multinodular goiter in the 50 patients with the monolobar disease. Postoperatively all patients continued to have normal blood levels of T_3 , T_4 and TSH, which were measured at intervals of 3 months for a duration of 18 months, indicating preserved function in the unaffected lobe.

Discussion

Multinodular endemic goiter is a multistage disease that has different clinical features corresponding to different pathological stages. If we look at the pathophysiology of multinodular goiter, the thyroid gland first goes through a phase of global hyperplasia and then through a phase of colloid storage. Both these phases are accompanied by enlargement of the thyroid gland. Later on, active lobules form as a result of fluctuating stimulation by TSH. Hemorrhage and central necrosis will then ensue and necrotic lobules will coalesce to form nodules surrounded by scar tissue and sometimes calcification [10]. In other words, nodularity develops in an already enlarged gland either because of hyperplasia or colloid accumulation as entailed by the natural history of the disease [11]. Therefore, if the contralateral lobes in our series were in the early stages of the disease, they should have shown some degree of enlargement. The disease is slowly developing and passes through different stages of enlargement with the ultimate formation of nodules.

Considering ethnic and geographical factors, there is a wide variation in the volume of the thyroid gland of normal subjects. Critical review of the literature has shown a range of volumes of 10–25 ml in non-endemic areas, and 30–35 ml in endemic goiter areas, correspond-

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Fig. 5. Photograph showing a normal right lobe (left-hand arrow) and an enlarged isthmus (right-hand arrow). Notice the clear plane between the normal lobe and the isthmus.

ing to a single lobe volume of 4–11.5 and 14–16.5 ml, respectively [12–14]. In our study, 92% of patients with monolobar goiter were found to have a contralateral lobe volume corresponding to that of normal subjects in non-endemic goiter areas.

It is not uncommon for volume values given for normal subjects to be considered as goiterous for others. There is marked global variation regarding the volume of the thyroid gland in normal subjects in both iodine replete and deplete areas. It is important to know the reference values of the thyroid volume in a population free of iodine deficiency and its determinants. Physiological factors such as body surface area and lean body mass account for much of the variation of thyroid volume [15, 16]. Genetic effects are important in the regulation of thyroid size, however the magnitude may vary between various populations [17]. Generally, the long-term influence of a different iodine intake results in considerable differences in thyroid volume as early as in childhood. By adolescence, the volume approaches what might be defined as

normal thyroid. In Sudan the reference range of thyroid volume in an iodine replete region, namely Khartoum province, is 6.44 ± 2.44 ml, compared to a mean volume of 22 ml in endemic goiter regions in the West [18]. In a comparative epidemiological study performed in two regions with a slightly different iodine intake in Denmark, 4,649 subjects from the general population were examined. Median thyroid volume at ultrasonography was found to be 11.9 ml in a mild iodine-deficient area and 13.6 ml in a moderate iodine-deficient area [19]. In two other epidemiological studies done separately in goiter-endemic areas in Germany and Senegal, the volume of the thyroid gland for normal subjects in Germany was found to be 50 ml, a volume twice that found in Senegal [20, 21]. Ahidjo et al. [22] reported values for normal thyroid volume in a Nigerian population lower than those among Caucasians.

FNAC of the thyroid is a quick, safe, accurate, and inexpensive procedure. Its outcome compares well with the results of tissue biopsy. The sensitivity of the thyroid FNAC ranges from 80 to 98%, and its specificity from 58 to 100%. The cytohistological concordance rate for some diseases like colloid goiter in endemic goiter areas approaches 90% [23]. Although in nodular thyroid disease the role of core biopsy may outweigh FNAC, the latter can be advocated in the medical management of all non-palpable or minimally enlarged thyroids in patients suspected of having thyroid pathology [24]. In our study, FNAC was performed on the contralateral lobes to exclude the presence of diffuse hyperplasia and colloid abundance which may signal early stages of goiter [25, 26]. Moreover, if multiple core biopsies are needed, then this may be associated with tissue damage and bleeding. FNAC is much less invasive and can be performed safely through multiple passes.

Based on our findings, the confinement of the disease to one lobe only poses very interesting questions. Firstly, why the contralateral lobe is refractory for the disease? Secondly, after reaching such advanced stages, why should there be a delay in the appearance of the disease on the contralateral lobe should it develop at all?

With the etiopathogenesis of endemic goiter in mind, the volumes obtained – which are equal to or less than those for normal subjects in endemic goiter regions – as well as the morphological and the cytological features of the contralateral lobes will all defy the presence of any of the stages of endemic goiter [27, 28]. There is substantial evidence that the contralateral lobes are disease-free and, therefore, it is unlikely that they are lagging behind the goiterous ones.

In the literature some diseases are reported to present in an asymmetrical pattern or to affect only one side of the body, like the epidermal nevi of the epidermolytic hyperkeratotic type and dermal neurofibroma in segmental neurofibromatosis type 1. These cutaneous lesions could be explained on the bases of somatic mosaicism, and in the case of segmental epidermal nevi of the hyperkeratotic type the affected skin was found to have keratinocytes with a mutated keratin gene [29, 30]. Other examples of asymmetrical diseases are Caroli's disease and Protues syndrome. Monolobar Caroli's disease, reported in the literature [31–33], is a congenital disorder characterized by segmental saccular dilatation of intrahepatic bile ducts [34]. The most acceptable theory explaining its pathogenesis is ductal plate malformation. Because the majority of cases of monolobar Caroli's disease are case reports, there have been no investigations into its etiopathogenesis. However, Ghosh and Emery [35, 36] could demonstrate how differences in liver blood flow and hypoxia during infancy could bring about differences in the histology of the two lobes of the liver that make them react differently to noxious stimuli later in life. Proteus syndrome is a complex disorder consisting variably of disproportionate, asymmetric overgrowth of body parts, particularly involving the skeleton, epidermal nevi and vascular malformations. The etiology of this syndrome is not known, but the best working diagnosis is somatic mosaicism [37, 38]. Disease asymmetry may sometimes be caused by locoregional factors as in asymmetrical idiopathic pulmonary fibrosis caused by gastroesophageal reflux disease [39]. Moreover, the process of thyroid gland organogenesis and the molecular basis of its development are rather complex. The genetic bases of thyroid developmental abnormalities are largely unknown, though mutations that take place in the regulatory genes are believed to be responsible for these developmental abnormalities [40].

To conclude, we report a new phenotype of endemic goiter where only one lobe of thyroid gland showed advanced forms of the disease that required operation, and in the presence of a structurally and functionally normal contralateral lobe. We think that molecular studies are needed to unravel this mysterious form of disease and open avenues in understanding the pathogenesis of a very important endemic disease that is widely spread over the world.

Acknowledgement

Supported by the University of Medical Sciences and Technology, Khartoum, Sudan.

Disclosure Statement

The authors declare that no financial or other conflicts of interest exist in relation to the content of the article.

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