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Thyroid Cancer in Suppressed Contralateral Lobe of Patients with Hot Thyroid Nodule

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We studied 60 patients with thyrotoxicosis due to single toxic nodule. At surgery in 3 patients (5%) a papillary carcinoma has been detected in the contralateral suppressed lobe. Thyroid function tests and thyroid scan confirmed thyrotoxicosis. Thyroid stimulating hormone (TSH) was undetectable in all patients. It is common opinion that differentiated thyroid tumour growth is TSH dependent. On the basis of our study two hypotheses are possible: (1) the development of thyroid carcinoma precedes the adenoma and suppressed TSH levels inhibit tumour growth; (2) suppressed TSH levels do not protect patients from the occurrence of cancer. In the evaluation of hot thyroid nodule we suggest careful ultrasonographic control in order to look for nodules outside the adenoma. A complete surgical examination of the whole thyroid gland is required and intraoperative biopsies are advocated in abnormal areas.
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INTRODUCTION

IT IS WELL KNOWN that hyperfunctional thyroid nodules can be malignant [1–7]. Interestingly, thyroid cancer can develop in the suppressed contralateral lobe in patients with hot thyroid nodule. The present study indicates a 5% incidence of papillary carcinoma in the suppressed lobe of the thyroid gland which has a contralateral hyperfunctioning nodule.

PATIENTS AND METHODS

This study includes 60 patients (Table 1) with a diagnosis of solitary hot thyroid nodule, referred to our clinic in the 3-year period from January 1989 to December 1991. At clinical examination the patients had no cervical adenopathy and presented one palpable thyroid nodule which was hyperactive (hot) at thyroid scan (1.85 MBq of ^{131}[I] orally) and not suppressible by triiodo thyronine (T_3) administration (T_3 100 μg daily for 8 days). The remaining thyroid parenchyma was suppressed at thyroid scan and appeared free of nodules at ultrasound examination. The data available at this point were believed to be sufficient for the diagnosis of an autonomously hyperfunctioning nodule. Thyroid surgery was performed after antithyroid drug therapy (propylthiouracil). Unilateral thyroid lobectomy, intraoperative biopsy and histological examination were performed. The histological appearance of the lobe revealed normal thyroid tissue containing a follicular adenoma within a capsule (Fig. 1a). All patients underwent peroperative palpation of the contralateral lobe and 3 patients presented an abnormal hard area measuring less than 1 cm in diameter. The areas immediately examined by the pathologist (intraoperative biopsy) revealed malignancy (Fig. 1b). Nearly total thyroidectomy was performed. Thyroid tissue was subjected to careful histological examination and no other malignancy was found. The patients subsequently received substitutive (in cases of adenoma) and suppressive (in cases of malignancy) hormone therapy with l-thyroxine. At 24, 12 and 6-month follow-up no recurrence of tumour was detected on ^{131}[I] whole-body scintigraphy and thyroglobulin serum levels were persistently low (<10 ng/ml).

Table 1. Patients (n = 60) *with solitary hyperfunctioning thyroid adenoma*

History	Physical examination	Laboratory tests and imaging studies
Age (years) 50 ± 10	Size (cm) 3 ± 1.2	T_3-RIA (ng/dl) *211 ± 15 **105 ± 10
Sex (female/male) 45/15	No fixation, tenderness, adenopathy	T_4-RIA (μg/dl) *13.4 ± 1.2 ** 7.8 ± 3.0
Presence of nodule (months) 24 ± 16		TSH-IRMA (μU/ml) *<0.06 **1.2 ± 0.7
No previous radiation, local symptoms, family history for thyroid cancer		Scan patterns: hot nodule and suppression of the remaining thyroid gland
		U.S. examination: solid mass, size 2.7 ± 0.8 cm

T_3, Triiodo thyronine; T_4, thyroxine; TSH, thyroid stimulating hormone; RIA radioimmunoassay, IRMA, sensitive immunoradiometric assay. Data are presented as mean ± 1 S.D. *Before, **after antithyroid drug therapy.

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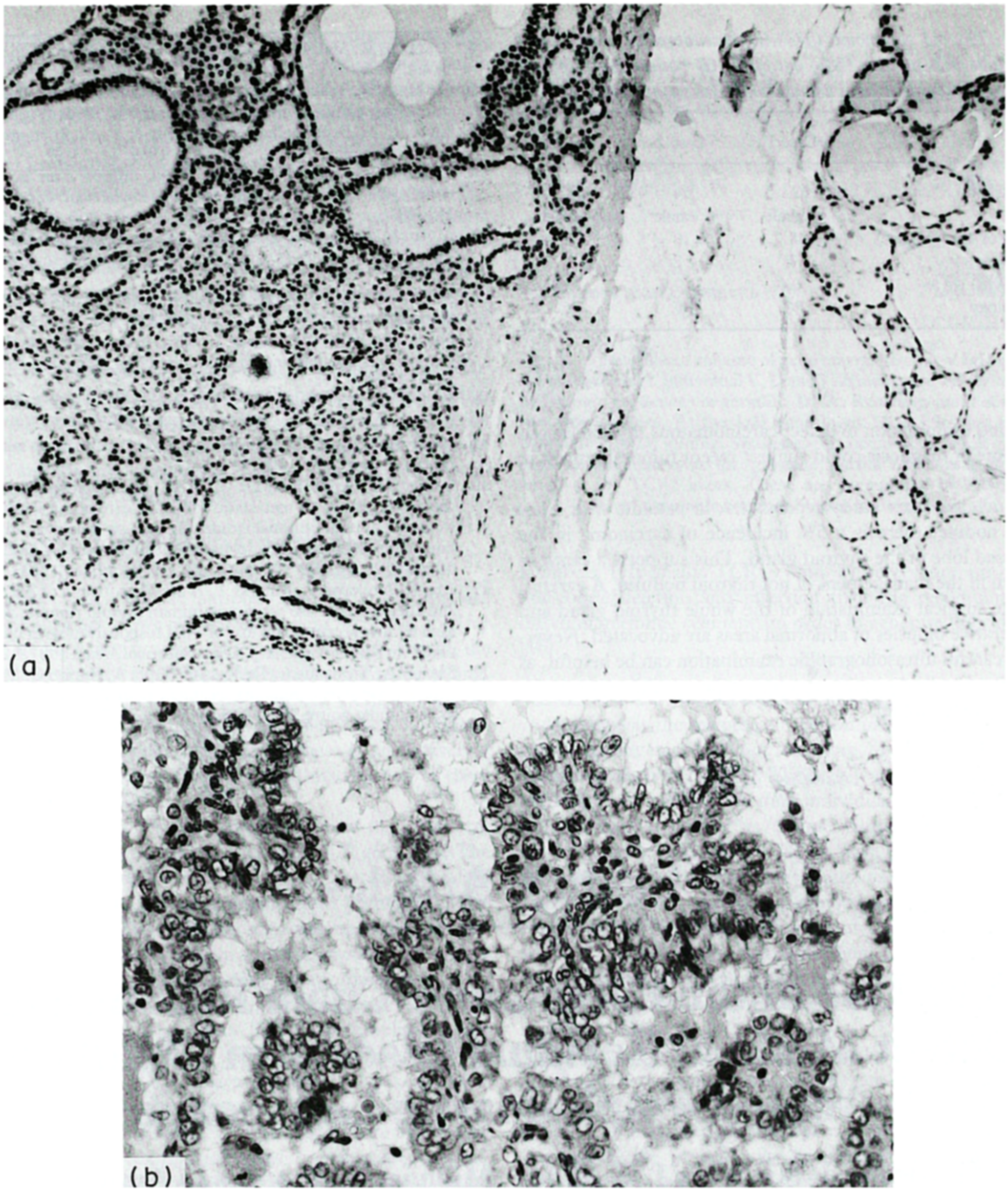

Fig. 1. (a) Case 1—Follicular adenoma, right lobe (×100). Adenomatous nodule shows a definite, fine and fibrous capsule: it is well delimited from normal parenchyma. Neoproliferation is formed by microfollicular arrangement with cubic cells. (b) Case 1—Papillary carcinoma, left lobe (×400). The tumour is formed by fine vascular axis lined with multilayered epithelium. The neoplastic cells show optically clear nuclei with occasional inclusions.

DISCUSSION

Almost all toxic solitary nodules are adenomas and only rarely are they carcinomas [2, 8]. It has been reported that positive associations exist between Graves' disease and thyroid cancer [9]. Thyroid stimulatory immunoglobulins, present in the sera of patients who have coincident autoimmune thyroid disease (like Graves' disease), may induce tumour growth. Congenital metabolic defects with thyroid hyperplasia and elevated thyroid stimulating hormone (TSH) levels in humans can lead to carcinomatous degeneration if patients have been untreated for many years [10]. Differentiated tumours have normal thyroid stimulating hormone (TSH) receptors and TSH-dependent growth, whereas anaplastic cancers lack high-affinity receptors and show TSH-independent growth [11]. This TSH-dependent growth supports the indication for long-term suppressive hormone therapy both for goiter and after limited thyroid surgery for benign and malignant lesions. Our observations can be interpreted in at least two ways: (1) if thyroid carcinoma precedes the thyroid hyperfunctioning adenoma, suppressed TSH levels may inhibit carcinoma growth; (2) the suppressed TSH levels do not protect patients from the occurrence of cancer. This latter hypothesis is in agreement with a previous observation in a patient with goiter who developed cancer during continuous, prolonged suppressive thyroid therapy [12]. The failure of

Table 2. Thyroid carcinoma (TC) in the suppressed controlateral thyroid lobe in 3 patients (5%) out of the 60 patients with solitary hyperfunctioning thyroid adenoma (TA) described in Table 1

	Case 1	Case 2	Case 3
Age (years)	62	54	68
Sex	Female	Female	Female
Presence of TA (months)	8	10	12
TA size (cm)	3	2	3
TC size (cm)	0.9	0.7	0.8
TC histology	PC	PC	PC

ultrasound examination to detect carcinomatous thyroid lesions at the time of diagnosis could suggest recent tumoral growth in our 3 patients.

In conclusion, our study reports that in patients with a hot thyroid nodule, there is a 5% incidence of carcinoma in the suppressed lobe of the thyroid gland. This supports a cautious approach in the management of hot thyroid nodules. A careful, complete surgical examination of the whole thyroid gland and intraoperative biopsies of abnormal areas are advocated. Nevertheless, careful ultrasonographic examination can be helpful, as well as fine-needle aspiration cytology, when nodules outside the adenoma are identified.

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Feature Articles

The Use of the Polymerase Chain Reaction to Detect Minimal Residual Disease in Childhood Acute Lymphoblastic Leukaemia

Colin G. Steward, Nicholas J. Goulden, Michael N. Potter and Anthony Oakhill

INTRODUCTION

SEVENTY PER CENT of children with acute lymphoblastic leukaemia (ALL) can now be cured by conventional chemotherapy [1]. Successful treatment began in the 1940s when prolonged survival was first reported following the use of aminopterin [2]. The concept of a remission was thus proposed [3] and during the 1950s and 1960s the use of combination chemotherapy, for inducing remission, and maintenance therapy to consolidate that remission brought about the first true cures [4].

In adult ALL, there are an estimated 10^{12} leukaemic cells at diagnosis and a proportional number, therefore, are expected in children. Typically, induction therapy continues for 28 days, by which time the blasts have cleared from the peripheral blood and the full blood count has returned to normal. Examination of bone marrow in nearly all children at this time will reveal less than 5% blasts by light microscopy. This then is the definition of haematological remission, but the patient may still harbour up to an estimated 10^{10} malignant cells [5]. These are collectively termed minimal residual disease (MRD) and the aim of maintenance or continuing chemotherapy is the elimination of the majority of this disease.

At least 25% of patients will have a relapse in their bone

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