Good prognosis in thyroid cancer found incidentally at surgery for thyrotoxicosis

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Summary

An analysis of the outcome of thyroid carcinoma incidentally discovered in patients undergoing surgery for hyperthyroidism is presented. Among 986 patients with differentiated thyroid cancer, 23 had presented with symptoms and signs of hyperthyroidism. Graves' disease was diagnosed in 11, multinodular goitre in eight and toxic adenoma in four. Following thyroidectomy, histology revealed papillary (18), follicular (four) and Hurthle cell (one) carcinoma. Tumour size ranged from 4 mm to 5.5 cm, multifocality was detected in three patients, and lymph node involvement in one. Two patients (one with associated Graves' disease, one with multinodular goitre) relapsed locally and required further surgery; one developed distant metastases and died 7 years after initial presentation. Two patients died of unrelated causes; the remaining 20 patients are alive and well with a median follow-up of 16 (1–34) years. Differentiated thyroid cancer found incidentally at surgery for hyperthyroidism has a good prognosis.

Keywords: thyroid neoplasms; thyrotoxicosis; thyroidectomy

Previous studies have suggested that thyroid cancer occurs more frequently in patients operated for hyperthyroidism than in euthyroid patients.^{1–4} The reported incidence of thyroid carcinoma found at surgery in hyperthyroid patients ranges from 0.21% to 8.7% depending on the criteria used to select patients for surgery, patient characteristics and history of previous neck irradiation. More recently, it has been suggested that thyroid cancer associated with Graves' disease is highly aggressive and should be treated vigorously.⁵ Other investigators⁶ have not confirmed this finding and the issue remains controversial. We report our experience in patients found to have differentiated thyroid cancer at thyroidectomy for hyperthyroidism.

Patients and methods

Between 1949 and 1997, 986 patients with differentiated thyroid cancer were treated at the Royal Marsden Hospital, which serves as a tertiary referral unit for patients with thyroid disease. Twenty-three patients (19 women, four

men, median age at diagnosis 35 years, range 21–78 years) had presented with clinical features of hyperthyroidism. The duration of hyperthyroidism ranged from 4 months to 13 years (median 3 years). Graves' disease was diagnosed in 11 patients based on clinical findings, the presence of circulating thyroid antibodies and a uniformly increased ¹³¹I thyroid uptake scan appearance.

Toxic multinodular goitre was diagnosed in eight patients and autonomously functioning thyroid adenoma in four patients based on clinical and scan appearances. Graves' disease with a palpable nodule was not diagnosed in this series.

Subtotal thyroidectomy was performed initially in all cases. Indications were: recurrent hyperthyroidism after medical treatment (7), physician preference (5), large goitre responding poorly to medical treatment (4), persistent drug effects (3), enlarging nodule (2) and patient preference (2). In 13 patients, total thyroidectomy was subsequently performed followed by 3 GBq of ¹³¹I to ablate residual tissue.

All patients were followed-up according to our thyroid cancer protocol at intervals increasing from 6 months to yearly. At each visit, patients were clinically assessed and serum thyroglobulin was estimated. Where whole body ¹³¹I scans demonstrated persistent uptake, further ablation with radioiodine was given.

Results

Eighteen papillary, four follicular and one Hurthle cell carcinoma were found incidentally in the thyroidectomy specimens. In three cases, more than one focus of cancer was identified. Tumour size ranged from 4 mm to 5.5 cm; 12 tumours were less than 1 cm (T1), five were 1–2 cm and five were over 2 cm in diameter. Five (45%) of the tumours in the Graves' patients, two (50%) in the toxic adenoma patients and four (57%) in the multinodular patients were over 1 cm in diameter. Only one patient had evidence of lymph node involvement at presentation.

Follow-up ranged from 1–34 years with a median of 16 years. Two patients suffered a local recurrence; one with associated Graves' disease, the other with an underlying multinodular goitre. A 2.5 cm follicular thyroid cancer was discovered at thyroidectomy in the Graves' patient. She underwent total thyroidectomy and received ablative radioiodine but despite this, developed lymph node recurrence 5 years after presentation. Block dissection of

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Accepted 2 September 1988

lymph nodes was performed but two years later she had developed brain metastases and died 7 years after initial diagnosis.

The patient with multinodular goitre and recurrent thyroid cancer had been found to have an 8 mm Hurthle cell carcinoma at the time of subtotal thyroidectomy. Ten years later a 1 cm palpable nodule was discovered in the thyroidectomy scar and was found to contain recurrent cancer. She underwent completion total thyroidectomy. She remained disease-free thereafter and died of heart disease 17 years after initial presentation with no evidence of recurrent thyroid cancer at death.

There was one further death in a patient with associated Graves' disease unrelated to thyroid cancer (gall bladder cancer). The remaining 20 patients are alive and well with no evidence of recurrent disease.

Discussion

In this series of patients with occult thyroid malignancy and hyperthyroidism, we have not found evidence of increased tumour aggressiveness over a long period of follow-up. Only two patients developed local recurrence and only one distant metastases. Tumours in patients with Graves' disease were no larger than in other hyperthyroid patients and behaved no differently from those in non-Graves' patients. These results contrast with those of Belfiore *et al*⁵ who reported a high incidence of local invasiveness, lymph node involvement and distant metastases in their patients with Graves' disease and thyroid cancer. However, all but two of their Graves' patients had palpable nodules in contrast to the present study (none had nodules) which could indicate that tumours in the previous study were detected later and hence had a poorer outcome.

Only three patients had evidence of multiple foci in histological specimens. A higher frequency may have been found if all patients had

Learning points

- tumours discovered incidentally at thyroidectomy in patients with thyrotoxicosis generally have a good prognosis
- occult thyroid tumours in patients with Graves' disease behaved no differently from those in non-Graves' patients

undergone total thyroidectomy. Similarly, elective node dissection on all patients may have detected a higher incidence of nodal involvement. Nevertheless, the prognosis of our patients remained good and certainly we would have expected to detect metastases during the long period of follow-up.

The good outcome of the patients in our series is similar to that found in previous studies.⁶⁻⁸ Possible factors contributing to the high survival and low incidence of recurrences include young age at presentation and more aggressive treatment. In this series, we treated patients with less favourable prognostic indicators (older patients, T2 and T3 tumours) with more radical surgery and ablative iodine. However, treatment alone does not explain the initial lack of invasiveness and metastases observed in this study.

Care is needed in interpreting histology as the diffusely hyperplastic gland of Graves' disease may simulate malignancy; the cases in this series were all diagnosed by experienced pathologists according to established criteria.⁹

In summary, our results do not suggest increased aggressiveness in incidentally discovered thyroid carcinomas associated with hyperthyroidism. Further work is needed to define the optimal treatment for this group of patients.

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