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Thyroid Carcinoma

Presentation of a Clinical Material with Special Aspects on the Classification and Operative Treatment

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ABSTRACT

During the years 1969–1975, 58 patients were treated for thyroid carcinoma. 48 patients had differentiated and 10 had anaplastic carcinomas. The material is presented with special attention given to diagnostic methods and treatment for the differentiated forms. The value of cytological examination of fine needle biopsy is clearly documented. 40 patients with differentiated carcinomas were treated with total thyroidectomy, with low complication rate. Accidental persistent recurrent nerve paralysis as well as persistent hypoparathyroidism occurred in less than 3%, Subdivision of papillary and follicular carcinomas on the basis of their local growth pattern is emphasized as being of value in the determination of subsequent therapy.

INTRODUCTION

The incidence of thyroid carcinoma has increased during recent years as suggested by several authors (1, 4, 10). Possible explanations could include the use of better-defined criteria for diagnosis as well as factors such as increasing exposure to carcinogens.

Management of the patient with thyroid carcinoma is a challenging problem. Surgical excision is generally recognized as the preferable primary treatment for carcinoma of the thyroid gland. Different opinions still exist concerning the extent of the surgical procedure. To clarify some of the diagnostic and therapeutic problems connected with thyroid carcinoma during the past years we present a review of all patients observed through 1969–1975 at the University Hospital, Uppsala. Special interest is given to the differentiated forms of carcinomas and their treatment.

Table I. *Thyroid carcinoma—material and diagnosis*

	No. pats.	% pats.
Differentiated	48	83
Papillary	25	43
Follicular	21	36
Medullary	2	4
Undifferentiated	10	17
Small-cell anaplastic	3	5
Giant-cell anaplastic	3	5
Carcinosarcoma	4	7

MATERIAL

All patients (=58) were operated for histologically verified primary carcinoma of the thyroid gland. The tumour classification, sex and age distribution are shown in Tables I and II. Most of the patients (72%) came from the hospital service area (a population of 230000) and the remaining patients (28%) were referred to us from hospitals outside this area.

A histo-pathological subclassification (8, 9) of the papillary and follicular carcinomas is shown in Table III.

Symptomatology, clinical observations and diagnostic procedures

Differentiated carcinomas. The main symptoms of patients with differentiated carcinomas appear in Table IV. More than 50% had a solitary nodule while 25% presented

Table II. *Thyroid carcinoma—material, age and sex distribution*

	Age		Sex
	Range	Mean	Male : Female
Differentiated	23–81	53	1 : 4
Papillary	23–76	49	1 : 4
Follicular	27–81	58	1 : 4
Medullary	31–57	44	– : 2
Undifferentiated	49–87	65	2 : 1
Small-cell anaplastic	49–72	63	1 : 2
Giant-cell anaplastic	68–87	75	2 : 1
Carcinosarcoma	47–74	60	3 : 1

Table III. *Thyroid carcinoma—subclassification of differentiated carcinomas and stage*

	No. pats.	% pats.	Metastases regional	Metastases distant
Papillary	25			
Occult	6	24	4	
Intrathyroidal	18	72	1	
Extrathyroidal	1	4		1
Follicular	21			
Microinvasive	10	48		2
Macroinvasive	11	52		3

Table IV. *Thyroid carcinoma—main symptoms*

	No. pats.
Solitary nodule	25
Unilateral atoxic goitre	10
Bilateral atoxic goitre	3
Nodular toxic goitre	4
Lymph nodes in neck	2
Distant metastases	4

as non-toxic multinodular goitre, unilateral or bilateral. Four toxic goitres were found to contain carcinoma. Fifteen of the patients had been previously treated for goitre, fourteen for atoxic and one for toxic goitre. None of them had had continuous thyroid hormone substitution. Four patients reported previous irradiation of the neck, 5, 30, 35 and 40 years, respectively, before surgery for thyroid carcinoma.

In fourteen patients (30%) a correct diagnosis was possible on clinical grounds in combination with preoperative cytological examination. In 10 cases (20%), where cytology had aroused suspicion of malignancy, cancer could be demonstrated histologically in the frozen section. In another two patients, who were operated with no suspicion of cancer, a frozen section gave the diagnosis. The diagnostic value of preoperative fine needle biopsy and histological examination of the frozen section is illustrated for all the material in Tables V and VI. The diagnostic accuracy of fine needle biopsy has improved and the results from 1974–75 are presented separately in Table VII.

Anaplastic carcinomas. The anaplastic carcinomas in general were clinically obviously malignant with rapid local growth.

OPERATIVE PROCEDURES

Differentiated carcinomas. The surgical procedures performed are listed in Table VIII. 83% of the patients with differentiated carcinomas had a total thyroidectomy. It was performed as a primary operation in 23 cases, secondary in 17.

Total thyroidectomy was combined with removal of the lymph nodes in the pre- and paratracheal area. Nodes in the tracheooesophageal groove were removed if they appeared to be involved. In one case with extensive metastases of papillary cancer a unilateral radical neck dissection was performed.

In the operative procedure special attention was paid to visualizing the recurrent nerve, the inferior artery and the parathyroids. The inferior artery was freed laterally and the trunk ligated in continuity. The parathyroids were, if possible, dissected free and left intact. If the vascular supply was damaged, the gland was removed and autotransplanted to the sternocleidomastoid muscle. Suction drainage was always used.

The vocal cords were inspected before and after the

Table V. *Thyroid carcinoma—the diagnostic value of fine needle biopsy*

	No. pats.	Not performed	No signs of malignancy	Slight or moderate atypia	Grave atypia, cancer
Papillary	25	3	7	3	12
Follicular	21	3	5	3	10
Medullary	2	–	–	1	1

Table VI. *Thyroid carcinoma—the diagnostic value of frozen section*

	Frozen section				
	No. pats.	Not performed	No signs of malignancy	Malignancy suspected	Cancer
Papillary	25	9	4	2	10
Follicular	21	10	–	7	4
Medullary	2	1	–	–	1

Table VII. *Thyroid carcinoma—the diagnostic value of fine needle biopsy 1974–75*

	No. pats.	Not performed	No signs of malignancy	Moderate atypia	Grave atypia or cancer
Papillary	10	–	3	1	6
Occult	3	–	2	–	1
Intra-Extrathyroidal	7	–	1	1[a]	5
Follicular	10		2	2	4
Microinvasive	6	1	2	2	1
Macroinvasive	4	1	–	–	3
Medullary	1	–	–	1	–
Anaplastic	5	–	–	–	5

[a] Frozen section was not positive.

operation. The postoperative serum calcium level was followed daily, for 7 to 10 days.

Anaplastic carcinomas. The anaplastic carcinomas were so advanced that surgery was only palliative. In one patient the anaplastic carcinoma (small cell type) was encapsulated and was possible to resect completely.

Further therapeutic procedures. After surgery *radioactive iodine* was used to estimate the activity of residual thyroid tissue and to discover possible metastases. Radioactive iodine was used therapeutically if there were significant remnants or metastases, especially in follicular carcinomas and elderly patients.

External radiotherapy was given only to anaplastic carcinomas and to one case with low differentiated follicular carcinoma.

Permanent *suppressive therapy with thyroid hormone* was given to all patients.

COMPLICATIONS OF THE OPERATIVE PROCEDURE

Mortality

There was no per- or immediate postoperative mortality.

Postoperative bleeding

3 patients had postoperative bleeding which required reoperation with hemostasis. In no case was tracheostomy necessary.

Table VIII. *Thyroid carcinoma—operative procedures in the differentiated forms*

	No. pats.
Total thyroidectomy[a]	40
Lobectomy	5
Bilateral subtotal resection	3

[a] 17 were performed as secondary operations.

Paralysis of recurrent nerve

In 4 patients nerve excision was necessary to ensure removal of the neoplasm. Unilateral transient paralysis, lasting for 3 months, occurred in another 2 patients. One patient suffered an accidental and persistent unilateral paralysis. This patient had had total thyroidectomy as a secondary procedure. In no case there was any nerve complication on the side opposite the cancer.

Postoperative hypoparathyroidism

Two patients (5%) required vitamin D supplementation implying a persistent postoperative hypoparathyroidism. One of these patients had previously been unsuccessfully explored for hyperparathyroidism but the parathyroid adenoma was not found until the definitive operation for thyroid carcinoma. Another 2 patients had initial substitution with D-vitamin for two months. Both patients are now without substitution and symptomless but with a slightly lowered serum calcium level (2.10–2.20 mmol/l).

Thus, the frequency of accidental persistent hypoparathyroidism was less than 3%.

RECURRENCE AND SURVIVAL

Differentiated carcinomas

Three of the patients with differentiated carcinomas died of the primary disease, one with papillary and two with follicular tumours. They all had advanced tumours at the operation. Another patient had died from intercurrent disease.

Three patients with papillary carcinomas had recurrences in regional lymph nodes which were

operatively extirpated in two patients and treated with radioiodine in one.

In four patients with follicular carcinomas metastases caused further progress of their disease. These patients had locally advanced disease at the primary operation.

Anaplastic carcinomas

In the anaplastic cancer group all the patients died within one year, except the patient who was operated for an encapsulated anaplastic carcinoma and who is still well 6 years after operation with no signs of recurrence.

DISCUSSION

The association between thyroid carcinoma and radiation is well documented (7, 15). The radiation induced tumours are often said to be of the papillary type and less malignant. In our material four patients (nearly 10%) had previous irradiation. Two of these patients had tumours of the papillary type but the other two had follicular and medullary carcinomas, respectively.

A contributing factor to the development of carcinoma after irradiation may be an elevated TSH-level due to slight thyroid hypofunction. The importance of TSH-stimulation as an etiological factor for thyroid carcinoma has been shown experimentally (16). Such a factor may be responsible for a higher cancer frequency in patients with goitres or patients where medical or surgical treatment has resulted in lowered thyroid function. In the present study 25% of the patients had had previous treatment for goitre. An earlier report (11) from our clinic has shown the high frequency of subtle hormone deficiency after surgical treatment of thyreotoxicosis. This underlines the importance of a lifelong follow-up after thyroid surgery as well as after medical treatment of goitre, not only for the control of thyroid function but also because of the enhanced risk of cancer development.

There are increasing reports of the coexistence of thyroid carcinoma and hyperparathyroidism (6, 12). Irradiation therapy has also been claimed as an etiological factor for hyperparathyroidism (17). In our series two patients (one papillary and one follicular carcinoma) had concomitant verified parathyroid adenoma, another two (both follicular carcinomas) had hypercalcemia which was normalized after surgery though no parathyroid abnormality was found. None of these patients had had previous irradiation.

Carcinoma of the thyroid gland can present in different ways. Usually only anaplastic and some follicular tumours have the classical clinical appearance of malignancy. Most of the differentiated carcinomas present in a form indistinguishable from that of a benign goitre. This is clearly demonstrated in the present study. It is therefore important to look for signs indicating malignancy, such as unilateral or asymmetric goitre, especially in combination with change in size. The solitary nodule always involves a very high risk of malignancy, which is also demonstrated by this material. The aim should be to recognize papillary carcinoma presenting only with enlarged lymph nodes in the neck. In our material two cases were diagnosed in this way, both had occult tumours.

It is essential to reach the diagnosis of thyroid carcinoma preoperatively as it influences the choice of surgical procedure and diminishes the need for reoperations. In our material the pre- and peroperative diagnosis proved correct only in about 50% mainly because diagnostic procedures were not used to the full extent during the first years of the study. However, during the latter part of the period the routine use of fine needle biopsy has led to increased accuracy. The problem remains of differentiating atypical follicular adenoma from encapsulated, highly differentiated follicular carcinoma and of finding a minimal papillary cancer.

Different opinions still exist concerning the extent of surgery for differentiated carcinomas. Follicular carcinomas are always able to take up iodine for visualization and treatment of metastasis and this uptake is highly improved after removal of the thyroid gland. Also some papillary carcinomas can take up radiaoctive iodine, especially if they contain a follicular component. Total thyroidectomy seems reasonable on these grounds and also because of the reported high degree of multicentricity of all differentiated forms of thyroid carcinomas (3, 14). Because of this multicentricity there is always a risk of recurrence in the remnant. No serial sectioning has been done in this material but there were clearly visible bilateral or multicentric tumours in 30% of patients. The tendency for multicentricity was most obvious for the occult papillary tumours and microinvasive follicular tumours.

If a total thyroidectomy is done it is easier to diagnose a possible recurrence with radioiodine and

fine needle biopsy. Recent reports of improved prognosis after more extensive operations further advocate total thyroidectomy (13). The main argument against total thyroidectomy has been the hazard of a higher complication rate. Our series, however, shows that total thyroidectomy is possible to perform with minimal risk of complications.

No prognostic conclusions can be drawn from this material because of the limited follow-up time. However, the subclassification of the differentiated forms seems valuable as a help in determining the prognosis for a particular patient. Furthermore it is helpful in deciding on the need for subsequent therapy, especially radio-iodine.

CONCLUSIONS

Differentiated thyroid carcinomas often present as solitary nodules or goitres often clinically indistinguishable from benign goitre.

Carcinomas can be combined with toxic goitre. Many of the patients with thyroid carcinoma have had previous thyroid disease indicating a slight thyroid hormonal hypofunction as a possible etiologic factor. All patients with previous thyroid disease should be continuously followed and protected from thyroid dysfunction.

Fine needle biopsy has proven of great value for the diagnosis. Still remain difficulties to cytologically diagnose microinvasive follicular and occult papillary carcinomas. All possible diagnostic methods should be widely used as reoperations should be avoided because of their higher complication rate. Also with the frozen section technique it is difficult or impossible to differentiate between some types of adenomas and highly differentiated follicular carcinomas. Because of these diagnostic problems total lobectomy is indicated in all cases of solitary adenomas.

Total thyroidectomy seems to be the treatment of choice for all differentiated thyroid carcinomas because of the better possibilities of postoperative follow-up and treatment and also because of their tendency to multicentricity. Total thyroidectomy can be performed with a low rate of complications.

Anaplastic thyroid carcinomas usually have a rapid local growth, and can be verified with fine needle biopsy and if locally advanced preferably treated by palliative resection and external radiotherapy.

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