CARCINOMA OF THE THYROID

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Introduction

Goitre is far more common in women than in men and it follows that carcinoma of the thyroid is equally more common. The discrete nodule, although it is an unusual finding in men, is however, more likely to be malignant than when found in women. Cancer of the thyroid, unlike cancer elsewhere in the body, is more malignant in the aged than in the middle aged or young. The nodular goitre in children, however, must be looked upon with grave suspicion as it may well prove to be malignant, or at any rate, is more likely to recur after operation and again after re-operation, the final recurrence being frankly malignant.

The incidence of thyroid cancer throughout the general population is very low, whereas the hospital incidence is a little over 2 per cent of all those goitres admitted. The goitre patients accepted by hospitals, however, are selective inasmuch as being suspect, have been referred, not necessarily because of the goitre, but because of an associated toxicity or because of its increase in size with accompanying pressure symptoms, discomfort or change in consistency. Any one of these latter symptoms would bring its attention to the patient and general practitioner, perhaps giving rise to the suspicion of malignancy.

Thyroid clinics throughout the world being specialized and often having radioiodine facilities, are bound to have difficult cases and cases of thyroid cancer referred to them by general hospitals, resulting in a still greater selectivity and a higher incidence of thyroid malignancy at such units. There is, however, a wide variation in the statistics of thyroid cancer emanating from various well known thyroid clinics, ranging from six to thirty per cent. in the non-toxic goitre. This wide statistical variation can be partly explained by the well known difficulty in differentiating the multinodular goitre, with its lower incidence of malignancy, from the discrete nodule with its much higher incidence. A further reason for the wide variation in statistics is the divergent views held by many Pathologists on the criteria of malignancy, for there is no doubt that certain slow growing types of thyroid cancer can give rise to more diffi-

culty in pathological diagnosis than does carcinoma of any other organ of the body.

In a recent survey at our own clinic (Piercy, 1955) we found that of the 2,000 thyroid operations performed in the past six years, just over three per cent. were for cancer of the thyroid. Analysing this figure further showed that eight per cent. of the non-toxic nodular goitres and 20 per cent. of the discrete non-toxic adenomata were malignant, and that only one per cent. of the malignant tumours were associated with thyrotoxicosis. The ages of the patients with cancer ranged between eight and eighty years; only 2 per cent. being found in men.

Pathological Classification

The microscopic classification of *differentiated* malignant thyroid tumours can be difficult as there are often several cell types throughout the tumour. When the usual criteria of malignancy have been fulfilled, such as irregular and abnormal cell pattern, invasion of capsule and blood vessels, anaplasia and mitoses, the attempt is made to classify the tumour by the cellular structure that predominates. It follows, therefore, that frequently the more sections of a tumour studied the greater the difficulty in its classification.

The highly malignant and *undifferentiated* type of carcinoma is also often difficult to classify, many displaying sarcomatous tendencies and others being so undifferentiated that the type of malignancy cannot be determined.

Classification. Although all thyroid carcinomas could come under the general term 'adenocarcinoma,' it is preferable to divide them into the two main groups *differentiated* and *undifferentiated* and sub-divide these two groups into the cellular type predominating. This method of classification both describes the type and correlates to some extent its clinical course and prognosis. The majority arise in pre-existing adenomata, the remainder arising 'de novo' in a lobe not the site of an adenoma.

Classification of Carcinoma of Thyroid.

A. *Differentiated*

(1) Papillary Carcinoma

- (2) Follicular Carcinoma (alveolar adenocarcinoma)
- (3) 'Hurthle cell' adenocarcinoma.
- B. *Undifferentiated* Carcinoma: which includes
 - Small cell (carcinoma simplex)
 - Pleomorphic (giant celled)
 - Carcinomata displaying sarcomatous tendencies.
- C. *Lymphomas*
 - Reticulum cell Sarcoma
 - Lymphosarcoma
 - Hodgkin's disease.

I. PAPILLARY CARCINOMA (Fig. 1)

Approximately half of all malignant thyroid tumours are predominantly papillary in type, yet containing follicles; the occasional tumour being a pure papillary type.

Taking all differentiated carcinomas, the presence and amount of papillary tissue determine prognosis, the more papillary tissue present, the slower growing and less malignant the tumour. The pure papillary tumour is a slowly growing neoplasm, often giving rise to a chain of large soft secondary nodes, perhaps as large as the thyroid lobe itself (Fig. 1); whilst the primary carcinoma in the lobe may be too small to be detected by the

naked eye. In the past, these large soft glands were erroneously considered to be 'aberrant thyroid nodes,' and not associated with a primary tumour of the thyroid. The prognosis of these purely papillary tumours is in the main good. They occur most commonly under the age of fifty years, the majority metastasising to the cervical and innominate lymph nodes, whilst a small percentage metastasise to the lungs, resembling pulmonary tuberculosis or giving a fine 'snow storm' effect. Those growths which contain follicular structures as well, may occasionally metastasise to the bones. It must be recognized that in a small percentage of cases a mixed papillary carcinoma will not follow the accepted slow low grade malignant picture, but will prove to be invasive having a rapidly fatal termination.

2. FOLLICULAR CARCINOMA (alveolar adenocarcinoma) (Fig. 2)

Approximately one-third of all thyroid carcinomas are predominantly follicular in type. They have a mixed cellular structure with, as their name implies, 'follicles' in different stages of activity. Papillary tissue is almost always present but to a lesser extent. It is possible for the tumour tissue

FIG. 1.—Papillary carcinoma in the sectioned right lobe above with a chain of invaded cervical lymphatic nodes.

FIG. 2.—Follicular adenocarcinoma, the growth having broken through the capsule of the adenoma.

FIG. 3.—Undifferentiated small cell carcinoma of the left upper lobe with a blood-borne secondary deposit in the lower right lobe.

to be so well differentiated as to resemble hyperplastic thyroid. It is not uncommon for this type of cancer to commence in a pre-existing adenoma which has been present for many years. The suspicion of malignancy arises when the nodule, which has remained stationary and unchanged for a long period, begins to increase in size, changes in consistency and causes pressure discomfort and referred pains. The follicular carcinoma is more inclined to metastasise early to lungs and bones by way of the blood stream and may lead to pathological fractures, whilst early invasion of the capsule can occur with involvement of the cervical nodes.

The prognosis in the follicular carcinoma is less good than in the papillary type and, although the tumour is resistant to radiotherapy, fortunately something like a quarter of them contain functioning follicles, as shown by radioactive iodine uptake, and are therefore amenable to radioactive iodine therapy.

3. 'HURTHLE CELL' ADENOCARCINOMA

This comparatively rare tumour often forms follicles and may be included with the follicular cancers, following much the same pattern in regard to progress, prognosis and therapy.

Undifferentiated Carcinoma

Approximately 25 per cent. of thyroid carcinoma are undifferentiated in type, consisting of a regular cell pattern without follicles or papillary elements. These include mainly the small cell tumour or carcinoma simplex, and the Pleomorphic or giant cell tumour. They are all highly malignant and are most commonly found in the upper age groups.

FIG. 4.—Large pleomorphic giant cell carcinoma.

SMALL CELL TYPE (carcinoma simplex) (Fig. 3)

This most frequent type of undifferentiated carcinoma commonly arises in patients over 50 years of age. The unencapsulated growth usually commences in an apparently normal thyroid gland without previous evidence of goitre. It is highly anaplastic and spreads rapidly by local invasion and metastasises extensively by way of the lymphatics and blood stream. The prognosis is bad, as the growth has usually spread before being recognized; it may temporarily respond, however, to irradiation.

PLEOMORPHIC GIANT CELLED CARCINOMA (Fig. 4)

These highly malignant vascular anaplastic tumours, at one time, were thought to be sarcomatous. They arise in large pre-existing goitres of many years duration, and spread locally with great rapidity. They appear in the elderly and usually cause death within a few months from rapid local invasion of the tissues of the neck, often before metastases have had time to appear. The giant cell carcinoma, unlike other anaplastic tumours, is resistant to irradiation and the prognosis is usually hopeless from the onset.

Lymphomas

LYMPHOSARCOMA

RETICULUM CELL SARCOMA (Fig. 5)

These two primary sarcomatous thyroid growths run much the same clinical course and there is an abundance of reticulum cells and lymphocytes in the thyroid for their origin (Winship, 1955). They

FIG. 5.—Reticulosarcoma with invaded nodes.

occur most commonly in elderly females and have been found both with and without the history of pre-existing goitre. The tumour increases rapidly in size, the growth quickly involving all of the thyroid and metastasising to the cervical and mediastinal lymph nodes. At this unit we have found several such growths presenting in pre-existing lymphadenoid goitres. Although the prognosis in lympho and reticulum sarcoma is not good, they are radio sensitive and temporarily respond to irradiation which is also an important factor in their diagnosis. If the tumour is seen when still localized to the thyroid, surgery is indicated to be followed by X-ray therapy. (Fig. 5).

Prognosis in carcinoma of the thyroid is governed by several factors:—

(a) Age of the patient—unlike carcinoma elsewhere in the body, it is invariably more highly malignant in the elderly than in the middle aged and young.

(b) The stage of the growth found on clinical examination—the prognosis is in inverse proportion to the certainty of diagnosis.

(c) The speed of onset—the more rapid an increase in size, the less favourable the prognosis.

(d) The greater the cellular differentiation of the tumour, the more favourable the prognosis.

Clinical Classification

Clinically, carcinoma of the thyroid may be conveniently classified into:—

- (1) Obvious carcinoma
- (2) Suspect carcinoma
- (3) Hidden carcinoma.

1. CLINICALLY OBVIOUS CARCINOMA

The patient, usually in the upper age groups, complains of an increase in the size of her goitre, radiating pain, and hoarseness of the voice due to tracheal pressure or involvement of a recurrent laryngeal nerve. The mass is hard, fixed, nodular and tender. Firm lymph nodes are often present in the neck. In this obvious example the malignancy is advanced, the growth having broken through the true capsule of the thyroid and invaded the cervical tissues. The prognosis is very bad, the patient usually dying within a year in spite of thyroidectomy and irradiation.

2. CLINICALLY SUSPECT CARCINOMA

Malignancy is suggested when a nodular goitre or a discrete adenoma, which has been stationary for many years, *gradually* begins to increase in size. The patient complains of discomfort in the goitre often with a sense of constriction in the neck. On examination the nodular mass is found to be tender and firm.

The prognosis is very much better in the suspected case, as it is likely that the carcinoma is still contained within the capsule of the adenoma and can be satisfactorily removed. The growth is most often differentiated in type and commonly seen in the middle age group. It must not be confused with the *sudden* tenderness and increase in size of an adenoma resulting from a haemorrhage within it.

3. CLINICALLY HIDDEN CARCINOMA (see Fig. 2)

First diagnosed either during a partial thyroidectomy for a nodular goitre or after routine post-operation microscopy. It must be appreciated, however, that carcinoma of the thyroid, unlike carcinoma of most other organs, can be notoriously difficult to recognize at the time of operation and may easily be confused with degenerative, cystic and fibrous processes. The prognosis is excellent in these cases of obscure carcinoma, if the growth has not already invaded the blood vessels and given rise to secondary deposits.

In considering the all important question of prognosis based on clinical classification, we find that the prognosis in clinically obvious carcinoma is bad, in clinically suspect carcinoma is good, whereas the prognosis in clinically hidden carcinoma is usually excellent.

FIG. 6.—Rapidly growing reticulosarcoma showing diagnostic needle puncture.

Considerations in regard to Partial Thyroidectomy for Nodular Goitre as a Precaution against Carcinoma

The ideal procedure would be the removal of all non-toxic nodular goitres referred to hospital, both as a precaution against clinically hidden cancer being present, and as an insurance for the future. The indication for operation being still greater when such a goitre is present in men and in children.

Operation should *always* be undertaken for any nodular goitre at the first suspicion of malignancy, such as an unusually firm nodule, its gradual increase in size, or evidence of tenderness or pressure.

Every discrete non-toxic adenoma should be widely removed, as it has been shown at this clinic that, of those proven by radioactive iodine to be cold nodules at least 20 per cent. were malignant (Greene, 1956).

It has been suggested after animal experiment, that following partial thyroidectomy, small doses of thyroxine or thyroid should be given to prevent excessive secretion of the pituitary hormone T.S.H. in order to lower the incidence of adenoma and carcinoma production (Doniach, 1955). It has

been our practice to give thyroid medication following operation for cancer, both to maintain the thyroid balance and with the above theory in view.

Treatment

Thyroidectomy is the treatment of choice.

(a) Clinically obvious carcinoma

The involved lobe is completely removed including invaded lymph nodes and muscle; a total or near total lobectomy being undertaken on the opposite side to allow, if necessary, for radioactive iodine to concentrate in local remnants or in local or distant metastases. The choice of the post-operative therapy would depend on whether the cancer was of a type sensitive to irradiation or had an uptake of radioiodine, thereby making this form of treatment applicable.

(b) Carcinoma found initially at operation.

When carcinoma is first recognized during an operation (see Fig. 2) for an adenoma or a nodular goitre, a total or near total thyroidectomy is undertaken, the *complete* removal of the invaded lobe being considered essential. Post-operative treat-

FIG. 7.—The same after X-ray therapy.

ment by means of radioiodine or irradiation to be considered along the lines indicated in (a).

(c) When unsuspected malignancy is diagnosed initially by post-operation microscopy.

If the operation was adequate inasmuch as all pathological tissue, innocent and malignant had been removed, keeping the patient under observation would be sufficient unless the carcinoma was undifferentiated and anaplastic in type, or had invaded beyond the capsule of the adenoma. In the latter circumstances a total thyroidectomy would be indicated, or alternatively, the remaining tissue destroyed by an ablation dose of radioiodine.

(d) Rapidly growing undifferentiated carcinoma.

Operation is often undertaken in the late stages to relieve pressure, to institute a tracheotomy, and to resect tissue for microscopic pathological diagnosis of the growth.

In the early stages, total thyroidectomy, if possible, is undertaken including removal of invaded

nodes or muscle, to be followed by irradiation, or occasionally radioactive iodine, if an uptake of the Isotope is present or can be induced.

Needle puncture biopsy is occasionally indicated in a rapidly advancing growth (Fig. 6), for if proven to be sarcomatous it will temporarily respond to irradiation as will any invaded mediastinal nodes (Fig. 7).

It is to be reiterated that if for various reasons it is impracticable to remove all non-toxic nodular goitres when the prognosis of an unsuspected malignancy would still be excellent, at any rate operation must be undertaken at the first suspicion of malignancy when results are still good, and not left until the condition is obvious when the prognosis is bad.

BIBLIOGRAPHY

- DONIACH, I. (1955), *Proc. roy. Soc. Med.*, **49**, 173.
 GREENE, R. (November, 1956), Hunterian Lecture, R.C.S.
 PIERCY, J. E. (1955), *Proc. roy. Soc. Med.*, **49**, 173.
 WINSHIP, T., and GREENE, R. (1955), *Brit. J. Cancer*, **9**, 401.