

Carcinoma of the Thyroid Gland

A Review of 106 Cases

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CARCINOMA OF THE THYROID GLAND has attracted the attention of the medical profession more and more in recent years. The disease has been recognized pathologically as a carcinoma that develops as other malignant neoplasms do and causes death if uncontrolled. Many clinicians, however, are reluctant to accept this fact. They are lulled into a sense of security by the fact that course of the disease may be protracted over a period of many years. Recent long term follow-up studies are eliminating this misconception. Because biopsy of the thyroid gland is more than a minor operation, indications for this procedure need clarification and acceptance. In addition, opinions as to methods of treatment of the disease are far from unanimous.

This presentation will review 106 unselected cases in which the patients were treated at the Los Angeles County General Hospital, at Harbor General Hospital and in the private practice of one of the authors. Ninety-three of the patients were treated primarily, while 13 had had previous treatment. The purpose of the study is to shed light on a few characteristics of the disease and to suggest a rationale of treatment for papillary carcinoma.

INCIDENCE BY AGE AND SEX

Chart 1 shows the age of the patients. Unlike most cancers, which affect primarily the older age groups, cancer of the thyroid has a biphasic curve with



Chart 1.—Age of patients at time of diagnosis of carcinoma of the thyroid gland (106 cases).

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• In a review of 106 cases of carcinoma of the thyroid gland, it was noted that a solitary thyroid nodule is the most outstanding single physical sign in this disease. It should be investigated by biopsy of a specimen removed at operation. Patients and physicians were sometimes guilty of delay in this regard.

Papillary carcinoma involved multiple foci within the gland in at least half of the cases and there was a high incidence of regional lymph node metastasis associated with this type.

Doubt was cast on conclusions by other investigators that carcinoma of the thyroid rarely is lethal in patients less than 40 years of age.

peaks in the fourth and seventh decades. It affects females preponderantly, the ratio of females to males in this particular study being more than 4:1 (87 females, 19 males). In the older age groups, however (over 60 years), the ratio was 2.4:1 (24 women, 10 men). These findings agree with those of Sloan,⁸ who also pointed out that this ratio is low in childhood too. In the present series so few of the patients were less than 20 years of age that no conclusions could be drawn in this regard.

PATHOLOGICAL CLASSIFICATION

Table 1 shows the incidence of various pathologic types of carcinoma in this series. For clinical purposes a relatively simple classification is used without regard to niceties of pathologic detail. In all cases in which there were elements both of follicular and papillary types histologically, the classification assigned was *papillary*, for it is the authors' conviction

TABLE 1.—Incidence of Pathologic Types of Carcinoma in Present Series Compared with Incidence Reported by Other Investigators

	Incidence (Per Cent) in Various Series			
	Current Series 106 Cases	Cope 190 Cases	Sloan 282 Cases	Frasell & Foote 301 Cases
Papillary	61	47	50	46
Follicular	23	24	25	7
Hurthle cell	5	0.5	5	9
Undifferentiated ..	6	24	20	19
Lymphoblastoma ..	4	0.5
Other	4	19

TABLE 2.—Duration of Symptoms Before Diagnosis

	Number of Cases					
	All	Papillary	Follicular	Hurthle Cell	Undifferentiated	Lymphoblastoma
Less than 6 months.....	23	12	5	1	3	2
6 to 12 months.....	10	7	2	1
1 to 3 years.....	27	29	5	2	1
3 to 5 years.....	6	3	1	1	1
5 years or more.....	30	16	9	3	2
	96	57	22	5	8	4

Unspecified: Papillary, 8; Follicular, 2.

tion that these tumors behave as papillary carcinomas. Giant cell types and small cell types were included with the undifferentiated tumors. Lymphoblastoma was included because there were four cases which clinically appeared to be primary thyroid cancer, but subsequently proved to be lymphoblastoma. The incidence of the various types in this series was compared with that in three other series in Boston and New York. In order to obtain some uniformity of classification for purposes of comparison, mixed types were considered as papillary, giant cell and small cell types as undifferentiated. There was a considerably higher incidence of the relatively benign papillary type in the present series than was reported in the eastern series. There were also considerably fewer of the malignant and undifferentiated type.

SYMPTOMS

Most patients complained of a mass in the thyroid area. About one third also complained of pressure. Only one patient had pressure symptoms without noticeable mass. Two were asymptomatic, the mass being noted on routine physical examination. Two patients sought aid because of symptoms suggesting toxicity but only one of these had thyrotoxicosis. Symptoms, however, directed attention to the gland and the necessity for exact diagnosis.

Of more interest, perhaps, than the actual symptoms is the delay from onset of symptoms to diagnosis (Table 2). It is to be noted that many patients had symptoms for more than five years before the diagnosis was made. Remarkably, two such patients had undifferentiated carcinoma. Some of the patients had sought aid from physicians during the interval before the diagnosis was made.

PHYSICAL FINDINGS

The solitary nodule was the striking physical finding among patients with thyroid carcinoma (Table 3). It was noted in approximately half of the patients. This accords with the well known relation of a solitary nodule to carcinoma. The finding of a multinodular or diffusely enlarged gland does not exclude cancer. In addition, if a nodular thyroid

TABLE 3.—Observations on Physical Examination

	No. of Cases
Solitary nodule	54—with nodes 12
Multiple nodules	19—with nodes 1
Diffuse enlargement	24—with nodes 1
Mass replacing gland.....	6—with nodes 0
Palpable cervical nodes.....	19
Neck normal on physical examination.....	4
Dominant nodule in multinodular gland..	3
Dominant nodule in diffusely enlarged gland	6
Palpable nodes only.....	8*

*Two had previous treatment.

TABLE 4.—Primary Treatment

Total thyroidectomy	25	with neck dissection	13
Total lobectomy	32	with neck dissection	6
Subtotal thyroidectomy	20		
Subtotal lobectomy (local excision of nodule).....	12		
Biopsy and radiation.....	3		
Biopsy only	3		

gland contains a dominant solitary nodule, it should be treated in a manner analogous to an undiagnosed lump in the breast—by open biopsy. In only one in five cases in the present series were there palpable cervical nodes. In six such cases the lesion was papillary carcinoma whose symptoms were first manifest by metastasis to cervical lymph nodes—the old “lateral aberrant thyroid.” In cases in which the neck was normal on physical examination, symptoms developed as a result of metastatic lesions elsewhere in the body, investigation of the thyroid having been eventually brought about through study of these distant growths.

PRIMARY TREATMENT

Owing to the multiplicity of the sources of the patients and to changing concepts as to proper management, there was no uniformity of methods of treatment. Table 4 shows the initial therapy that was given to these patients. Total thyroidectomy was done in only 21 instances. A subtotal lobectomy as listed in the table implies simply a local excision of the nodule. Neck dissection either limited or radical was combined with total thyroidectomy in 12 instances, and with lobectomy in six.

TABLE 5.—Foci in Thyroid

	Single	Multiple
Total thyroidectomy (21):		
Papillary	11	5
Follicular	0	2
Other	3	0
Subtotal thyroidectomy (47):		
Papillary	20	10
Follicular	10	0
Other	7	0

SINGLE OR MULTIPLE FOCI IN THYROID

Because there is considerable confusion as to the amount of thyroid gland which should be removed with a carcinoma, a review of the number of foci of tumor within the gland was carried out (Table 5). All cases of lymphoblastoma and 11 cases from one source where the data on this point were not available, were excluded. This study was based on routine multiple block sections and not on a large number of serial sections. All cases in which distinct multiple foci were not noted were considered as having a single focus. Even with these rigid restrictions it was immediately apparent that in about half of the cases of papillary carcinoma there were multiple foci within the gland. Russell,⁶ doing whole gland serial sections to discover multiple foci, found such foci in 11 of 12 papillary carcinomas. He set forth the concept of the thyroid gland as "a large lymphatic lake with the capsule being the first limiting barrier to tumor cells. These findings strongly suggest that total thyroidectomy should be employed in the treatment of thyroid carcinoma, especially of the papillary type.

ASSOCIATED PATHOLOGIC CHANGES

Associated pathologic changes noted in the thyroid gland in cases in which the gland was removed because of carcinoma are listed in Table 6. The data were derived, of course, from cases in which enough of the gland was removed to determine whether such changes were present. The incidence of associated diseases in the glands containing carcinoma was no greater than that in the thyroid gland in the general population. These data are in agreement with those of Sloan.⁸ The four cases in which the lesion seemed to arise in an adenoma, may well have been cases of carcinoma arising de nova and subsequently betraying their true nature by developing histologic criteria of malignant growth. The evidence at hand is not convincing that carcinoma is more likely to develop in a patient with nontoxic nodular goiter or any other minor thyroid abnormality than it is in the general population. In this series none of the males had associated pathologic changes in the gland. This strengthens the common opinion that a

TABLE 6.—Associated Pathologic Changes in Thyroid Gland*

None	51
Nontoxic nodular goiter.....	18
Adenoma	6
Thyroiditis	4
Hypertrophy with involution.....	1

*No male had associated thyroid disease.

TABLE 7.—Data on Clinical Diagnosis of Cervical Node Involvement Compared with Actual Occurrence of Involvement (Excluding Cases of Lymphoblastoma)

	No. of Cases
Cases in which nodes were removed.....	28
Nodes clinically palpable.....	19
Nodes pathologically positive.....	26
Cases of papillary carcinoma.....	20
Nodes clinically palpable.....	14
Nodes pathologically positive.....	20

solitary nodule of the thyroid in a male is almost invariably carcinoma. These facts support the thesis that carcinoma of the thyroid arises directly from the gland itself and not from some preexisting disease within the gland.

INVOLVEMENT OF NODES

Nodes were removed for pathologic study in 28 of the cases in the present series, exclusive of cases of lymphoblastoma (Table 7). In only 19 of these 28 cases had nodes been palpable clinically, although in 26 cases nodes were found to be involved. With regard to cases of papillary carcinoma only, nodes were removed in 20 cases and all the nodes contained metastatic growth, although in only 14 cases had palpable nodes been noted. Thus, in only one case of nonpapillary carcinoma was a node that was not palpable found to be histologically "positive." This accords with data set forth by Macdonald and Kotin⁴ in 1953, namely, that 43 per cent of papillary carcinomas were found to have spread to cervical lymph nodes whether or not such nodes were palpable clinically. It is in agreement also with observations by Frazell and Foote³ who found 61 per cent of nodes positive in 67 patients without palpable nodes.

METASTASIS

Table 8 shows the nature of spread of the various types of carcinomas as observed in the present series. Of the papillary type, about one third disseminated to lymph nodes, while only about one in ten infiltrated beyond the gland locally or spread to distant sites. In the case of follicular carcinomas, about one in four spread to nodes and about the same proportion to distant sites. Hurthle cell carcinomas tended to remain confined to the thyroid gland or to the local area in the neck. Not many of the undif-

TABLE 8.—Data on Metastasis from Carcinoma of the Thyroid Gland

	None	Local Infiltration	Nodes	Bones	Chest	Other
Papillary	34	7	20	2	6	2
Follicular	15	1	6	5	2	1
Hurthle	5	1
Undifferentiated	4	2	2	1	1*

*Site unspecified.

ferentiated carcinomas extended to distant sites. This is probably owing to the fact that the patient dies so early of rapid local growth of the primary lesion that there is no time for distant extension.

FOLLOW-UP

Seventy-four patients had been observed for more than one year at the time of this report. The study was not sufficiently protracted to permit drawing conclusions as to survival rate. However, it is planned to carry out a long term follow-up program with special emphasis on carcinoma of the papillary type. Cope⁵ and co-workers reported a five-year survival of 43 per cent in papillary carcinoma, 35 per cent in follicular and only 11 per cent in undifferentiated. Shallow, Wagner and Colcher⁷ had a five-year survival of 40 per cent among 85 patients with carcinoma of the thyroid gland who were observed for five years or more, but these investigators did not say how many cases in the series were lost to follow-up. In the present series were two patients with carcinoma of undifferentiated type who were alive more than five years after the onset of disease. These were the same two patients who had symptoms for more than two years before the diagnosis was made. Of the six patients alive with disease at the time of report, three had papillary carcinoma with recurrent neoplasm that probably would soon cause death. Apparently then, any thyroid carcinoma may eventually cause the death of the host by local growth or metastasis.

Fourteen patients died of the disease, six of them of distant metastatic lesions—in the lungs in most cases. Nine patients died of unrelated causes; four of them had thyroid carcinoma present at the time of death.

Crile¹ stated that carcinoma of the thyroid gland is rarely lethal under the age of 40 years, no matter what the histologic structure. In a study in which the period of follow-up was from three to fifteen years, he noted a mortality rate of 5 per cent under age 39, 55 per cent between ages 40 and 60, and 85 per cent over 60. Cope⁵ and co-workers expressed the belief that death from thyroid cancer is extremely rare under age 39. In the present series, despite the limited period of follow-up, eight of the 23 patients who died were under 60 years of age, and in five of these eight cases death was due directly to thyroid carcinoma. One patient died of metastatic lesions at age 39. These data seem to justify skepticism of the conclusions of Crile and Cope in this regard.

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