Surgical Thyroid Disease in Northern Thailand

A Study in Geographic Pathology

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STUDIES in geographic pathology provide exceptional opportunities to examine familiar diseases in special environments in which there may be significant local differences in important variables. Particularly fertile fields for inquiry are found in some developing countries in which geographically limited populations often represent a stage of health care no longer extant in other parts of the world.

Northern Thailand is an area in Southeast Asia in which iodine deficiency goiter is endemic. Iodized salt was not made available to the population of this region until late 1965, and then only in very limited areas. In addition, the affected population is not geographically mobile and patients with thyroid disease tend to reside in areas in which they were born.

Diseases of the thyroid are an unusually good example of changing patterns of health: thyrotoxicosis and nodular colloid goiter are declining while there is an increasing incidence of thyroid carcinoma and Hashimoto's thyroiditis. Although a number of different environmental influences may be responsible for some of these changes, the most important exogenous substance affecting thyroid physiology is dietary iodine. The effect, if any, of excess dietary iodine in the changing incidence of thyroid disease remains to be determined with certainty, however, a recent retrospective study has demonstrated a statistically significant increase in lymphocytic infiltration of the thyroid gland as well as an increase in thyroiditis, after beginning thyroid prophylaxis.

There is a dual purpose to this report; (1) to describe the incidence of surgical disease of the thyroid gland observed at Chiangmai Hospital over a six-year period, and (2) to compare these data with those of Weaver et al, from a study of surgical thyroid disease in Michigan, in order to assess the distribution and incidence of thyroid disease and changes in morphology of the thyroid gland before the introduction of widespread iodine prophylaxis. Two different populations similar in number but separated by 8,000 miles and 40 years are contrasted.

Materials and Methods

The ethnic origin of the population under study is almost exclusively Thai although the geographic area encompassed contains a variety of other groups. Many of the latter, however, are limited to more or less remote mountainous and jungle regions in which distance and lack of transport prohibit patients from ready ac-
cess to health care facilities. Other than lack of transportation there was no selection of patients for socioeconomic reasons inasmuch as health care services at Chiangmai University Hospital are available to all citizens regardless of ability to pay. A map of Chiangmai Province (Figure) which shows the geographic origin and incidence of patients according to the various administrative subdivisions (amphurs) of the province tends in part to reflect the availability of transport with respect to demand for health care.

A Thai government project to begin the use of an iodate salt in control of endemic goiter was begun in 1963, but it was not until December 1965 that first supplies were actually distributed in northern areas. Distribution thus far has been limited to only selected areas in six of 17 amphurs in Chiangmai Province (A. Chandrapanond, personal communication to the authors, 1967). Supplies of salt are sold to village retail stores. At the same time noniodate salt was not withdrawn so that the consumer is offered a free choice of product.

Prices of iodate and noniodate salt are about the same although there tends to be some slight increase in price of iodate in the rainy season due to difficulty in transportation. The recent introduction and very limited distribution of iodate do not significantly alter the contention that the population under investigation has been exposed to prolonged iodine deficiency although there are several months overlap in a few rural areas.

A total of 261 surgical specimens were reviewed microscopically. These represented total, subtotal, and segmental resections of the thyroid submitted to the Department of Pathology from January 1961 through December 1966.

All microscopic material was reviewed using the morphologic criteria of Weaver et al.4 According to their classification, glands were separated into the following categories: (1) nodular colloid goiter; (2) nodular colloid goiter with lymphocytes; (3) hyperplasia; (4) thyroiditis, using Hazard's criteria to differentiate Hashimoto's thyroiditis from lymphocytic thyroiditis; (5) adenomas (trabecular, follicular, and Hürthle); and (6) carcinomas (papillary, follicular, mixed papillary and follicular medullary with amyloid stroma, and anaplastic forms).

Results

Nodular Colloid Goiter.—A total of 170 glands had microscopic features consistent with nodular or simple colloid goiter. No attempt was made to morphologically differentiate involuted hyperplastic glands from diffuse or nodular colloid goiter. Mean age and sex distribution are given in Table 1. These data do not substantially differ from other reports.2,4 Although the mean age for males was 7.4 years older than for

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Table 1.—Surgical Thyroid Disease in Northern Thailand:—Age and Sex Distribution in 261 Cases

<table>
<thead>
<tr>
<th>Classification</th>
<th>Cases</th>
<th>Age (yr)</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular colloid goiter</td>
<td>138</td>
<td>2</td>
<td>170</td>
<td>35.8</td>
</tr>
<tr>
<td>Nodular colloid goiter with lymphocytes</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>34.0</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>7</td>
<td>0</td>
<td>7</td>
<td>29.6</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td>33.8</td>
</tr>
<tr>
<td>Adenomas</td>
<td>45</td>
<td>15</td>
<td>58</td>
<td>35.4</td>
</tr>
<tr>
<td>Carcinomas</td>
<td>11</td>
<td>6</td>
<td>17</td>
<td>45.5</td>
</tr>
</tbody>
</table>

females, this may or may not be a significant difference (P = 0.05). Glands from this period showed very limited numbers of lymphoid nodules or diffuse interstitial accumulations of lymphocytes. When present, lymphocytes were usually confined to areas of regressive change, particularly within or adjacent to the fibrous pseudocapsules of large nodules. Many glands contained definite areas of focal hyperplasia in both active and involuted patterns. Several nodular colloid goiters also contained discrete follicular adenomas. The true incidence of these coexisting lesions is not known in this material.

Only two patients had nodular colloid goiters with significant lymphocytic infiltration, an incidence of 0.8%. In neither of these glands was the degree of lymphoid infiltration marked but averaged about one lymphoid nodule per medium-power field. A pattern of extensive diffuse interstitial infiltration was not encountered.

Hyperplasia.—Seven patients were judged to have hyperplasia by the conventional criteria of diffuse change character- ized by papillary epithelial hyperplasia, tall columnar cells, and pale-staining colloid with scalloped edges. Glands having these features accounted for only 2.8% of the total. The age and sex distribution are found in Table 1. Many nodular colloid goiters, however, contained focal hyperplastic areas and were occasionally given the preoperative designation of toxic nodular goiter. Data from the study period relating thyroid function tests to such glands are too few to be meaningful, but the morphologic impression remains that there is more focal and less diffuse hyperplasia in thyroid glands from this area as compared to those examined in the Michigan study.4

Thyroiditis.—This group included seven patients, or 2.8% of the total. Age and sex are summarized in Table 1. Each of these cases was classified as lymphocytic thyroiditis. No examples of Hashimoto's thyroiditis or Riedel's struma were detected in this study. In glands classified as lymphocytic thyroiditis, changes were often slight to moderate or suggested some evidence of resolution.

Adenomas.—One of the surprising comparative findings of this study was the high incidence of adenomas. The 58 lesions classified as adenomas comprised 22.6% of the total. Sex and age distribution are recorded in Table 1. Data from the Michigan study are found in Table 2. Conservative morphologic criteria were applied with full knowledge of the occasional difficulty in distinguishing between true adenomas and focal adenomatous hyperplasias in nodular colloid goiters.

We were able to confirm the findings of Weaver et al4 of the frequent occurrence of lymphoid elements in areas immediately adjacent to adenomas although the remainder of tissue examined was free of lymphocytes. Of 58 adenomas, 55 were follicular and 3 trabecular. Although Hürtle cell foci were occasionally seen, no adenoma was observed in which this cell type predominated.

Carcinomas.—The 17 patients in this group represented 6.1% of the total. Papillary carcinomas were most common. There were three anaplastic neoplasms and one medullary carcinoma. Details of age and sex are presented in Table 1. As in other parts of the world, thyroid carcinoma in northern
Thailand is chiefly a disease of adult women over 40 years of age. Also, as is generally true elsewhere, anaplastic neoplasms were found in patients about one decade older than those with differentiated tumors. No lymphomas or sarcomas were encountered.

Comment

Weaver et al., in summarizing the effect of iodine therapy and prophylaxis on the morphology of the thyroid gland, were able to make the following observations: (1) lymphocytic infiltrates in thyroid glands were rare and focal in the preiodine period; (2) after iodine was widely introduced into the diet in Michigan, the incidence of lymphocytic infiltrates in thyroid glands was significantly increased; and (3) lymphocytic thyroiditis and Hashimoto's thyroiditis which were absent in the preiodine era appeared with increasing frequency after the introduction of iodine.

This study confirms the paucity of lymphocytic infiltrates in thyroid glands from another area of endemic goiter before iodine prophylaxis. Whether this will change with prophylaxis remains to be determined. Although there were a few examples of lymphocytic thyroiditis, there was no Hashimoto's thyroiditis.

The incidence of follicular adenomas in this study is much higher when compared with the data of Weaver et al. The adenoma:carcinoma ratio in the Michigan Study was 1.5:1. Use of this ratio would project about 32 fewer adenomas for our series than were actually observed. If the microscopic interpretation of this material was correct only half the time in spite of strict histologic criteria, the incidence would still be nearly five times that observed in the Michigan study in glands from the preiodine era (Table 2). An attractive conclusion is that there were many adenomas in thyroid glands in northern Thailand during the period studied and therefore presumably this is a geographic difference of considerable interest. However, Weaver et al. postulate that the increased incidence of adenomas in their series from 1959 to 1963 is a result of surgical selection based on the high incidence of cancer appearing as a solitary nodule. We also believe this is a factor in selection. Additional factors, however, may be suggested from consideration of the low level of awareness and lack of concern about sickness as well as indifference to the cosmetic effect of goiter in the average patient in this region. Many patients, particularly from rural areas, seek medical attention only when something is seriously wrong; the observation of advanced stages of many diseases, particularly neoplasms is commonplace. Many patients with adenomas (or carcinomas) probably do not see a physician about their goiter until they become symptomatic. Until more is known about how patients with adenomas and other thyroid diseases are first detected and finally selected for surgical treatment, this high incidence of adenomas must stand subject to revision.

The low incidence of 2.6% of diffuse hyperplasia in this population is an interesting finding which contrasts sharply with the 14.4% noted by Weaver et al. in the preiodine era in Michigan (Table 2). Nevertheless, this low incidence of diffuse hyperplasia closely parallels the clinical observation that exophthalmic goiter with smooth symmetrically enlarged glands is rarely seen in this population (M. Keoplung, personal communication to the authors, 1967). Lack of environmental iodine as a possible local variable in the incidence of diffuse hyperplasia was noted by these authors, who suggested a decreasing incidence was due to the availability of iodine. This deficiency would not appear to be of equal significance in northern Thailand.

A real increase in carcinoma of the thyroid during the past three decades has been described for various areas of the United States. The incidence of 6.1% in this study is approximately one half that reported in the Michigan study for 1958 to 1963 but is almost five times the incidence these authors determined for pre-iodine years, 1915 to 1920. Age, sex, and morphologic distribution of thyroid carcinomas does not vary significantly from that reported previously from other parts of the world. Although it can be stated that thyroid carcinoma is significantly less common in Northern Thailand than in Michigan at the present time, a changing incidence in northern Thailand has yet to be demonstrated.
Summary

The incidence of surgical thyroid disease, in an area of northern Thailand characterized by a high incidence of endemic goiter, has been determined for a six-year period prior to iodine prophylaxis.

This study confirms the low incidence of lymphoid infiltrates in thyroid glands from a geographic area deficient in dietary iodine and corroborates the low incidence of lymphocytic thyroiditis and absence of Hashimoto's thyroiditis.

Compared with a population in Michigan during a period before iodine prophylaxis, there was a much higher incidence of adenoma and a much lower incidence of diffuse glandular hyperplasia.

Carcinoma of the thyroid gland in this population is almost four times more common than the preiodine prophylaxis era in Michigan 40 years before.

Surgical thyroid disease in northern Thailand has been studied to serve as a baseline for future comparison in order to anticipate the predictable evolution of thyroid disease under the influence of widespread iodine prophylaxis and changing methods of treatment.

References


CENTRAL SURGICAL PAPERS

The papers read at the Central Surgical Association's meeting this year will be published in the September and October issues of the Archives because of late receipt of the discussions for these papers.