MANAGEMENT OF PATIENTS WITH CANCER OF THE THYROID

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CARCINOMA OF THE THYROID IS NOT A COMmon disease. The incidence based on statistics from death certificates shows that the death rate in this disease is approximately one per 100,000.[5] Of course, these figures do not show the prevalence of the disease among the living. This is unknown because published statistics vary so greatly. The reported occurrence of carcinoma in nontoxic nodular goiters varies from 3.6 to 17.1% and in solitary nodules from 9 to 33%.[1, 2, 4, 6] These data concern only surgical patients and do not apply to the general population.

The wide variation in figures is due to inaccuracy in distinguishing clinically between single and multiple nodules of the thyroid and to the unavoidable selection of cases. Some of the disparity is also due to the lack of uniform criteria for evaluating pathologic findings. Certainly the low incidence of malignant tumors in some areas reflects the failure of pathologists to recognize cancer of the thyroid.

PROBABLE POPULATION WITH DISEASE

For more than 50 years it has been assumed that cancer of the thyroid was more frequent in goitrous than in nongoitrous regions. No large-scale investigation has been carried out but the few limited surveys conducted in the last 15 years indicate that cancer of the thyroid is equally distributed throughout all areas and has no relationship to goitrous regions. The reported inequality appears to be related to local interest in the disease rather than any geographic differences.

Carcinoma of the thyroid rarely is associated with thyrotoxicosis. Malignant tumors are found in approximately 2½% of toxic goiters whether they be nodular or diffuse in morphology.[7]

Like other disorders of the thyroid, cancer is found predominately in women. Approximately 65% of all patients with cancer of the thyroid are women. Presumably this is associated with the influence of estrogenic hormones though their increased production during pregnancy apparently does not accelerate the growth of cancer of the thyroid.[9]

Thyroid nodules are uncommon in men but, when present, are three times more likely to be carcinoma than similar nodules in women. Nodules in children also should be viewed with suspicion. It has been estimated that almost 50% of nodules in children are malignant. Although the majority of patients are in the fifth and sixth decades of life, approximately 15% are younger than 30 years. In the series of 850 childhood cancers of the thyroid which Winship and Rosvoll have collected during the last 20 years, two patients were aged 4 months when the diagnosis was established and 12 children had tumors at birth which later proved to be carcinoma.[13]

In most instances the etiology of cancer is not known; however, in the case of cancer of the thyroid it is now generally acknowledged that previous radiation may result in the production of a malignant neoplasm. In 1949 Quimby and Werner suggested such a relationship.[8] Since then, numerous investigators have verified their thesis. In the collected series of childhood thyroid carcinomas the clinicians attempted to obtain a history of previous radiation to the head and neck area in only about half of the patients. Of this group 74% had been treated by roentgen-ray therapy from 3½ to 14 years before the diagnosis was established. Doses ranged from 140 to 2600 R with an average of 512 R. In the greatest number of cases roentgen therapy had been directed to the mediastinum and neck during infancy for a so-called enlarged thymus gland. The second largest group had

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been treated during early childhood for enlarged tonsils and adenoids while others received treatment for hemangiomas, acne, eczema, nevi and numerous other benign lesions. The average interval between radiation and the histologic diagnosis of cancer was 8½ years.[13]

Though thyroid cancers have been produced in animals by the use of both roentgen-rays and radioactive iodine, malignant tumors have not been produced by radioactive iodine in the human. At this time there is no explanation for what appears to be a different effect from equivalent amounts of external and internal radiation. The hazards of ^{131}I in the young have not been delineated. Too few patients have been followed for a sufficient period for a definitive statement to be made concerning the safety of even small amounts of radioactive iodine. Therefore, it would be advisable to employ radiotherapy in any form with great caution in the head and neck region of young people.[15]

CLASSIFICATION OF TUMORS

The treatment of carcinoma of the thyroid depends to a large extent on the histologic type. For this reason it is well to have an understanding of the classification of cancers of the thyroid. Malignant tumors of the thyroid can be classified in three groups:

1. Papillary—62%;
2. Follicular—20%;
3. Undifferentiated—18%.

Included in the papillary category are all cases showing papillations. These tumors are almost always mixed and multiple sections show varying numbers of functioning follicles. Follicular carcinomas are composed of malignant follicles only. The undifferentiated carcinomas are a more heterogeneous group and comprised those malignant tumors with neither papillations nor follicles. These tumors are likely to be solid and to have a uniform cell type in contrast to the well-differentiated cancers. There are many variants in this category but there are three main subgroups: small cell, medullary and the uncommon spindle and giant cell carcinomas. Except for some of the medullary tumors, these are highly malignant and rapidly growing cancers.[14]

Carcinoma of the thyroid usually is manifested first by a nodule in the neck, either in the thyroid or in a cervical node. In adults the nodule is more apt to be in the thyroid whereas an involved cervical node is usually the first sign of disease in children. The evaluation of thyroid nodules depends to a large extent on physical examination. Radioiodine scans are of limited value since they seldom detect cancers less than 2 cm and the majority of cold areas prove to be degenerating nodules or microfollicular adenomas.

TREATMENT

For practical purposes the well-differentiated tumors of the thyroid (papillary and follicular) can be treated alike. Virtually all aspects of therapy for these types can be discussed on the basis of the management of a single nodule in the thyroid gland. Obviously a painless, slowly growing lymph node in the neck which reveals metastatic thyroid carcinoma will lead to surgery on the thyroid. Whether the nodule is in the lateral cervical region or in the thyroid, adequate therapy should be undertaken and an attempt made to eradicate the cancer. As adequate therapy we accept a lobectomy for a small cancer involving only one lobe. The routine removal of the isthmus together with a total lobectomy is advisable. If at the time of operation an abnormal contralateral lobe is palpated, then and only then should a "near-total" lobectomy be performed on the opposite lobe. A "near-total" lobectomy removes all the thyroid tissue except for a remnant in the tracheoesophageal groove which will tend to protect the parathyroid glands. If it becomes necessary later to ablate the thyroid, this can be accomplished with a relatively small dose of radioactive iodine. Hypoparathyroidism is sometimes a worse disease than papillary carcinoma.

The large majority of investigators have found bilateral involvement in 20 to 33% of glands rather than the 87% reported by Clark and associates.[3] Tollefsen and DeCosse routinely perform a lobectomy and neck dissection for differentiated cancer of the thyroid. After a 10-year follow-up of a large series, only 3.7% of their patients had developed recurrent tumor in the remaining contralateral lobe.[12] Therefore, total thyroidectomy is seldom necessary and should not be performed routinely.

After the lobe has been removed, it should be submitted for frozen section if this service

is available. The diagnosis of carcinoma of the thyroid is somewhat difficult by frozen section but it usually can be established and this is helpful in determining the need for immediate further surgery. When the diagnosis of carcinoma has been made by frozen section, the surgeon should open the carotid sheath and examine carefully for enlarged lymph nodes. If none is found, no further procedure should be carried out at this time.

If disease is demonstrated in the lateral cervical nodes, a neck dissection should be performed immediately. It is usually not necessary to do a classical radical neck dissection including the sternomastoid muscle and internal jugular vein as is done for carcinoma of the tongue or the floor of the mouth. In most cases of papillary and follicular carcinoma the sternomastoid muscle is not involved and a satisfactory modified neck dissection can be performed leaving it intact. If involved nodes are present on both sides of the neck, a bilateral modified neck dissection is indicated.

Patients with undifferentiated thyroid cancer are usually in the older age group and seldom present themselves for treatment before the tumor is extensive. In this situation it is recommended that as much of the tumor as possible be resected. Roentgen-ray therapy can be used for controlling residual disease and for palliation.

In some institutions all patients with cancer of the thyroid receive prophylactic or therapeutic roentgen-ray therapy postoperatively. How much effect this has had on the survival of the patients is difficult to evaluate; however, Sheline et al.[10] and Smedal and associates[11] have described some very favorable results in patients whose tumor was not amenable to surgical excision. There is also a growing series of children with known residual carcinoma who have been controlled for long periods by the judicious use of roentgen therapy.[13] This is of special value in those patients in whom carcinoma must be left on the larynx or trachea.

Radioactive iodine is often of value in the treatment of patients with inaccessible metastatic follicular carcinoma. It is not generally appreciated that papillary carcinomas may contain a large follicular element, enough in some cases to pick up therapeutic amounts of ^{131}I. There are now 21 patients in the childhood series whose lungs have cleared after the use of radioactive iodine and some have lived for more than 10 years. All these patients had mixed papillary and follicular carcinoma.[13]

EVALUATION OF THERAPY

It is extremely difficult to evaluate any form of therapy when dealing with cancer that grows as slowly as well-differentiated carcinoma of the thyroid. Many therapists have attempted to control the growth of inaccessible cancer of the thyroid with large doses of desiccated thyroid. Few are enthusiastic about the results and unfortunately this method of therapy has been unsuccessful in our hands.

To evaluate fully the results of therapy in thyroid cancer it is necessary to follow patients for at least 20 years; however, many authorities have demonstrated that death from this disease most frequently occurs in the first five years. Two factors influence the prognosis in thyroid carcinoma. The first is the cell type and the second is the extent of the disease. In the large group of children nearly all of those with undifferentiated carcinoma died within the first five years. The same was true in the series of 126 adults seen at the Washington Hospital Center. The 10-year survival rate for the adults with cancer of the thyroid is 74% and 85% of the children have lived 10 or more years. Cancer of the thyroid is an unpredictable disease. Two patients have had a recurrence of papillary carcinoma after 20 years and others have lived with carcinoma continuously for more than 35 years.[13]

The existing controversy concerning methods of therapy is due to the tremendous variations in the clinical behavior of cancer of the thyroid and to judgments based upon statistically insignificant numbers of patients inadequately followed. Even the few investigators with large series are in disagreement. In spite of these differences, evaluation of the published data and personal experience suggest that patients with well-differentiated cancer of the thyroid should be treated conservatively.

SUMMARY

The clinical aspects of patients with cancer of the thyroid were discussed with remarks on etiology, physical findings and the relationship between the various cell types and methods of therapy.

Recommendations for conservative surgery were offered on the basis of the natural his-

tory of the disease. Comments were made on the effects of radiation on inaccessible cancer of the thyroid followed by a brief discussion of survival.

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