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Secondary Malignancy of the Thyroid Gland and Its Management

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Background: Secondary cancer of the thyroid gland is widely acknowledged as infrequent but is a persistent problem requiring ongoing awareness, particularly with respect to clinical recognition and treatment.

Methods: From 1978 to 1993, a 15-year period, patients demonstrating secondary involvement of the thyroid gland as a surgical problem were collected and analyzed with regard to pathology, demography, behavior of primary and secondary disease, treatment, and patient outcome.

Results: In the 15-year span, 11 patients with secondary involvement of the thyroid gland were recognized, consisting of 3 men and 8 women with primary lesions occurring in oral cavity, esophagus, stomach, colon, pancreas, breast, skin, unknown, kidney, and lung. Needle biopsy produced a 90% malignancy rate but in only half of such cases was the diagnosis specific for secondary malignancy. Eight of 11 underwent palliative surgery, usually total thyroidectomy. No patient survived >2 years. There was no undue surgical morbidity. One patient died of pulmonary embolus postoperatively.

Conclusions: Secondary cancer of the thyroid is rare and can be detected by fine-needle aspiration biopsy in the face of clinical findings. Where indicated, palliative thyroidectomy can be effective, because other methods of treatment appear ineffective.

Key Words: Thyroid—Cancer, secondary—Metastases—Goiter.

Nodular disease of the thyroid gland is common affecting 5% of the North American population, but secondary malignancy as a cause of nodularity is infrequent. Major institutions (1–3) can only report totals of 12–17 patients discovered during a 20-year period. Autopsy findings of malignancy metastatic to the thyroid gland vary from 2 to 26.4% of cases studied (3), and the more painstaking the pathological study of the thyroid is, the more frequent becomes the rate of metastatic disease. It may simply be that the clinical involvement of the thyroid gland by secondary malignancy is infrequently sought for and appears overshadowed by the classic sites where metastases are found. The infrequency of secondary malignancy in thyroid, particularly as an isolated finding, dictates for the surgical oncologist a need to renew awareness of the condition, its clinical features, and appropriate investigation and management.

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METHODS

From 1978 to 1993, a 15-year period, patients demonstrating secondary involvement of the thyroid gland as a surgical problem were collected and analyzed. Patients with direct extension of tumor from primary lesions in the head and neck area such as larynx were excluded, excepting one case that presented as an unusual and remitting form of thyroid disease. All cases of lymphoma were also excluded, again with one exception, which behaved as

a nonlymphomatous malignancy and illustrated an important point in diagnostic pitfalls. Patients were analyzed as to pathology, demographic features, behavior of primary and secondary disease, treatment protocols and their implication for patient benefit.

RESULTS

In the 15-year span, 11 patients with secondary involvement of the thyroid gland were identified consisting of 3 men and 8 women ranging in age from 45 to 89. Excepting two individuals, all patients were older than 50 years. Primary malignant sites included oral cavity 1, esophagus 1, stomach 1, colon 1, pancreas 1, breast 1, skin 1, unknown 1, kidney 1, lung 2. Pathology of secondary disease showed squamous cancer 2, adenocarcinoma 6, melanoma 1, fibrosarcoma 1, and non-Hodgkin's lymphoma 1. Nine of 11 patients underwent fine-needle aspiration biopsy (FNAB) of the thyroid gland showing inflammation 1, cellular 1, anaplastic cancer 2, papillary cancer 1, melanoma 1, and metastatic adenocarcinoma 3. Eight of nine FNAB reports were correct for malignancy for a true positive rate of 90%. Six of the 11 patients had established malignant disease.

In one patient, thyroid disease was clinically occult. Four patients presented themselves with apparent "malignant pseudothyroiditis" characterized by variations of hyperthyroxinemia, elevated thyroid antibody titers, and thyroid tenderness. Six patients presented themselves with a thyroid mass clinically suspect for malignancy because of bulkiness, firmness, bilateral involvement, and variable degrees of pressure symptomatology. Thyroid technetium-99 scanning was carried out in 9 of 11 patients, indicating the presence of a hypofunctioning nodule(s).

The clinical behavior of thyroid secondary disease was of interest. The occult case was detected during a neck dissection for metastatic squamous cell cancer of regional nodes from an oral primary controlled by radiation. One patient presented with a thyroid abscess that responded completely to repeat needle aspiration and antibiotic therapy. A subsequent barium swallow revealed a cervical esophageal malignancy with fistula formation that proved to be irresectible. Two patients were diagnosed with anaplastic cancer by FNAB and underwent total thyroidectomy. One eventually proved to be a non-Hodgkin's lymphoma by manifesting gastric and small-bowel involvement 6 months after surgery. She underwent chemotherapy with a fatal outcome. The second such patient developed an acute abdomen 6 months after total thyroidectomy, and laparotomy revealed a duodenal perforation and peritoneal carcinomatosis due to anaplastic adenocarcinoma of the pancreas. Our melanoma patient had undergone a local resection 3 years previously. Before planned thyroidectomy she developed small-bowel obstruction due to metastatic melanoma and died shortly after. Two lung cancers appeared to be preterminal and received no surgical treatment. Our renal case had undergone a nephrectomy 7 years before surgery and had already undergone parotidectomy, orchiectomy, and soft-tissue resections for metastatic renal cell carcinoma. Our fibrosarcoma patient was admitted with a rapidly growing bulky mass that could not be completely resected. Its primary site was not established. Our breast cancer patient had undergone mastectomy 3 years previously, and thyroidectomy revealed a metastatic breast cancer that developed almost synchronously with chest wall recurrence, for which she received radiation therapy; she died 18 months later (Figs. 1 and 2). Our colon case presented with pressure symptoms a year after colectomy and postoperative irradiation. She died of abdominal recurrence after 1 year (Table 1).

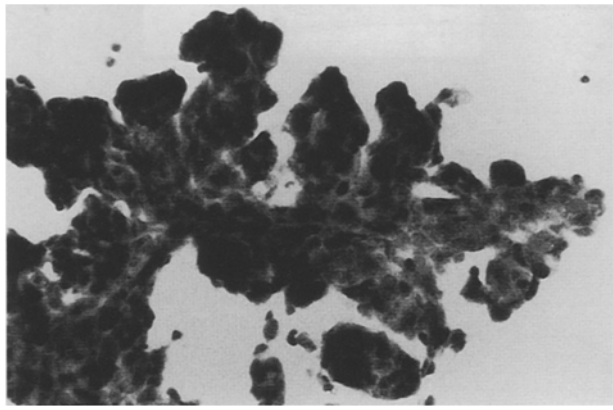

FIG. 1. Cytologic appearance of fine-needle aspiration biopsy with diagnosis of papillary carcinoma of the thyroid representing secondary disease from a breast primary (Papanicolaou stain ×250).

Of the 11 cases, 4 initially showed an unidentified primary, for a 36% rate. Duration of preexistent malignancy varied from 0 to 7 years, and survival of our patients varied from 1 to 24 months, with one patient lost to follow-up and presumed to be dead. Three patients underwent no surgical procedure (melanoma 1, lung 2). Surgical procedures included

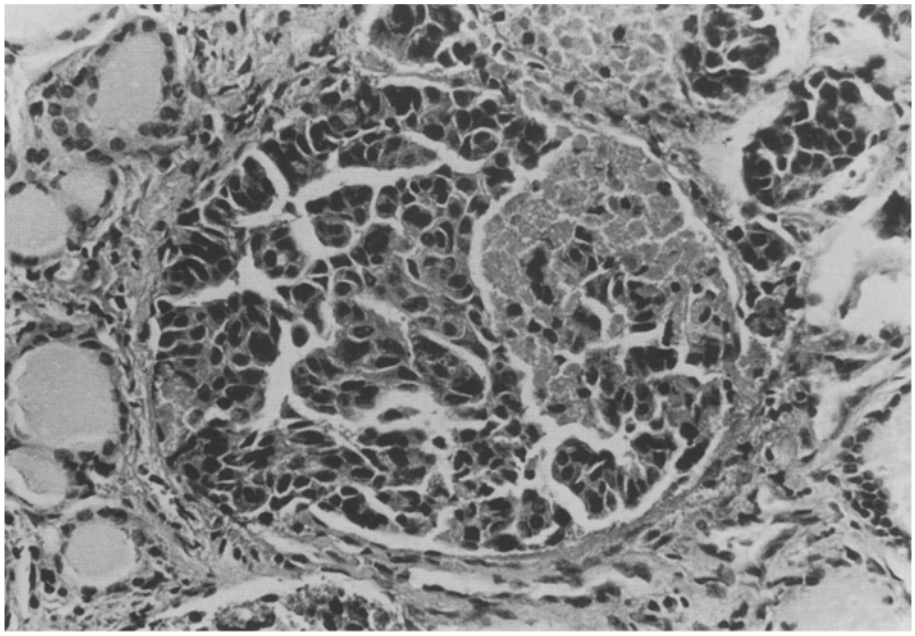

FIG. 2. Histologic section of papillary breast adenocarcinoma metastatic to thyroid gland (H&E stain ×222).

near-total thyroidectomy and modified neck dissection 1 (oral), near-total thyroidectomy 5 (stomach, kidney, colon, pancreas, breast), partial thyroidectomy (fibrosarcoma) 1, exploration only (esophagus) 1. There was no substantial morbidity, but one patient died on her 1st postoperative day of pulmonary embolus. No recurrence of tumor developed in the thyroid region after complete resection in six patients. Radiation was given to the head and neck 3 (2 postthyroidectomy), pelvis 1, chest wall 1. Chemotherapy was received by three patients for primary problems.

DISCUSSION

Although secondary thyroid disease appears to be rare, the use of FNAB has altered this view somewhat, with frequencies ranging from 0.1% occurrence in 25,000 thyroid FNABs during 20 years (4) to 5.7% occurrence in 70 patient FNABs during 1 year (5) and 1% occurrence in 549 FNABs during 7 years (6). Our 11 patients made up 0.6% of our thyroidectomy experience during the study period.

In an autopsy study of incidental thyroid metastases (3), primary sites were shown to be breast

TABLE 1. *Summary of patients with secondary thyroid cancer showing primary sites, duration of diagnosis, treatment, and survival*

Case no.	Age (yrs)	Sex	Primary	Clinical	FNAB	O.R.	Path	Result
1	72	F	Oral	Occult; found at neck surgery	0	+	S	DOD
2	59	F	Esophagus	Fistula; thyroid abscess	pus	+	S	Dead; pulmonary embolus
3	62	F	G.I.?	Goiter; occult primary	CA	+	L	DOD
4	73	F	Pancreas	Goiter; occult primary	CA	+	A	DOD
5	46	F	Colon	Goiter; postcolectomy	CA	+	A	DOD
6	52	M	Kidney	Multiple metastectomy	0	+	A	DOD?
7	89	F	Unknown	Goiter	Cellular	+	S	DOD
8	48	F	Breast	Obstructive goiter; synchronous breast recurrence	CA	+	A	DOD
9	50	F	Melanoma	Goiter; bowel obstruction due to secondary	CA	+	M	DOD
10	62	M	Lung	Terminal	CA	−	A	DOD
11	67	M	Lung	Terminal	CA	−	A	DOD

FNAB, fine-needle aspiration biopsy; CA, cancer; DOD, died of disease; G.I., gastrointestinal.

25%, lung 25%, melanoma 10%, kidney 10%, gastrointestinal tract 8%, with a wide range of other primaries. Where secondary thyroid disease was clinically detectable, kidney primary occurred in 57% and breast and lung occurred in ~10–12%. In another autopsy study (3), 39% of melanoma, 21% of breast, 12% of kidney, 11% of lung, and 10% of head and neck primaries had metastasized to thyroid. Pooling the reported secondary thyroid cases (1–9) along with our own patients resulted in a total of 111 such cases, which showed primary sites to be kidney 25 (23%), breast 18 (16%), lung 17 (17%), melanoma 6 (5.4%), larynx 5 (4.5%), colon 5 (4.5%), and esophagus 3 (2.7%). The remaining primary sites or lesions included stomach, sarcoma, cervix, "lymphoma," nasopharynx, mesothelioma, bladder, and anus.

The inclusion of lymphoma appears inappropriate in view of its multicentric nature, but it has been included in reviews (3) and reports (8). Our series included one such case in which the thyroid disease was diagnosed and treated as an anaplastic malignancy of thyroid until its gastrointestinal involvement manifested itself 6 months later. This case behaved as a solid cancer and was similar to a case previously reported (8).

In one study (3), 5 patients with a larynx primary were described among 17 cases, but pains were taken to affirm that this did not represent direct invasion. Our series included one cervical esophageal malignancy, which presumably did represent direct extension but manifested itself as an acute thyroid abscess that responded completely to needle aspiration and antibiotic drugs and resembles another such reported case (8).

Secondary thyroid lesions present themselves like primary thyroid problems including symptoms of dysphagia, dysphonia, and a thyroiditis-like picture (7). The thyroid scintiscans in these patients are usually cold, although one functioning nodule has been reported (5).

Usually the primary cancer is evident. A third of our cases showed an occult primary lesion that was only determined metachronously and has been similar to the experience of others (1,4, 5,8). The interval between primary site treatment and secondary disease varies with the primary's behavior but has been reported as high as 23 years for hypernephroma. Lengthy duration can also be seen in breast and gynecological cancer as well as melanoma (1, 4,8). One of our patients with hypernephroma presented 7 years after nephrectomy, but he had had other metastatic sites involved as did four of our other patients, a not unusual occurrence (1,3).

Needle aspiration biopsy of thyroid mass represents an ideal method of diagnosis of metastatic malignancy of the thyroid gland and in our experience showed a 90% positive rate for cancer, although specific secondary diagnosis was lacking in four of nine cases. FNAB has been used to diagnose metastatic thyroid disease and thereby indicate the underlying primary tumor (6). Ultrasonography (8) can indicate the extent of clinically occult disease and guide fine-needle aspiration for establishment of tissue diagnosis. Schmid et al. (4) note that FNAB biopsy of renal and mammary metastases are indistinguishable cytologically from primary papillary and follicular cancers of the thyroid gland, but otherwise FNAB is reliable in diagnostic information. The FNAB diagnosis of anaplastic cancer may represent secondary disease from an inapparent malignancy of the gastrointestinal tract or lung (6). All authors (1–9) affirmed the value of fine needle biopsy but some of the larger series (1,3,8) actually had not used FNAB in their patients. Cytologist review of our cytology specimens confirmed the diagnosis of secondary carcinoma reinforced by results of total pathological studies.

FNAB diagnosis permits intelligent treatment. When patients are well and symptomatic, thyroidectomy provides effective palliation (1,3,9). The extent of thyroidectomy is dictated by individual circumstances. Survival results of thyroidectomy reflect the behavior of the underlying primary. In our own experience, survival did not exceed 2 years, although one patient was lost to follow-up. Reported survivals can be lengthy, particularly for renal cell carcinoma, which can vary from 7 months to 8 years (1,3,9), but the overall prognosis here is limited. Postoperative adjuvant chemotherapy and radiation therapy have been reported (1), but their value as policy has not been established.

Secondary cancer of the thyroid gland is uncommon but persistent and requires recognition. Although any primary lesion may give rise to such metastatic disease, the usual primary sites are kidney, lung, and breast. FNAB is the key to appropriate diagnosis, which permits appropriate management. Surgical resection of the affected thyroid tissue provides reasonable palliation with little morbidity. When the patient's condition is hopeless and terminal, no surgical intervention appears indicated, which occurred in three patients in our series. The overall survival depends on the behavior

of the underlying primary lesion, and renal cell carcinoma, a common primary site, is compatible with lengthy survival.

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