

DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS OF LONG-TERM RADIOISOTOPE SCANNING IN THE MANAGEMENT OF THYROID CANCER

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It is widely accepted that total or extensive subtotal thyroidectomy followed by ablative doses of radioiodine (^{131}I) is the treatment of choice for thyroid cancer of differentiated cell types (1-5). This combination of surgery and ^{131}I has been shown to be more effective than surgery alone (6).

At the present time the recurrence rate of thyroid cancer, once all tumor tissue has been completely ablated with ^{131}I , is not known. Furthermore, the diagnostic importance of long-term followup scanning after total tumor ablation has not been established. In view of the fact that the combination of surgery and ^{131}I ablation appears to increase survival rates (6), it would seem to be essential that the patient be free of all ablatable cancer tissue. It is important therefore to determine the actual incidence of recurrence following total tumor ablation and also to determine how long scanning should be continued in the absence of detectable tumor tissue. To obtain information concerning such problems, a prospective study of thyroid cancer patients was initiated in 1949 at the Los Angeles Wadsworth Veterans Administration Hospital. It is the purpose of this paper to report the initial results of this study.

MATERIALS AND METHODS

The patient procedures used in this study are reported in detail in a previous communication by Blahd, et al (7). In brief, they consist of the following:

Therapeutic procedures. Total or extensive subtotal thyroidectomy was followed by ablative doses of ^{131}I . Repeat ^{131}I doses were administered at 4-6-month intervals until ablation of all functioning tumor tissue and postsurgical thyroid tissue remnants had been achieved. After the total ablation, all patients were maintained on maximum tolerated doses of thyroid extract which varied from 4 to 10 grains daily.

Followup procedure. Thyroid medication was discontinued for 4-5 weeks prior to ^{131}I scanning. Ten

units of thyroid-stimulating hormone (TSH) was administered daily for 3 days, and scan of neck, chest, and body was obtained 24 hr following an oral dose of 5 mCi of ^{131}I . (The scan dose of ^{131}I was given 24 hr after the last dose of TSH.)

From 1950 to 1960, a total of 31 patients with histologically proven carcinoma of the thyroid were treated by means of surgery and ^{131}I . For purposes of this report we have included only those patients who had been followed for 10-21 years after surgery and ^{131}I treatment. Total ablation was considered to have been achieved when two consecutive 5 mCi ^{131}I post-therapy diagnostic scans performed at 6 and 18 months did not show evidence of functioning tissue or regenerated thyroid tissue. After total ablation was achieved, yearly scans were performed for the first 5 years and subsequently every 2 years thereafter. Whenever functioning tumor tissue was detected, further ^{131}I ablation therapy was instituted.

RESULTS

Postsurgical total ablation was usually achieved between 12 and 24 months in all patients with total doses of ^{131}I that varied from 75 to 475 mCi. Individual doses ranged from 75 to 100 mCi of ^{131}I . Of the original 31 patients treated between 1950 and 1960, 18 fulfilled the criteria set forth for inclusion in this study. Table 1 gives the relevant clinical data of these 18 patients. They were all males. The ages ranged from 33 to 75 years with a current mean age of 46 years. Eight patients were between 20 and 30 years of age at the time of their first treatment with ^{131}I . Six patients had papillary carcinoma, four had follicular carcinoma, and the remaining eight had mixed papillary and follicular

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TABLE 1. CLINICAL DATA

Patient	Tumor histopathology	Site of initial metastases	Recurrence		Followup period (yrs)
			Yrs after 1st ablation	Site	
1	Papillary and follicular	None	NR*	—	16
2	Follicular	None	NR	—	19
3	Follicular	Cervical	2	Local†	16
4	Follicular	None	8	Local	17
5	Papillary and follicular	Cervical	NR	—	14
6	Papillary and follicular	Cervical	7	Local and cervical	12
7	Papillary and follicular	Cervical	3	Local and cervical	18
8	Papillary and follicular	None	NR	—	17
9	Papillary and follicular	Cervical	NR	—	11
10	Papillary and follicular	Cervical	NR	—	14
11	Papillary	Cervical and thoracic	6	Local	21
			10	Local	
12	Follicular	None	NR	—	18
13	Papillary	Cervical and thoracic	6	Cervical and thoracic	12
			8	Cervical and thoracic	
14	Papillary	None	NR	—	10
15	Papillary	None	NR	—	12
16	Papillary	Cervical	NR	—	10
17	Papillary	Cervical and thoracic	9	Local and cervical	12
18	Papillary and follicular	None	5	Local	10

* NR: no recurrence.

† Local: indicates thyroid bed area.

carcinomas. Initially, ten patients had metastases in either the cervical or the thoracic region before ¹³¹I ablative treatment. The remaining eight patients did not have extrathyroidal metastases. Eight patients had been followed for periods of 15–21 years and ten patients had been followed for 10–14 years. The mean followup period was 14 years.

Tumor recurrence. Six of the ten patients who had metastases at the time of initial surgery and ¹³¹I treatment and two of the eight patients who did not have demonstrable metastases initially were later found to have abnormal ¹³¹I focal concentrations. In four of these eight patients who had evidence of recurrence, the recurrence was located in the thyroid bed area; in the remaining four, both local and extrathyroidal ¹³¹I foci were observed. The site of recurrence was in all instances the same as that of the original metastasis before ¹³¹I treatment (Table 1). All eight patients who showed recurrence were treated again with ¹³¹I and complete ablation was achieved (Fig. 1). In two patients, the recurrence occurred within 5 years; in the remaining six, it occurred more than 5 years after complete ¹³¹I ablation. The recurrence rate was essentially the same for papillary, follicular, and the mixed variety of carcinomas. Patients with anaplastic tumors did not survive long enough to be included in this report.

DISCUSSION

The 18 patients included in this prospective study represent a very select group. They are all male

veterans in the age range of 33–75 years. All had either total or subtotal thyroidectomy followed by tumor ablative treatment with ¹³¹I. All patients had yearly scans for the first 5 years and every 2 years thereafter. All were subjected to the same therapeutic regimen.

The incidence of extrathyroidal metastases in the present study is 56% (10 of the 18 patients). Haynie, et al (4) studied a group of 200 thyroid cancer patients and reported an initial extrathyroidal metastatic incidence of 41%. Metastases were mainly to the lymph nodes, and in a few instances, to the lungs and bones. Haynie, et al also observed no tumor recurrence in patients followed for 3 years who were clinically free of disease following ¹³¹I therapy (4). It is interesting to note that in our series only two of the eight patients had tumor recurrence within 3 years. The remaining six had their first recurrence 5–10 years after total ¹³¹I ablation therapy. Thus, continued absence of ¹³¹I concentration for 3 or 5 years is no assurance that tumor recurrence will not occur later. In no instance in our study were the metastatic lesions clinically palpable. Thus, the only possible means of detecting tumor recurrences is by isotope scanning.

In the present study it is not known how many of the recurrences in the thyroid bed area involve malignant tissue; however, four patients had both local (thyroid bed area) and extrathyroidal recurrences strongly suggesting tumor metastases. We have considered extrathyroidal localization of ¹³¹I other than

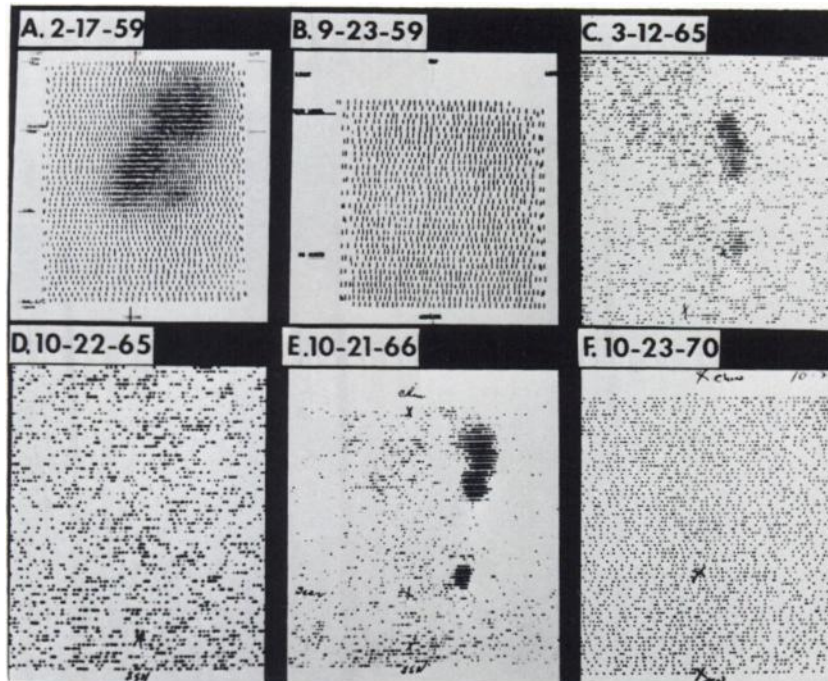


FIG. 1. Patient with papillary cancer of thyroid (No. 13 in Table 1). First scan obtained after administration of 100 mCi of ^{131}I shows remnant of thyroid tissue and area of cervical metastasis adjacent to superior pole of left lobe (A). Total ablation was achieved with 210 mCi of ^{131}I (B). For next 5 years, there was no evidence of ^{131}I localization, but scan at end of 6 years showed ^{131}I accumulation in neck (C). Patient was again treated with 92 mCi of ^{131}I and total ablation was apparently achieved (D). One year later recurrence was again noted (E). Total ablation was achieved with additional 200 mCi of ^{131}I . There has been no evidence of any recurrence for last 4 years. Latest scan (F) does not show any evidence of recurrence.

salivary gland, esophagus, and stomach as indicative of metastatic deposits. Many investigators may consider extrathyroidal ^{131}I localization as lateral aberrant thyroid. In our study we have considered all extrathyroidal cervical region ^{131}I localization as indicative of cervical metastasis from thyroid.

This study indicates that long-term followup ^{131}I scanning is essential in the management of patients with thyroid cancer, especially for those patients who have metastases at the time of original ^{131}I ablation therapy. Since only two of the eight patients without initial metastasis had local recurrences, it appears that the tumor recurrence rate for this group of patients is low. In contrast, six of the ten patients with initial metastases showed tumor recurrence. Recurrence occurred as late as 5 to 10 years after total ^{131}I ablation; hence, complete absence of tumor recurrence for 5 years does not preclude the need for continued periodic diagnostic scanning.

It has been shown that the mortality rate is lower in patients treated by means of surgery and ^{131}I total ablation than the mortality rate in the patients who have been treated with surgery alone. Varma, et al (6) followed 263 patients treated by means of combined surgery and ^{131}I and 50 patients treated with surgery alone. Patients were followed for a mean duration of 6.2 years (range, 2–20 years). The mortality rate for patients more than 40 years of age was 10.3% for the combined group and more than 50% for the surgical group (6). Patients with papillary carcinoma showed significantly better survival than the patients with other histological tumor cell types. Patients with extrathyroidal metastasis

showed a higher death rate. When ^{131}I therapy was discontinued short of total tumor ablation, the death rate was 20 times higher than the death rate when total ablation was achieved. Thus, total ablation of initial and recurrent functioning tumor tissue would seem to be appropriate in the management of thyroid cancer patients.

In our study all patients were treated with maximum tolerated doses of thyroid extract which varied from a minimum of 4 grains to the maximum of 10 grains daily. We did not measure TSH levels during the suppression period. Now, with the availability of radioimmunoassay for TSH measurement, it should be possible to assess the degree of TSH suppression by exogenous thyroid hormones. It is possible the incidence of recurrence may depend very much on the degree of TSH suppression by exogenous thyroid extract.

In the present study all patients who had detectable tumor recurrence were treated with ^{131}I . The total dose (including the first ^{131}I ablation dose) did not exceed 500 mCi. Eight patients were young adults between the ages of 20 and 30 years at the time of initial treatment. No complications from therapeutic doses of ^{131}I have been observed during the 10–21-year patient followup period. One patient had tumor recurrence after a second ^{131}I ablation (Fig. 1). He was treated again and total ablation was achieved.

The therapy regimen employed in this series of patients would not have been possible without the availability of diagnostic radioisotope scanning. Radioisotope scanning would appear to be an excel-

lent means of detecting early tumor recurrence since by the time recurrent thyroid cancer becomes clinically apparent, the disease may be far advanced. Although routine long-term scanning of all thyroid cancer patients without selection may not be justified, it appears justified to continue life-long scanning of patients with initial extrathyroidal metastasis since they represent a high-risk group.

SUMMARY

The diagnostic significance of long-term post ^{131}I ablation scanning was evaluated in 18 patients with thyroid cancer. Each patient had been treated with surgery followed by total ablation of tumor tissue with ^{131}I . Patients were followed by means of annual scans for the first 5 years and thereafter by scans every 2 years. Followup intervals were 10–21 years (mean, 14 years) after the ^{131}I treatment. Tumor recurrence occurred in some patients 5 or more years after continued absence of tumor for the first 5 years.

Since tumor recurrence is more common in those patients who had tumor metastases initially, it is recommended that diagnostic scanning be continued annually for all thyroid cancer patients for the first 5 years and beyond this period for those with initial tumor metastasis. It is also recommended that the patient who shows recurrence be treated with ^{131}I until total ablation is again achieved. There have been no long-term harmful effects associated with therapeutic doses of ^{131}I for either initial or recur-

rent thyroid cancer in the dose range employed in this series of patients.

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