THYROID CANCER FOLLOWING $^{131}$I THERAPY OF HYPERTHYROIDISM

John B. Lima
Kaiser Foundation Hospital, Oakland, California

Boris Catz
University of Southern California School of Medicine, Los Angeles, California

S. L. Perzik
Loma Linda University School of Medicine, Loma Linda, California

A review of the literature has uncovered three cases of carcinoma of the thyroid following the use of $^{131}$I in the treatment of hyperthyroidism (1–3). To this group we wish to add another case (Table 1).

REPORT OF A CASE

P.G. (Colh.#18-07006), a 36-year-old, white female housewife was admitted to the hospital on May 14, 1968, with bilateral exophthalmos of 3-year duration. She had been in excellent health until 4 years prior to admission when she developed symptoms of nervousness, cardiac palpitation and heat intolerance. A diagnosis of hyperthyroidism was

Received Jan. 1, 1969; revision accepted July 11, 1969.
For reprints: S. L. Perzik, 300 S. Beverly Dr., Beverly Hills, Calif. 90212.

<table>
<thead>
<tr>
<th>Source</th>
<th>Sex</th>
<th>Preliminary findings (pre $^{131}$I)</th>
<th>Age at first $^{131}$I dose (yr)</th>
<th>First $^{131}$I dose (mCi)</th>
<th>Total $^{131}$I dose (mCi)</th>
<th>Age at D$_{x}$ of cancer (yr)</th>
<th>Pathological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheline, G. E. et al (1)</td>
<td>F</td>
<td>Diffusely enlarged thyroid gland (1.5–2x normal)—no nodules</td>
<td>9</td>
<td>1.2</td>
<td>5.4</td>
<td>17</td>
<td>GROSS: 3 encapsulated nodules (largest = 2 cm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PBI = 9.6 µg%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MICRO: Radiation changes 2 follicular adenomas</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMR = +62%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 follicular carcinoma in the largest nodule</td>
</tr>
<tr>
<td>Karlan, M. et al (2)</td>
<td>F</td>
<td>Diffusely enlarged thyroid gland (3x normal)—no nodules</td>
<td>11</td>
<td>1.25</td>
<td>3.25</td>
<td>13</td>
<td>GROSS: Several nodules (largest = 3 cm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PBI = 16.7 µg%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MICRO: Radiation changes Papillary carcinoma in the largest nodule</td>
</tr>
<tr>
<td>Burke, G. et al (3)</td>
<td>F</td>
<td>Diffusely enlarged thyroid gland (2–3x normal)—no nodules</td>
<td>26</td>
<td>4.7</td>
<td>4.7</td>
<td>36</td>
<td>GROSS: Multinodular gland</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PBI = 12.4 µg%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MICRO: Radiation changes Well differentiated Follicular carcinoma</td>
</tr>
<tr>
<td>Lima, J. B. et al</td>
<td>F</td>
<td>Small thyroid—no nodules</td>
<td>32</td>
<td>5.0</td>
<td>9.0</td>
<td>36</td>
<td>GROSS: 4.0 gm thyroid parenchyma with fibrous streaks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PBI = 9.5 µg%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MICRO: Encapsulated nodule showing microcarcinoma with a follicular pattern</td>
</tr>
</tbody>
</table>

JOURNAL OF NUCLEAR MEDICINE
made and confirmed by an $^{131}$I uptake of 78%, with a PBI of 9.5 μg% and a $T_3$ resin uptake of 42%.

The patient was given 5 mCi of $^{131}$I on December 10, 1964, after which her symptoms gradually abated until December 16, 1965, when it was noted that the left palpebral fissure was larger than the right. Hertel measurements which previously had been 16 mm bilaterally, measured 20 mm in the left eye and 18.5 mm in the right eye. Repetition of the laboratory studies showed the PBI to be 7.3 μg%. The radioactive iodine uptake was 63%.

Because of continuation of nervousness and progression of ophthalmopathy, an additional 4 mCi of $^{131}$I were administered on March 31, 1966, following which a transition to hypothyroidism occurred.

On May 12, 1966, she was started on 1 grain of thyroid a day, and her eyes measured 19 mm in the right and 22 mm in the left with the exophthalmometer. Although she had no eye pain, diplopia or epipora, she did notice occasional blurring of her vision. By February 1967 she was taking 3–4 grains of thyroid a day; and while on this regimen, there was further increase in her proptosis, associated with remittent diplopia. Reevaluation prior to admission in May 1968 revealed that the radioactive iodine uptake was 16% while on 4 grains of thyroid daily, suggesting lack of suppression. The long-acting thyroid stimulator was positive, the $T_4$ by column was 4.3 μg% and the $T_3$ uptake by the red cell was 14%. Her eye measurements were OD 19½ mm, OS 22 mm. A total thyroidectomy was performed on May 15, 1968, because of the persistence and progression of the ophthalmopathy.

**PATHOLOGY**

See Figs. 1–4. The thyroid weighed 4 gm. It showed a tan parenchyma streaked with gray con-
nective tissue. In the right lower lobe was a 2.5-mm nodule.

The parenchyma of the thyroid showed increased connective tissue both in the septa and between the follicles. Most of the follicles were of normal size with cuboidal epithelium containing granular, pale cytoplasm. In places there were hyaline droplets, some pigmented a faint brown, and occasional Hurthle cells were seen. The colloid was pale, scalloped and vacuolated. There were moderate numbers of atypical, enlarged and bizarre hyperchromatic nuclei. Other follicles were small and atrophic with flattened epithelium and densely staining colloid.

The right lower lobe nodule had a fibrous capsule. It contained follicles of variable size, and in places, its stroma was hyalinized and edematous. One portion of the nodule showed small follicles with atypical cells containing enlarged, vesicular nuclei. In this area there was also some loss of follicular structure with cords of the same atypical elements.

The parenchymal changes were interpreted as indicating reaction to irradiation. The right lower lobe nodule was a follicular carcinoma.

The patient was last seen on September 15, 1968. The diplopia and the conjunctival infiltration were less. The eye measurements were OD 18 mm and OS 19 mm. She has been maintained on 4 grains of thyroid daily.

DISCUSSION

All of the four cases listed in Table 1 occurred in females. No nodules were noted at the onset of $^{131}$I treatment. The interval between treatment and the diagnosis of cancer was 2−10 years.

An analysis of these cases may suggest the possibility that the time interval between the first doses of $^{131}$I and the detection of the thyroid carcinoma is too short to imply carcinogenesis. However, thyroid malignancy was found by Winship (4) to occur 3.6−14 years after childhood irradiation, and Nishiyama (5) reported an average of 8.8 years between exposure to childhood radiation and the diagnosis of carcinoma of the thyroid. The patient reported in this paper had thyroid carcinoma which was discovered at surgery 4 years after $^{131}$I was administered.

SUMMARY

A case of carcinoma of the thyroid gland discovered 4 years after radioactive iodine treatment for Graves' disease has been presented.

REFERENCES


