Outcome of 309 Patients with Metastatic Differentiated Thyroid Carcinoma Treated with Radioiodine

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Abstract: From 1969 to 1990 there were 309 patients with differentiated thyroid carcinoma (241 papillary and 68 follicular) treated with radioactive iodine for functioning node metastases alone (n = 191) or distant metastases (n = 118) with or without node metastases. These patients represented 32.7% of 945 patients treated in our institution during the same period. Initial treatment included near-total thyroidectomy and 131I ablation of postsurgical thyroid residue, followed by l-thyroxine suppressive therapy. At the end of follow-up (mean 5.8 years), 146 patients (76.4%) in the group with nodal metastases were considered cured, as assessed by clinical and laboratory evaluation including whole body scan (WBS) and serum thyroglobulin (Tg) levels; 32 patients (16.7%) had persistent disease. Loss of 131I uptake in persistent metastatic lesions occurred in five patients (2.6%), and newly developed distant metastases occurred in eight patients (4.2%). Of the patients with distant metastases, 36.4% were cured by 131I. Distant metastases from papillary carcinomas had a higher cure rate than follicular carcinomas (p < 0.01). The metastases of four patients (5.2%) lost the property to take up radioiodine. Lung and bone metastases detectable by WBS but not by radiography were most likely to be cured by 131I. The overall survival at the end of follow-up was 95.8% in patients with only lymph node metastases and 76.0% in those with distant metastases. Tumor-related deaths were 3.6% of follow-up was 95.8% in patients with only lymph node metastases and 76.0% in those with distant metastases. Tumor-related deaths were 3.6%

Patients and Methods

From 1969 to 1990 there were 309 patients (220 women, 89 men; ages 5–81 years, mean 38.7 years) with functioning nodal or distant metastases from DTC treated at the Institute of Endocrinology of the University of Pisa. Initial treatment was surgery, performed in most cases at the Unit of Endocrine Surgery of the University of Pisa.

According to the WHO classification [3], histology was papillary thyroid carcinoma (PTC) in 241 patients and follicular (FTC) thyroid carcinoma in the remaining 68 patients. Lymph node metastases alone were present in 191 patients (61.8%) (164 papillary, 27 follicular; ages 5–80 years, mean 33.9) and distant metastases with or without associated nodal metastases in 118 patients (38.2%) (77 papillary, 41 follicular; ages 7–81 years, mean 43.9 years). The site of metastatic involvement in patients with distant metastases is reported in Table 1: For PTCs, the lung was the main site of metastases, whereas for FTCs, lung and bones were almost equally affected. Mean follow-up, from the time of diagnosis, was 5.8 years (range 3–22 years). For simplicity, lymph node metastases alone are referred to as "lymph node metastases"; and distant metastases, regardless of the presence of node metastases, are referred to as "distant metastases."

As shown in Figure 1, lymph node metastases were found within the first 6 months after surgery, at routine WBS, in 146 (76.4%) patients, including 83 of the 184 patients who had evidence of lymph node metastases at surgery, and were arbitrarily considered present since the time of diagnosis. In 45 patients (23.6%) nodal metastases were detected 1 to 9 years after the diagnosis, mostly within the first 3 years. A similar pattern was observed in patients with distant metastases: Most (73.7%) were detected within the first 6 months after surgery, and most of the remaining cases (26.3%) appeared within the first 3 years of follow-up.
Table 1. Site of metastatic involvement in patients with distant metastases.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Lung (% in 118)</th>
<th>Bone (% in 118)</th>
<th>Lung + bone (% in 118)</th>
<th>Others (% in 118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n = 118)</td>
<td>86 (72.9%)</td>
<td>16 (13.6%)</td>
<td>13 (11.0%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Papillary (n = 77)</td>
<td>70* (90.9%)</td>
<td>4 (5.2%)</td>
<td>2 (2.6%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Follicular (n = 41)</td>
<td>16* (39.0%)</td>
<td>12 (29.3%)</td>
<td>11 (26.8%)</td>
<td>2 (4.9%)</td>
</tr>
</tbody>
</table>

*Associated with lymph node metastases in 44 cases.

Fig. 1. Time of discovery of lymph node or distant metastases after initial treatment.

The patients were considered "cured" when they were clinically free of disease, had a negative WBS, and had undetectable (< 3 ng/ml in our assay) serum Tg off thyroid medication. The term "persistent disease" was applied to patients who appeared unchanged both clinically and at WBS regardless of serum Tg levels. The term "no uptake" was used for previously functioning metastases losing their function some time during the follow-up period.

Results

Radioiodine Treatment

Results of radioiodine treatment in patients with lymph node metastases are depicted in Figure 2. A total of 146 patients (76.4%) achieved definitive cure. They received a mean cumulative dose of 123 mCi 131I, delivered in a mean of 1.4 administrations, over a period of 2.9 years. Persistent disease was observed in 32 (16.7%) patients after a mean 131I dose of 301 mCi, administered over 3.8 years. In five patients (2.6%) functioning nodal metastases lost their ability to take up radioiodine after a mean 131I dose of 77 mCi. Eight patients (4.2%), all with papillary tumors, developed functioning lung metastases (radiography detectable in two cases) after treatment with 131I (mean dose 356 mCi). There was no statistical difference in the percentage of cure achieved between papillary and follicular carcinomas.

As shown in Figure 3, among patients with distant metastases of the papillary type the cure rate was significantly higher (45.5%) and the persistent disease rate significantly lower (49.3%) than that of patients with follicular carcinoma (19.5% and 80.5%, respectively) (p < 0.01 by chi-square analysis). In total, 43 patients (36.4%) were cured; the mean 131I dose achieving permanent cure was higher in patients treated for distant metastases (233 mCi) with respect to the dose required in patients with lymph node metastases alone (123 mCi). In four patients (5.2%) with papillary tumor the metastases lost the ability to take up radioiodine.