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FIVE-YEAR SURVIVAL IS SIMILAR IN THYROID CANCER PATIENTS WITH DISTANT METASTASES PREPARED FOR RADIOACTIVE IODINE THERAPY WITH EITHER THYROID HORMONE WITHDRAWAL OR RECOMBINANT HUMAN THYROTROPIN

Tala H, Robbins R, Fagin JA, Larson SM, Tuttle RM. **Five-year survival** is similar in thyroid cancer patients with distant metastases prepared for radioactive iodine therapy with either thyroid hormone withdrawal or recombinant human **TSH.** J Clin Endocrinol Metab. May 11, 2011 [Epub ahead of print].

BACKGROUND

Randomized trials have demonstrated that radioactive iodine (RAI) ablation of thyroid remnants is equally facilitated by withdrawal from thyroid hormone, inducing hypothyroidism, and by administration of recombinant human thyrotropin (rhTSH) (1,2). Reports have suggested that small-volume local nodal disease identified incidentally after remnant ablation appears to be effectively treated by either withdrawal or rhTSH preparation (2,3). This is a retrospective study to determine whether there is a difference in the short-term survival of patients with iodine-avid thyroid cancer metastatic to bone or lung (American Joint Committee on Cancer stage IV) and treated with RAI after either TH-WD or rhTSH administration.

METHODS

This 17-year retrospective study, conducted from 1993 through 2010, involved 175 patients with differentiated thyroid cancer with iodine-avid metastatic disease to bone (28%), lung (52%) or both (19%). Patients were excluded if the tumor was anaplastic or not iodine-avid or if there was metastatic disease to other organs. Patients were also excluded if there was inadequate follow-up or other malignancies or if the patients was <20 years old.

All patients treated with RAI for distant metastases were placed on a low-iodine diet and underwent formal whole-body and blood RAI clearance dosimetry studies to calculate a dose that delivered <2 Gy to the bone marrow and had less than 80 mCi whole-body retention at 48 hours. Thirty-eight patients had received one or more doses of RAI after thyroid hormone withdrawal prior to referral to the authors' center. Patients treated before 1998 received RAI after withdrawal; starting in 1998, when rhTSH became commercially available,

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patients were treated on the basis of individual patient and physician discussions. All rhTSH treatments were performed with a four-dose schedule that included two doses before a blood and whole-body dosimetry protocol to determine RAI activity and a second set of 2 rhTSH injections before RAI therapy. Thirty-five patients were treated only after thyroid hormone withdrawal, 58 patients were treated only with rhTSH, and 82 patients had thyroid hormone withdrawal with one or more initial treatments and subsequent RAI activities administered after rhTSH.

RESULTS

The clinical characteristics of the patients were not different when segregated by method of preparation for RAI therapy. There was no different in age, sex, evidence of metastases at diagnosis of thyroid cancer, distribution of the distant disease, size of lung metastases, or multiplicity of bone metastases. Patients who were prepared for RAI by thyroid hormone withdrawal only were treated twice, on average, with a cumulative median dose of 522 mCi. Patients prepared for RAI by rhTSH only were also treated twice, on average, with a cumulative median dose of 408 mCi. The patients who were treated with both thyroid hormone withdrawal and rhTSH received, on average, four doses of RAI, with a cumulative median dose of 967 mCi. But the median activity per dose was higher in patients prepared

with rhTSH only (median, 263 mCi; range, 30 to 514) than in patients prepared with thyroid hormone withdrawal only (median, 200 mCi; range, 30 to 480; P = 0.038). Despite the difference in cumulative dose or individual administrations, there was no significant difference in overall survival between patients who were treated with RAI by withdrawal only, rhTSH only or withdrawal followed by rhTSH after a median of 5.5 years (range, 0.8 to 21). In a multivariate analysis including clinicopathological features and methods of preparation, only age at diagnosis was an independent predictor of overall survival. Examining a subset of 73 patients who had only micrometastases in the lung, there was no difference in the survival curves (P = 0.79) whether they were prepared by rhTSH only (32.9%), thyroid hormone withdrawal only (21.9%) or thyroid hormone withdrawal followed by rhTSH (45.2%). The median survival of patient with micrometastases in the lung was 12.5 years.

CONCLUSIONS

This is the first report to show a similar 5-year overall survival rate in patients with thyroid cancer who had iodine-avid distant metastases in the lung and bone when prepared by thyroid hormone withdrawal or rhTSH with dosimetry determined RAI activity treatments. When examined by multivariate analysis, the method of preparation for RAI had no impact on overall survival.

This study confirms clinical observations that when rhTSH was used because either TSH levels could not be elevated or hypothyroidism was thought to be too clinically risky, there is some clinical benefit to RAI therapy of thyroid cancer with metastases (4). It is important to understand that rhTSH is not approved by the Food and Drug Administration for the treatment of metastatic thyroid cancer. Further caution must be used because the average RAI activity administered was higher when rhTSH preparation was used as compared with thyroid hormone withdrawal. The higher dose with rhTSH was due to the more rapid clearance of RAI in the nonhypothyroid state, allowing for higher activity to be administered before the limits to blood and whole body were achieved. This higher dose very likely resulted in a higher dose delivered to the iodine-avid lesions than with thyroid hormone withdrawal.

Clinically, it is exciting to think that patients with distant disease can be treated with less discomfort from hypothyroidism, but ultimately, I think that our standard empirical doses of RAI for distant *continued on next page*

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disease possibly will not result in the same results as achieved at this premier institution for thyroid cancer care. I cannot conclude that patients with iodine-avid distant disease will be adequately treated with rhTSH and empirical doses of RAI, but it is fair to say that a four-dose rhTSH-stimulated dosimetrydetermined treatment with RAI for a patient with RAIavid metastatic disease appears to be a reasonable alternative to traditional thyroid hormone withdrawal RAI treatments.

- Stephanie L. Lee, MD, PhD

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