Radioactive Iodine Rarely Induces Thyroid Storm

Patients with severe thyrotoxicosis can be treated, but they should receive β-blockers and counseling.

BY PAM HARRISON
Contributing Writer

TORONTO — The risk of provoking thyroid storm with administration of radioactive iodine appears to be vanishingly small even in cases of severe thyrotoxicosis, Vani Vijayakumar, M.D., said at the annual meeting of the Society of Nuclear Medicine.

Patients undergoing such treatment therefore do not need to be placed on thiouracil drugs first, provided that they receive concomitant β-blocker therapy and good counseling, added Dr. Vijayakumar of the nuclear medicine section at the University of Texas Medical Branch, Galveston.

In a retrospective study, Dr. Vijayakumar and her colleagues identified 122 patients who were treated for severe thyrotoxicosis between August 2003 and December 2004. Patients were judged to have severe hyperthyroidism when there were marked signs and symptoms of thyrotoxicosis, suppressed levels of TSH, and markedly elevated levels of free T4 or free T3.

The diagnosis of severe thyrotoxicosis also required radioactive iodine (I-131) uptake exceeding 30% at 4 or 24 hours after administration of I-131. Of the 122 patients identified with severe thyrotoxicosis, the diagnosis of Graves' disease predominated. For the group overall, TSH levels were between 0.01 and 0.06 mIU/L.

Most of the patients were females between ages 15 and 64 years, and the range of radioactive iodine uptake was between 31% and 92%. All patients were treated with 10-20 mCi of I-131 and were evaluated for any evidence of thyroid storm.

"Ninety-two patients had one radioactive iodine treatment, 21 patients had two radioactive treatments, and only a few had three treatments," Dr. Vijayakumar reported. Eight patients received no radioactive iodine treatment at all. Four patients were thyrotoxic and were placed on propylthiouracil (PTU); three patients were already on PTU and did not receive I-131.

Most patients were placed on β-blocker drugs at the time of initial I-131 therapy, and those drugs were continued for at least 2 months. Patients were educated about the signs and symptoms of thyroid storm before receiving I-131 treatment, Dr. Vijayakumar said.

At first follow-up 2 months later, "none of these patients had any symptoms of thyroid storm," Dr. Vijayakumar said. In a subset of 39 high-risk patients—defined as having I-131 uptakes in excess of 70%, marked signs and symptoms of hyperthyroidism, and markedly elevated free T4 or free T3 levels—I-131 treatment was well tolerated, and led to "marked clinical improvement." Again, none of these high-risk patients had any sign of thyroid storm.

"Thyroid storm after radioactive iodine is extremely rare," Dr. Vijayakumar concluded. "Hence, it is safe to treat these hyperthyroid patients in thyrotoxicosis with radioactive iodine, [although] simultaneous β-blockers are necessary, and patient education is also important. With all these measures in place, 4-6 weeks of prior medical treatment [with PTU] may not be necessary."

Thyroid storm, an acute, life-threatening thyroid hormone–induced hypermetabolic state that can occur in patients with thyrotoxicosis, is usually precipitated by stress such as surgery or infection.

Although thyroid storm is rare—occurring in 1%-2% of hyperthyroid patients—mortality approaches 20% if the condition goes unrecognized and untreated. Features of thyroid storm include a high fever, flushing, sweating, tachycardia, agitation, and delirium. The diagnosis of thyroid storm is largely clinical as thyroid function tests cannot differentiate between thyroid storm and thyrotoxicosis. ■

Hypothyroidism Linked to Lower Risk of Breast Cancer

BY CHRISTINE KILGORE
Contributing Writer

Women treated for hypothyroidism were less likely to develop primary breast carcinoma—and more likely to have more indolent disease when they did develop cancer—than women with normal thyroid function in a retrospective, case-control study.

The findings "strengthen the possibility of a significant role of thyroid hormones on breast cancer biology" and may indicate areas of intervention "for targeted preventive and therapeutic purposes," said Massimo Cristofanilli, M.D., and his associates at the University of Texas M.D. Anderson Cancer Center, Houston.

The investigators compared the medical records from 1,136 women with primary breast carcinoma with those of 1,088 healthy women who visited their breast cancer–screening clinic.

Approximately 240 women reported having symptomatic primary hypothyroidism and thyroid supplementation before they were diagnosed with breast cancer or before their screening visit.

The prevalence of reported hypothyroidism was significantly greater in the control group, compared with the breast cancer group (15% vs. 7%).

Women with primary hypothyroidism had a 61% lower risk of developing invasive breast cancer, and women with breast cancer were 57% less likely to have hypothyroidism, compared with healthy women, the investigators reported (Cancer 2005;103:1122-8).

After adjustment for confounders of breast cancer risk such as family history of breast carcinoma and history of pregnancy, the association between breast cancer and hypothyroidism "essentially was unchanged and [treated hypothyroidism] remained a strong protective factor against a diagnosis of invasive breast carcinoma," they said. The association was similar in all ethnic groups.

Among women with invasive breast cancer, patients with hypothyroidism were older at the time of diagnosis (59 vs. 51 years) and were more likely to be postmenopausal (82% vs. 64%) than patients with normal thyroid function.

The prevalence of reported hypothyroidism was significantly greater in the control group, compared with the breast cancer group (15% vs. 7%).

Among white women specifically, those with invasive cancer who had been treated for hypothyroidism were more likely to be diagnosed with early-stage disease (95% vs. 86%) and disease without pathologic lymph node involvement (64% vs. 56%).

They also had smaller pathologic tumor size than women with invasive cancer but normal thyroid function.

The investigators restricted part of their analysis to white women to have a more homogenous population and to eliminate the influence of ethnicity.

A possible association between thyroid disease and breast carcinoma has been debated for decades and remains controversial, the investigators say. Epidemiologic studies have had conflicting results, and large prospective studies have failed to clearly demonstrate a correlation. ■

Evidence Supports Aggressive Papillary Thyroid Ca Treatment

BY CHRISTINE KILGORE
Contributing Writer

Multifocal tumors in papillary thyroid cancer appear to often arise as independent tumors—a finding that supports the use of bilateral thyroidectomy and radioablation of remaining tissue, according to Trisha M. Shattuck of the University of Connecticut, Farmington, and her associates.

Papillary thyroid carcinoma is the most common cancer of the thyroid gland, and it is often multifocal—typically with a "primary" tumor greater than 1 cm in diameter and additional, much smaller "microcarcinomas."

Multifocal carcinomas have been associated with increased risks of lymph-node and distant metastases, persistent local disease after initial treatments, and regional recurrence—features that have suggested that patients be treated aggressively.

It has been unclear, however, whether multiple intrathyroid tumors are metastases of a primary tumor or whether they arise independently as individual carcinomas, the investigators said (N. Engl. J. Med. 2005;352:2406-12).

They examined tumor samples from 17 women with multifocal papillary thyroid carcinoma who underwent thyroidectomy. Using a polymerase chain reaction (PCR) assay involving the human androgen receptor gene, they analyzed tumor DNA for patterns of X-chromosome inactivation (inactivation of either the maternal or paternal X-chromosome).

Such patterns can be used to determine whether a tumor arose from one or multiple progenitor cells because the inactivated chromosome is stably transmitted from parent cell to progeny cell, the investigators explained.

Multiple tumor foci from 10 of the 17 patients were suitable for analysis; they yielded DNA of adequate quality and quantity and were heterozygous for the human androgen receptor gene polymorphism. A single X chromosome was inactivated in each focus, the investigators reported.

Tumors from 5 of the 10 patients showed discordant patterns of X-chromosome inactivation that indicated the tumors arose separately from different progenitor cells. Tumors in the other five patients showed patterns that could be interpreted as indicating either a shared or independent origin.

The findings "favor the independent clonal origins of the distinct foci in some [and possibly most] of these cases," according to the investigators.

The findings also "imply that any thyroid tissue remaining after surgery to treat papillary thyroid cancer in patients with multifocal disease may contain—or be likely to develop—additional foci of cancer that could become recurrences."

In an editorial, Robert D. Utiger, M.D., wrote that the evidence "supports the clinical finding that patients with papillary carcinoma who undergo thyroid lobectomy are more likely than those who undergo near total thyroidectomy to have recurrent carcinoma in the remaining lobe as well as elsewhere."

Annual estimates of thyroid cancer diagnoses have been growing faster than the population for several decades, and the proportion of these cancers that are papillary carcinomas is growing as well, said Dr. Utiger of Harvard Medical School, Boston (N. Engl. J. Med. 2005;352:2376-8). ■