Case Report

Recombinant TSH-Stimulated, Radioguided Differentiated Thyroid Carcinoma Surgery

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ABSTRACT

A novel approach to locating and surgically resecting occult metastatic foci in a 25-year-old female with a history of total thyroidectomy for differentiated thyroid carcinoma was attempted. Two iodine-131 (^{131}I) body scans were performed: one after the patient underwent a 2-3 week thyroxine withdrawal, and another the following week utilizing recombinant TSH-stimulation. Then the patient was treated with 151 mCi of ^{131}I , and 2 weeks later, without further hormonal manipulation, she had radioguided surgery. The two diagnostic ^{131}I body scans were negative, but the post-therapy scan was positive. Two weeks later after pre-operative skin marking, radioguided surgery localized metastatic foci in the central compartment neck just dorsal to the suprasternal notch. No other foci were identified with the probe at surgery. At pathology, 2 of the 12 nodes were positive, as well as a 1 mm metastatic focus in the fat. Provocative imaging protocols, aggressive radioiodine therapy, and the novel use of radioguided surgery to attempt a cure in an ^{131}I image-negative metastatic thyroid carcinoma patient was performed. No other cases using these combined diagnostic and therapeutic efforts have been reported in the literature.

INTRODUCTION

Iodine-131 (^{131}I) negative body scans in the follow-up of thyroid cancer patients are reported in about 25% of patients with suspected metastases. These patients have no physical examination or imaging evidence of disease, but have an elevated thyroglobulin (Tg) on laboratory testing. There is debate as to whether these patients should even be worked up any further if their Tg suppresses.¹⁻⁸ Multiple imaging modalities have been used both successfully and unsuccessfully in the search for their disease.^{1,9} Anatomic imaging such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound are usually negative within the neck. Sometimes CT will find nodular disease in the chest. Nuclear imaging with thallium-201 (Bristol-Myers Squibb Medical Imaging Co, Billerica, NJ), technetium-99m ($^{99\text{m}}\text{Tc}$) sestamibi (Cardiolite®, Bristol-Myers Squibb Medical Imaging Co) or tetrofosmin (Myoview™, Amersham, UK), and positron emission tomography (PET) imaging with ^{18}F fluorodeoxyglucose (FDG) have all had varying degrees of success.¹⁰⁻²⁹ Even if diagnostic imaging can localize the metastatic foci, there is no guarantee that additional surgery or radioiodine therapy will cure the patient.³⁰

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Presented is a case of diagnostically imaging a negative patient who reverted to positive post-therapy. This is not rare, but she further underwent post-therapy radioguided surgery to successfully localize the metastatic foci. Analysis of probe response using ^{131}I for various isotopic window settings demonstrates the device's varying response and indicates that the optimal setting for ^{131}I is not the setting provided by the manufacturer.

CASE REPORT

In Texas in 1999, a 25-year-old white female had a 2.5 cm thyroid nodule in the right thyroid lobe that proved to be papillary thyroid carcinoma by fine needle aspiration (FNA). After a total thyroidectomy, she received a large radioiodine dose in the hospital. She moved to Wisconsin and was seen at our facility. The follow-up physical examination revealed a well-healed scar, but no nodes or masses. She had a contrast neck CT in September 2000 that demonstrated the patient was status-post thyroidectomy and no residual thyroid tissue was seen (figure 1).

In January 2001, she underwent a routine thyroxin withdrawal ^{131}I body scan after having been on suppression, her thyroid-stimulating hormone (TSH) of 1.6 (normal 0.5-5 IU/mg) 4 weeks prior (negative scan is not shown). She was restarted on thyroxin and remained asymptomatic.

Approximately 1 year later, in January 2002, she had another routine thyroxin withdrawal negative ^{131}I body scan (not shown). Prior to the scanning her suppressed TSH was 1.6. However, this time she had additional Tg testing that revealed a rising level to 6.6 (normal <3.0 ng/ml in athyroid patients). This prompted an additional scan prior to replacing her on thyroxin suppression. She had one intramuscular injection of Thyrogen® (thyrotropin alpha, Genzyme Corporation, Cambridge, MA) on both Monday and Tuesday, a 4 mCi oral dose of ^{131}I on Wednesday, and body imaging on Friday. The scan was again negative (scan not shown), but we had an elevated and rising Tg level as laboratory evidence of metastatic disease.

^{131}I therapy was scheduled the following week. She received 151 mCi of ^{131}I without further recombinant TSH stimulation and one week later she had a positive post-therapy scan because of evidence of metastatic disease (figure 2). It is not routine to perform post-therapy scans in all patients, only those with occult disease. Her health status was discussed at length with the hope that ^{131}I dose that had localized her disease would also eradicate the disease. Otherwise, this process would have to be repeated.

Another option was discussed with the patient. Our oncology surgeon has vast experience in radioguided surgeries. However, prior to this case, the navigator probe gamma guidance system (United States Surgical Corporation, Watertown, MA) had only been used for lymphoscintigraphy in breast

and melanoma surgery and in parathyroid adenoma localization. Individuals had used ^{131}I compounds for medullary thyroid carcinoma, but not papillary or follicular thyroid carcinoma.^{1,31-37} Tumor localization with the probe in position during surgery has not been previously described in the literature for differentiated thyroid carcinoma. However, the concept and surgery are similar to other radioguided procedures. The patient agreed to attempt this procedure.

Figure 1. Negative CT scan of the neck in September 2000.

Figure 2. Post-therapy positive ^{131}I scan in February 2002.

Another option, sodium ¹²⁵I could be an intraoperative probe option assuming you knew preoperatively where to look. ¹²⁵I has such a low energy that it is not used clinically for imaging. The low energy photons may not have penetrated the sternum or clavicles that may have been helpful in this case.

The oncology surgeon was interested in operating to have a higher chance of cure. Without further stimulation or ¹³¹I dosing, we performed post-therapy imaging. There was only background activity in the thyroid bed. However, near the sternal notch was a single focus of abnormal activity. We marked the skin over the suspected lesion (scan not shown). At surgery, two foci of activity were identified that read 8-12 counts per second on the ¹³¹I setting just deep to the suprasternal notch. Anatomically the counts were coming from the central compartment that had not been resected during the multiple initial surgeries. The presence of the central compartment came as a surprise since this area is usually resected in thyroid cancer patients, and this is where the skin probe activity was detected. A probe check of the neck after central compartment node removal revealed only background activity. Surgical pathology found 2 out of 12 lymph nodes positive for papillary thyroid carcinoma. In addition, a 1 mm foci of metastatic thyroid carcinoma was found invading fat.

The post-surgical pre-thyroxin suppression Tg level had decreased from 6.6 to 1. She was placed back on thyroxin suppression and we continue to follow her. Several weeks after the surgery our radiation safety officer (JG) ran a series of tests on the probe (table 1). He found that the probe was most sensitive for detecting ¹³¹I with the threshold setting off instead of the on position as recommended. Unexpectedly, to completely remove any ¹³¹I background detection, the most sensitive isotopic window setting for this device was indium-111 (¹¹¹In).

DISCUSSION

Not everyone agrees that every differentiated thyroid cancer patient should receive radioiodine.¹⁻⁸ ¹³¹I body scan negative differentiated thyroid carcinoma presents a difficult dilemma for both the clinician and the patient. Two possible options were presented to the patient. The first is recombinant TSH stimulated ¹³¹I body scans. There is support for performing the scan while the patient is still on thyroxin.³⁸ Nuclear medi-

cine physicians would treat these patients with ¹³¹I at least once and follow with the Tg. In addition, nuclear medicine physicians who use recombinant TSH, use it under selected conditions such as Tg-positive, ¹³¹I negative body scan patients only.³⁹

The second option is post-therapy radioguided surgery. There is a precedent for using it under multiple neoplasms and multiple radiopharmaceuticals.³² There is one article in the literature of sentinel node lymphadenectomies in thyroid malignancies found in a similar clinical setting.⁴⁰ No literature for the indication presented by our patient was located, but the procedure worked well in this particular instance. The low background and tumor counts presented a unique situation for an experienced surgeon who was used to far greater count rates. In this instance an experienced user was able to successfully locate and remove the two nodes, though it is not certain whether or not the 1 mm fat invasion could be detected separately from the nodes because of proximity.

In conclusion, there may now be more options available for ¹³¹I scan negative thyroid cancer patients. More experience is needed to see if this exciting possibility works for many other patients.

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Table 1. Probe readings taken on March 22, 2002 7.5 h after administration of 25.3 µCi of ¹³¹I.

Energy Setting Window	Reading (10 sec count)	Background (10 sec count)
99mTc	2,878	0
111In	7,355	0
131I	3,374	0
125I	3,485	0
None	26,636	6

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