CLINICAL VIGNETTE

Thyroid Nodules and Goiters: To Suppress or not suppress

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Introduction

Thyroid suppressive therapy in euthyroid patients with solitary benign nodules or sporadic nontoxic multinodular goiters is controversial. This topic should not be confused with the work up and assessment of a thyroid nodule that could be malignant.

Case Report

A 28-year-old female was noted on physical exam to have left thyroid fullness. Ultrasound of her neck revealed an isolated left thyroid nodule. Fine needle aspiration revealed a cellular follicular lesion and she was advised to undergo a partial thyroidectomy as the lesion was greater than 4cm. Family history was remarkable for thyroid cancer in her maternal grandmother. There was no history of radiation exposure to the head and neck. Otherwise she has no significant past medical history and is on no medication.

She does not smoke, but drinks occasionally. Physical exam was remarkable only for the thyroid nodule. Laboratory evaluation reveals she is euthyroid.

Although surgery was recommended, the patient declined and asked if there were non-surgical options.

Thyroid suppressive therapy has been favored on and off in the last century. The role of thyroid hormone therapy for benign nodules has been studied extensively[1,2]. Suppressive therapy is based on the observed atrophy of the thyroid in patients receiving thyroid hormone. The normal endocrine feedback mechanism presumes that if enough thyroid hormone is present, then the thyroid gland no longer needs to function, consequently the thyroid will shrink, thus any thyroid nodule might also shrink in size as part of the total thyroid gland. At the very least it is thought a nodule would not enlarge further on suppression. It is also thought that administration of levothyroxine with TSH suppression may prevent the appearance of new nodules.

In this patient, her solitary nodule was truly an isolated nodule. Many presumed "single" nodules based on clinical exam could be the dominant nodule in a multinodular goiter. Treatment to shrink goiters has been advocated to decrease the physical sequelae of an enlarging neck mass. Diffuse goiters have been more responsive to suppressive therapy than nodular goiters. The patient's evaluation followed the recommended algorithm for a potential malignant nodule and she thus had the nodule biopsied. This showed the cellular follicular pathology. A second biopsy was performed in case the diagnosis was missed and this confirmed the results of the first biopsy.

As the biopsy results remained negative or equivocal the patient was advised to undergo partial thyroidectomy because of the chance that an underlying cancer could still be present, however, she declined and requested a non-surgical approach.

The rationale for suppressive therapy for solitary nodules was explained to the patient. Randomized controlled trials showed no decrease in the size of the nodules, while other trials have shown a 40-50% reduction in size. The trials that did not show benefit were criticized for being too small and with inadequate length of follow-up. The study that showed the significant reduction was a one-year randomized

controlled trial that showed the patients whose nodules decreased on suppression noted increase in nodule size when therapy was discontinued.

Nodules as part of a multinodular goiter responded better than solitary nodules. Additionally nodules that are higher in colloid content, and smaller, tend to respond better. While the response in various studies shows minimal decreases, it has been noted that the development of new nodules occurred much less frequently in those patients that are suppressed.

Results from multiple randomized control trials and three meta-analyses suggest that thyroid hormone in doses that suppress the serum TSH to subnormal levels may result in a decrease in nodule size and may prevent the appearance of new nodules in regions of the world with borderline low iodine intake. Results from the study done in iodine-sufficient populations are less convincing[3-5]. The large studies indicate that only about 17-25% of thyroid nodules shrink more than 50% with levothyroxine suppression of serum TSH[3-5].

Long term suppressive therapy with levothyroxine is associated with potential adverse effects on the cardiovascular and skeletal systems. Prolonged subclinical hyperthyroidism is associated with a significant decrease in bone density in postmenopausal women[6-8]. A three-fold increase in atrial fibrillation with increased morbidity and mortality from cardiovascular disease is seen in patients with subclinical hyperthyroidism[9-11].

The American Thyroid Association Guideline Taskforce on Thyroid Nodules strongly recommend against routine suppression therapy of benign thyroid nodules in iodine sufficient populations[12].

At best, the patient could be informed that a trial of suppressive therapy could be instituted, however it is unlikely that she would have a significant reduction in her thyroid nodule. If she had had a multinodular goiter the chances of suppression of further enlargement or new nodules was much better and would be recommended. A trial of T4 therapy was instituted at her request, but after several months the patient decided that she would prefer the certainty of a partial thyroid resection to the uncertainty of nodular transformation especially in light of the size of her nodule (4cm). Any increase in size of the nodule on close follow-up would mandate another biopsy. Rather than subject herself to repeated biopsies she underwent an uncomplicated partial thyroidectomy and is doing well. Had the nodule been under 2cm some clinicians would still prescribe a trial of T4 and many would just monitor the nodule closely as they have been shown to occasionally spontaneously regress.

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