

# Incidentally Found Thyroid Nodules Oft Malignant

BY NANCY WALSH  
New York Bureau

CHICAGO — A high rate of malignancy was found in a retrospective review of incidentally discovered thyroid nodules among patients with a history of other cancers, Dr. Scott M. Wilhelm reported at the annual meeting of the Central Surgical Association.

Traditionally discovered palpable nodules reportedly have a 5% malignancy rate, but some studies have suggested that nonpalpable nodules found during other radiographic procedures carry malignancy rates ranging from 8% to 29%.

Office-based ultrasound confirmed the presence of a nodule 1 cm or more in diameter in 35 of 41 patients who were referred for evaluation after CT scans identified thyroid nodules, said Dr. Wilhelm, assistant professor, Case Western Reserve University, Cleveland.

Most (78%) of the patients were female. The primary site in 23 of the patients was gastrointestinal, including colon, pancreas, and small bowel, whereas the primary site was breast in 11 patients and prostate in 4. Three patients had lymphoma, and nine had various other tumors.

In some patients, there was more than one primary tumor, Dr. Wilhelm said.

The remaining six patients had nodules that were smaller than 1 cm or had no nodules, and were considered to represent false-positive CT scans.

Biopsy results were benign in 15 (42.8%) of the 35 patients, malignant in 2 (5.7%), indeterminate in 16 (45.7%), and nondiagnostic in 2 (5.7%). The malignancies were papillary thyroid cancers, whereas the indeterminate biopsies were classified as follicular neoplasms or suspicious, but not definitive, for papillary thyroid cancer.

A total of 20 patients had diagnoses that warranted surgical resection. One additional patient whose biopsy was benign was subsequently picked up on an OctoScan study.

“At the time there was very little in the literature on this, so we offered her resection as well,” said Dr. Wilhelm.

Seventeen of the 21 patients underwent resection, with results including four papillary thyroid carcinomas, four micropapillary cancers ranging in size from 4 mm to 8 mm, and seven benign lesions.

Two thyroid metastases also were found, one from renal cell carcinoma and one from melanoma.

Three patients had a history of radiation exposure to the head and neck. In two of the three patients, the exposure had occurred

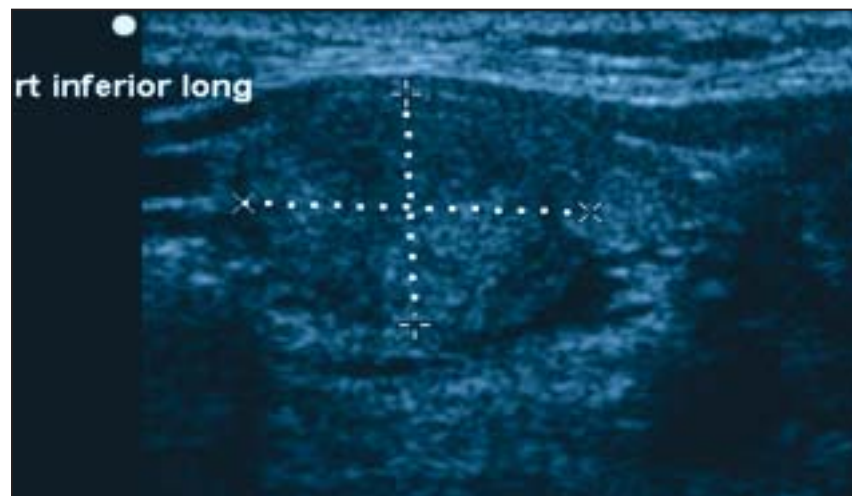
40 years earlier, during treatment for infantile thymus in one and for eczema in the other. Both patients had atypical biopsies and underwent surgery, but the pathologies were benign.

The third patient had been treated 10 years earlier for breast cancer, undergoing radiation therapy for a supraclavicular lymph node, and was found to have micropapillary thyroid cancer.

“The rate of malignancy in our incidental thyroid nodules was 24%, but we felt it appropriate to exclude the micropapillary cancers, so that left us with 15%, which is three times the rate of malignancy seen in traditionally discovered palpable nodules,” Dr. Wilhelm said at the meeting.

These microscopic foci are very common but pose little risk to patients. In autopsy studies that include these, up to 30% of the population will be found to have nodules, which is why they were excluded in this study, he said.

Some earlier studies did not specify whether micropapillary cancers were included, which may account



An ultrasound shows a heterogenous thyroid nodule with very irregular borders. It turned out to be a papillary thyroid carcinoma on pathology.

COURTESY DR. SCOTT M. WILHELM

for rates that were even higher than in this investigation.

The overall increase in thyroid cancer in recent years may be contributing to the high rates of malignancy: American Cancer Society data from 2002 show an actual number of 22,700 new cases and an estimated number of 33,550 for 2007.

“In this study, we also may have selected out patients with unusual genetics,” Dr. Wilhelm said. “We had nine patients who had two primaries and one who had three primaries. Two of the thyroid cancers were in these patients, so one patient wound up with four tumors and one with three. Clearly, there is something different about them.”

The study findings also show that ultrasound was superior to CT in identifying nodules.

The correlation of thyroid nodule size that was seen on ultrasound with that found on pathology was excellent, and thyroid ultrasound should be considered essential if size is to be used as the criterion for determining which lesions to biopsy, Dr. Wilhelm emphasized. ■

## Vitamin D Deficiency Occurs Even When Marker Is ‘Normal’

BY BARBARA RUTLEDGE  
Contributing Writer

TAMPA — Vitamin D deficiency is highly prevalent, even in patients whose 25-hydroxyvitamin D levels are within the “normal” range, Dr. Robert P. Heaney said at the annual meeting of the International Society for Clinical Densitometry.

That’s because the reference range for serum 25-hydroxyvitamin D (25[OH]D) levels is too low, said Dr. Heaney of Creighton University, Omaha, Neb. “Within the reference range, there is malabsorption of calcium and preventable fractures. These are as much expressions of nutritional deficiency as are the bleeding gums of scurvy.”

The Institute of Medicine reevaluated the nutrient intake recommendations for bone-related nutrients, including vitamin D, in the mid-1990s. The role of vitamin D intake in preventing rickets had long been recognized, and it was known that vitamin D was necessary for calcium absorption. Ten years ago, the unknowns were the vitamin D intake for optimal calcium absorption, possible links between vitamin D and other diseases, and how to determine whether a patient’s intake was sufficient.

“We’ve learned a lot since then,” said Dr. Heaney. “We know that 25(OH)D is the

functional status indicator, and we know that at levels below 20 nmol/L or 8 ng/mL, we get rickets and osteomalacia.”

The controversy lies in deciding where the normal range of serum 25(OH)D should be for optimal bone health. Although the low end of the reference range may vary from 38 to 50 nmol/L, an individual is at risk for osteoporosis at serum 25(OH)D levels below 80 nmol/L, according to Dr. Heaney, who argues that normal levels of serum 25(OH)D begin at 80 nmol/L. At levels between 20 and 80 nmol/L, increased bone remodeling, reduced calcium absorption, increased risk of falls, and increased risk of fractures occur.

Individuals might have inadequate vitamin D status even when serum 25(OH)D levels are well within the reference range. A study Dr. Heaney and colleagues conducted assessed serum 25(OH)D levels and calcium absorption in 34 healthy, postmenopausal women. The study showed that women whose serum 25(OH)D levels were at the lower end of the reference range had lower calcium absorption than women with higher levels. The study was conducted over 2 consecutive years in Omaha, in early spring, when serum vitamin D levels would be at their lowest levels.

Participants were given oral 500-mg cal-

cium supplements, and calcium absorption and serum 25(OH)D levels were measured. One year, the participants were pre-dosed with vitamin D supplementation, and the other year, they were not (Am. Coll. Nutr. 2003;22:142-6).

Vitamin D supplementation resulted in an increase in serum 25(OH)D from 50 to 83 nmol/L. Both of those values are considered to be within the reference range, but the two levels had different effects on calcium absorption efficiency.

At the lower serum 25(OH)D level of 50 nmol/L, calcium absorption efficiency was 22%, compared with 37% at the higher serum 25(OH)D level. Higher serum 25(OH)D levels were also associated with higher serum calcium concentrations and decreased serum parathyroid hormone levels.

Other studies have shown higher bone mineral density levels, decreased risk of fractures, or decreased risk of falling with levels of serum 25(OH)D above 80 nmol/L.

“Within the range of 25(OH)D levels commonly encountered, calcium absorption rises as 25(OH)D rises,” said Dr. Heaney. “Raising serum 25(OH)D levels from 50 to [about] 80 nmol/L improves calcium absorption, raises [bone mineral density], and reduces both fall and fracture risk.”

Sources of vitamin D are not equivalent. The high-dose (50,000 IU) vitamin D supplement that is available by prescription is ergocalciferol, or D<sub>2</sub>, which is less potent than cholecalciferol, or D<sub>3</sub>. Over-the-counter preparations of vitamin D in the form of cholecalciferol are available at lower doses.

A typical over-the-counter vitamin D supplement might contain 400 IU, but supplementation to increase serum 25(OH)D levels within an effective range usually requires much higher doses. Intake of 1,000 IU of vitamin D raises serum 25(OH)D by approximately 15-25 nmol/L.

In studies conducted by Dr. Heaney, dosages of 5,000-10,000 IU/day for a 4- to 5-month period in healthy adults have not caused elevated calcium levels in serum or urine. Vitamin D dosages in that range produce serum 25(OH)D levels comparable to those seen in outdoor workers at summer’s end.

Vitamin D intoxication should not be an issue unless the individual has regular dosages in excess of 10,000 IU per day.

“Our conclusion is that the safe upper limit level ought to be 10,000 IU per day,” said Dr. Heaney. “I don’t think many people would ever need that much, but it is nice to know that there is a therapeutic margin of safety.” ■