jnm / CASE REPORT

# DISAPPEARANCE OF AUTONOMOUS THYROID NODULE UNDER TSH STIMULATION

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***This report describes a case of an autonomous thyroid nodule that showed greatly decreased uptake of radioactivity following exogenous thyroid-stimulating hormone (TSH) administration whereas the previously suppressed thyroid parenchyma was clearly visualized. The cause of this phenomenon is not entirely clear.***

The autonomous thyroid nodule (ATN) actively traps circulating iodine, often at an accelerated rate, and is at least partially independent from the influence of endogenous thyroid-stimulating hormone (TSH) (*1*). In general, the laboratory findings include: (A) appearance of a "hot" area on the thyroid scintiscan with partial or complete suppression of the rest of gland, (B) nonsuppressibility of radioiodine uptake within the nodule by exogenous thyroid hormone, and (C) appearance of radioiodine uptake in other areas of the thyroid after exogenous TSH administration (*2*). We recently studied a patient with a functionally atypical nodule that had lost the ability to accumulate $^{131}I$ or $^{99m}Tc$-pertechnetate under exogenous TSH stimulation whereas the extranodular thyroid, previously suppressed, avidly concentrated both radionuclides.

## CASE HISTORY

A 30-year-old Latin American woman was referred to the nuclear medicine clinic for evaluation of a palpable thyroid nodule, which she first noted about 3 years ago. Recent tenderness caused her to seek medical evaluation. She had no family history of thyroid disease. On physical examination, a 3 × 2-cm firm, nontender nodule was palpated at the lower pole of the right thyroid lobe. The nodule moved freely with swallowing and no other abnormalities were noted within the remaining thyroid. Serum $T_3$ resin uptake was normal at 30% (range 25–35%) as was the serum $T_4$ value of 7.6 μg% (range 5.5–14.5 μg%). Radioiodine thyroid uptakes at 4 hr (6.2%) and at 24 hr (12.3%) were also considered to be within normal limits in our laboratory. (Normal RAI uptake at 4 hr 3–13%, 24 hr 7–32%.)

A thyroid scan was obtained utilizing a rectilinear scanner (Picker) equipped with 3-in. fine-hole collimator 20 min following the intravenous administration of 2 mCi of $^{99m}Tc$-pertechnetate. It revealed an area of radionuclide uptake limited to the palpable nodule (Fig. 1A). Administration of 75 μg of triiodothyronine for 5 days failed to cause a significant reduction in radioiodine uptake (24-hr uptake = 11%), confirming the suspicion of autonomous function. A thyroid-stimulation test was then performed using 10 units of TSH administered intramuscularly on three successive days. Repeat scans performed 24 hr after the last dose of TSH, using both $^{99m}Tc$-pertechnetate and $^{131}I$ indicated that the previously "hot" nodule had become "cold" relative to the extranodular thyroid (Fig. 2). Scanner was set for counting rate over the palpable nodule. In an additional $^{99m}Tc$ scan about 3 weeks later when the thyroid was no longer under the effect of the exogenous TSH, the original pattern of radioactivity accumulation within the nodule had returned (Fig. 1B).

## DISCUSSION

A study of the natural history of the ATN reveals that considerable variability may exist in the degree of autonomy from time to time. In general the ATN

Received April 17, 1974; revision accepted July 17, 1974.

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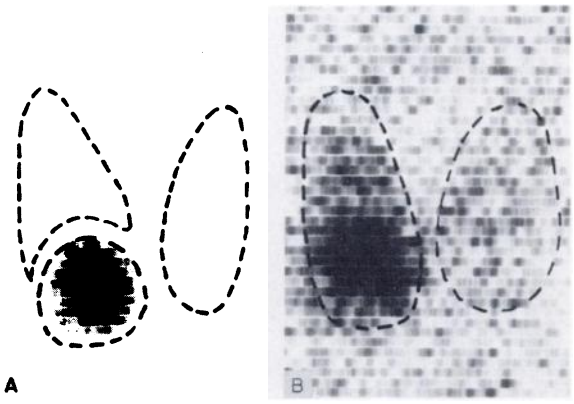


**FIG. 1.** Technetium-99m thyroid scans showing accumulation of radioactivity in region of palpable nodule with suppression of remaining thyroid parenchyma, (A) before and (B) about 3 weeks after TSH stimulation test.

maintains independence from the influence of endogenous TSH but may occasionally revert to partial TSH dependence. Thyroxine production by these nodules varies but often is sufficient to suppress the function of extranodular tissue through the normal pituitary feedback mechanism involving TSH (*2*). Progression into frank thyrotoxicosis is not typical but has been reported in 38% of the cases in one large series (*3*).

The kinetics of iodine metabolism between the ATN and extranodular thyroid parenchyma are characteristically a reduction in circulating TSH levels in response to the autonomous $T_4$ production with a resultant decrease in the rate of iodine or pertechnetate trapping by the normal extranodular thyroid tissue. The suppressed thyroid parenchyma can be stimulated by exogenous TSH administration producing the typical scan appearance of uptake in the previously "cold" areas without apparent change in the radioactivity of the "hot" nodule. Using finely focused collimation, Charkes, et al compared radioiodine uptake and clearance between ATN and adjacent thyroid parenchyma before and after TSH stimulation. The 24-hr $^{131}I$ uptake was considerably increased in the extranodular thyroid which had formerly been suppressed. None of the 17 patients in their study demonstrated a decrease in the rate of iodine concentration in the region of the functioning nodule (*4*). Other investigators have found similar results using dual labeling with iodine isotopes and autoradiography to study the functional characteristics of ATN. It has also been determined that thyroxine production is generally related to nodule size with thyrotoxicosis usually associated with nodules exceeding 3 cm in diameter (*5,6*).

The histopathology of the ATN is generally that of a nontoxic nodular goiter with follicular hyperplasia and a variable degree of colloid accumulation. Considerably more cellular hyperplasia is found in the ATN than in nonfunctioning thyroid nodules (*7*). Burke and Szabo, from a study of the in vitro behavior of excised ATN, reported that although the basal cyclic 3′5′, adenosine monophosphate (cyclic AMP) levels and 1-$^{14}$C-glucose oxidation in such nodules are not different from those in the extranodular normal thyroid tissue, TSH-induced cyclic AMP formation and glucose metabolism are several times greater than in the normal thyroid. This suggests that hyperresponsivity to TSH may play a role in the genesis of ATN (*8*).

The case described in this report presents a most unusual response to TSH stimulation. The absence of iodine or pertechnetate accumulation in the functioning nodule under TSH stimulation followed by reappearance of a hot nodule after the effects of the exogenous TSH had presumably disappeared suggests that the change was related to the TSH administration. Hazard and Vague postulate two explanations (*9,10*). First, it is possible that the ATN and the extranodular thyroid respond differently to the administration of TSH: the nodule is stimulated to discharge its iodine complement whereas the extranodular thyroid is stimulated to fix the iodine within its parenchyma. The second possibility is that under TSH stimulation the extranodular thyroid increases its trapping function far above that of the nodule resulting in a "steal" of iodine. The latter explanation seems more consistent in view of the reported observations regarding iodine kinetics in ATN but precise delineation of the mechanisms responsible for this interesting phenomenon must await further analysis.

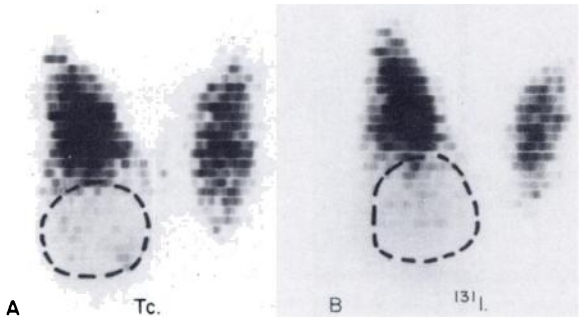


**FIG. 2.** Thyroid scans with (A) $^{99m}$Tc and (B) $^{131}$I following TSH stimulation. Thyroid parenchyma, previously suppressed, is now visualized whereas formerly hot autonomous nodule shows greatly diminished activity.

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