
Congenital Thyroid Disease Revisited: Migrational Anomalies and Dyshormonogenesis

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Nuclear medicine scintigraphy, in conjunction with other diagnostic tools, plays a vital role in assessing patients with congenital migrational anomalies. We present 5 patients, 4 of whom were hypothyroid and 1 patient who was euthyroid. Scintigraphic and ultrasonographic images were examined and correlated with laboratory results. These patients demonstrate the spectrum of migrational anomalies of the thyroid. Nuclear medicine scintigraphy was a valuable aid in establishing the location of the ectopic thyroid as well as its function.

Key Words: thyroid imaging; thyroid migrational anomalies; dyshormonogenesis

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Congenital thyroid diseases, including migrational anomalies and defects in hormone synthesis, are important causes of hypothyroidism in the neonatal period and during childhood. Disease is estimated to occur once in every 3000–5000 births (1). Congenital hypothyroidism is due to thyroid agenesis in 30% of cases, ectopic tissue in 60%, and defects in thyroid hormone synthesis in the remaining 10% (2). Evaluation of these patients includes history, physical examination, thyroid function tests and thyroid scintigraphy. Radioisotope evaluation provides important information concerning location of thyroid tissue, function of thyroid tissue present, and, together with pharmacologic intervention, can evaluate for dyshormonogenesis. We present a series of 4 patients with a spectrum of migrational anomalies and 1 case of dyshormonogenesis to illustrate the clinical utility of radioisotopic evaluation in congenital thyroid disease. Four hypothyroid patients and 1 euthyroid patient were referred for thyroid evaluation.

CASE HISTORIES

Patient 1

A 1-mo-old boy with abnormal thyroid screening studies was referred to rule out congenital hypothyroidism. Repeated labo-

ratory evaluation demonstrated a low T_4 of 3.0 $\mu\text{g/dL}$ (normal: 4.5–11.5 $\mu\text{g/dL}$) and an elevated TSH of 213 $\mu\text{U/mL}$ (normal: 0.4–6.0 $\mu\text{U/mL}$). There was no significant maternal iodine exposure. He had normal weight gain but had a history of mild neonatal jaundice. Physical examination was normal. Thyroid antibodies (antithyroglobulin and antiperoxidase) were all negative.

An ^{123}I scan was done to further evaluate ectopic thyroid tissue from a defect in thyroid hormone synthesis. This revealed an ectopic gland, at the base of the tongue, that was not apparent on physical examination. No thyroid tissue was present in the normal location. The ectopic gland was spherical in shape rather than the normal bilobate appearance (Fig. 1). The 6-hr uptake was elevated measuring 40% (normal range 5%–15%).

Patient 2

A 3-y and 8-mo-old girl was referred for short stature. Her growth rate was noted to decelerate at approximately 24 mo of age. Her birth history was unremarkable and the neonatal thyroid screen revealed an elevated T_4 of 13.0 $\mu\text{g/dL}$. Family history was negative for thyroid disease or significant birth defects. No thyroid-associated signs and symptoms were present. Physical examination was normal.

Laboratory evaluation revealed a low T_4 of 1.1 $\mu\text{g/dL}$, an elevated TSH of 236 $\mu\text{U/mL}$ with negative thyroid antibodies. The patient's bone age was delayed and was noted to be that of a 1-y-old. An ^{123}I scan demonstrated thyroid tissue in the sublingual area (Fig. 2). Iodine uptake at 6 hr was significantly low, measuring 3%, consistent with hypothyroidism.

Patient 3

A 13-y and 6-mo-old girl presented with a large asymptomatic neck mass. She was otherwise well and without signs or symptoms of hyper- or hypothyroidism. Family history was positive for hypothyroidism in a great aunt.

The physical exam was normal except for 2 soft, dense nodules in the neck. The first was a 3 × 4-cm mass in the left anterior neck. The second mass was approximately 3 × 3 cm in the midline. Careful examination revealed no clinical signs of hypothyroidism or regional adenopathy.

Thyroid function studies at that time revealed a normal T_4 of

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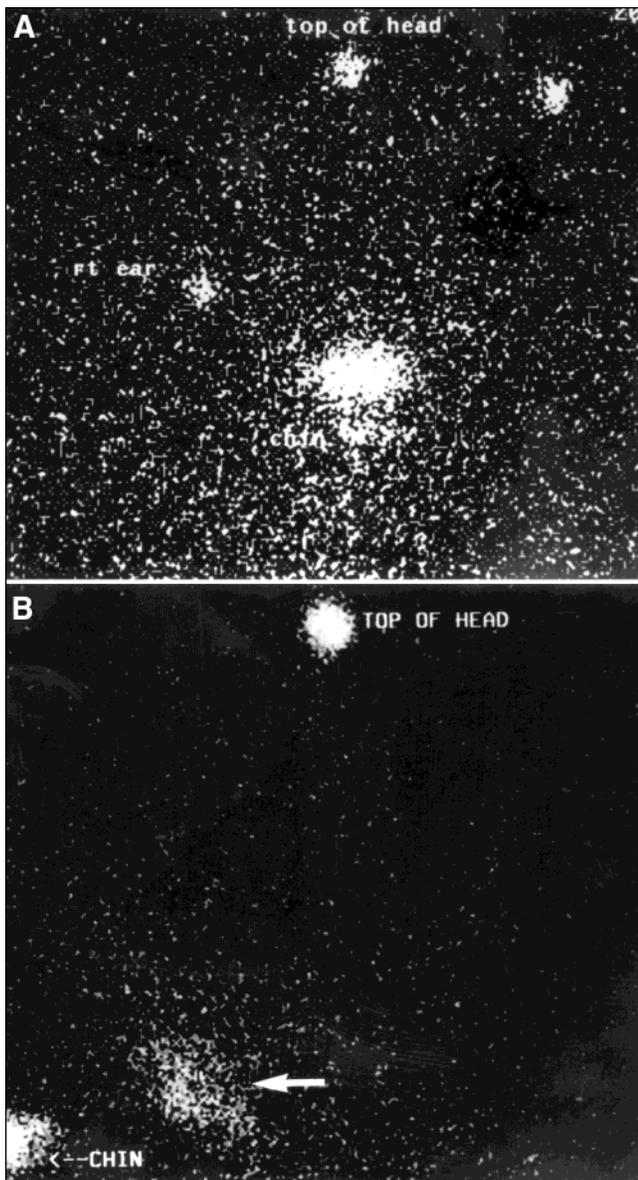


FIGURE 1. (A) Radioactive markers at top of head and sternal notch. (B) Six-hour ^{123}I scan shows an ectopic thyroid gland (arrow) at the base of the tongue. No thyroid tissue was present in the normal location.

5.3 $\mu\text{g}/\text{dL}$. The TSH was elevated at 9.2 $\mu\text{U}/\text{mL}$, and this was confirmed on repeat analysis 3 wk later. Both an ^{123}I scan and a $^{99\text{m}}\text{Tc}$ thyroid scan were performed revealing 3 masses in the neck in ectopic locations (Fig. 3) which correlated to the abnormalities on physical exam. A 6-h ^{123}I uptake was slightly elevated measuring 17.5%. The masses likely represented arrested development of the thyroid lobes and compensatory hypertrophy of other remnants of the thyroid “anlage” along the thyroglossal duct.

Patient 4

A 39-y-old woman presented with neck swelling. Thyroid function tests were normal. A $^{99\text{m}}\text{Tc}$ thyroid scan showed a multinodular goiter with persistent activity extending above the thyroid gland along the course of embryologic descent of the thyroid gland (Fig. 4).

Patient 5

A 10-y-old boy presented with a history of constipation and abdominal cramping. He also complained of cold intolerance. Family history was positive for thyroid disease. Physical examination revealed an enlarged thyroid gland with asymmetric enlargement of the right lobe.

Thyroid function tests showed a normal T_4 , T_4 uptake, free thyroxin index and an elevated TSH and T_3 RIA. An ^{123}I thyroid scan was performed and showed symmetrically increased uptake in both lobes of the thyroid gland (Fig. 5). The 6-h ^{123}I uptake was elevated measuring 18.6%. A perchlorate washout test was performed. Over a 3-h period after perchlorate there was a 30% decrease (18% uptake to 12% uptake) in the uptake consistent with a positive test. Serum antiperoxidase antibodies were demonstrated consistent with an organification defect.

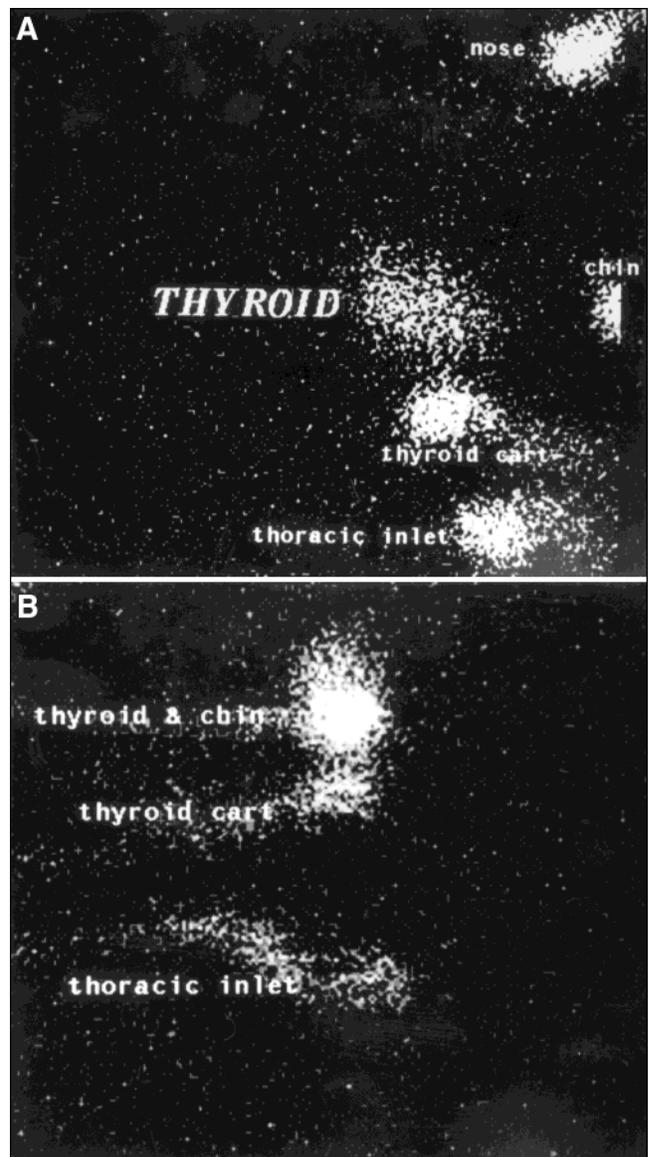


FIGURE 2. (A) Six-hour ^{123}I scan shows a small amount of thyroid tissue in the sublingual area. (B) No tracer uptake was seen in the region of the thyroid bed.

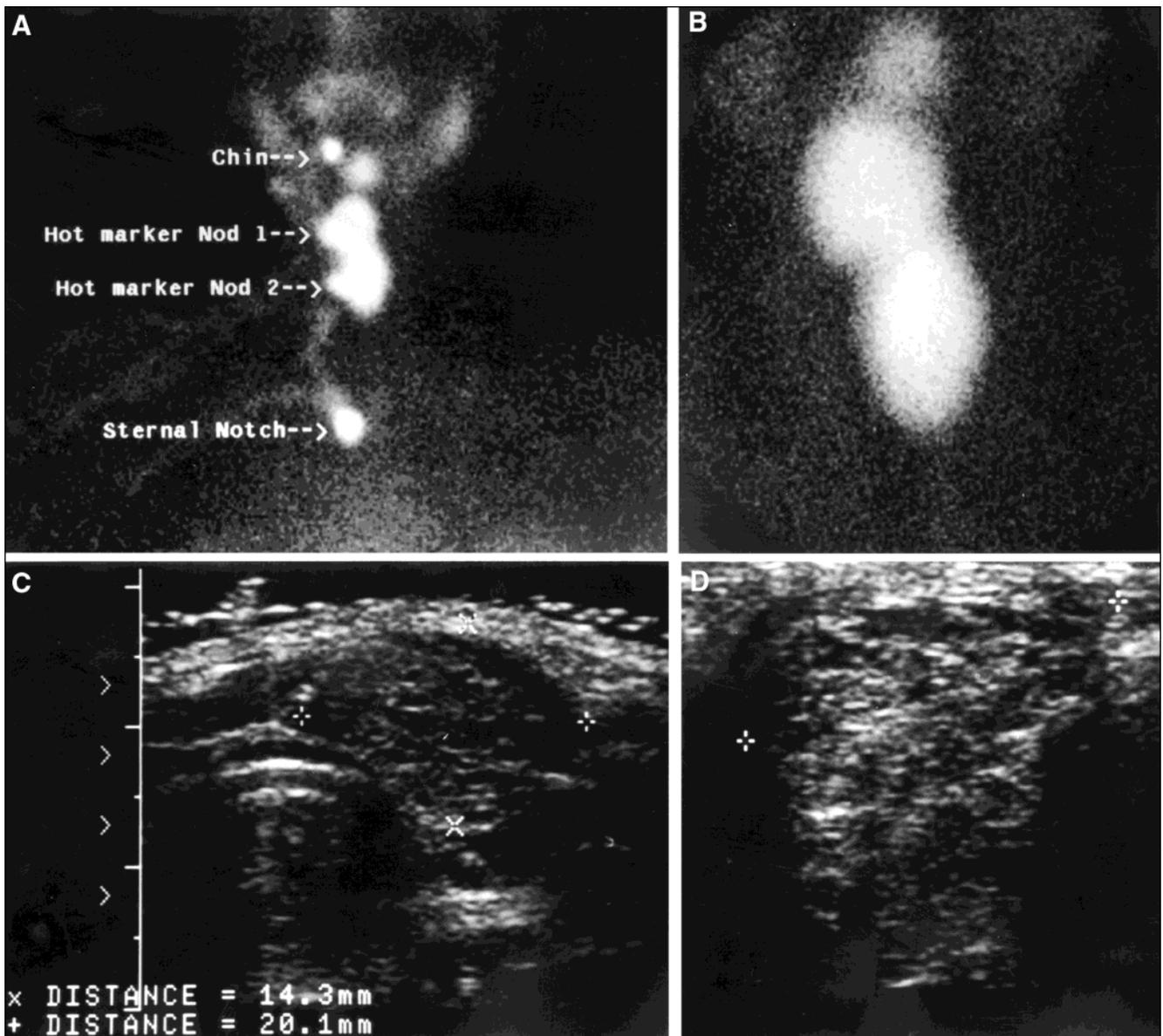


FIGURE 3. (A) Technetium-99m-sodium pertechnetate scan shows 3 areas of uptake aligned in a craniocaudal direction (arrowheads). These corresponded to the palpable masses. (B) Pinhole image of the thyroid shows nodules 1, 2 and 3. (C) High-resolution ultrasound shows 3 solid nodules corresponding to the clinically palpable nodules (crosshairs). (D) Magnified ultrasound of 1 nodule shows it to be a solid tissue.

DISCUSSION

Scintigraphic imaging of the thyroid is valuable to the clinician in both hypothyroid and hyperthyroid patients. Scintigraphy can determine the ectopic location of tissue, which is helpful if surgery is being considered since removal of this aberrant tissue may result in hypothyroidism.

The cases presented demonstrate a spectrum of thyroid migrational abnormalities. The embryology of the fetal thyroid is complex. The development of the thyroid begins as an invagination of the endoderm of the foregut at the floor of the pharynx. The pouch thus formed migrates downward toward the thyroid cartilage. By the seventh week of intrauterine life it reaches the thyroid cartilage, its definitive location. The thyroglossal duct then atrophies. The follicles begin to form and

produce thyroglobulin at about 8 wk, and at 10 wk the fetal thyroid can accumulate iodide. Pituitary thyroid stimulating hormone (TSH) production begins at approximately 12 wk gestation, but it is not until approximately 20 wk that the hypothalamic-pituitary-thyroid axis is fully functional (3,4).

An aberration in the migratory pathways of the rudimentary thyroid may lead to ectopy, which almost certainly results in inadequate blood supply to support normal thyroid function (3). This may manifest itself in 2 ways clinically. There may be an enlarged compensated gland with normal levels of T_4 and T_3 and elevated TSH, or clinical hypothyroidism with low levels of T_4 and T_3 with elevated TSH.

Thyroid evaluation generally begins with a history, physical exam and laboratory workup. If these studies reveal a euthyroid

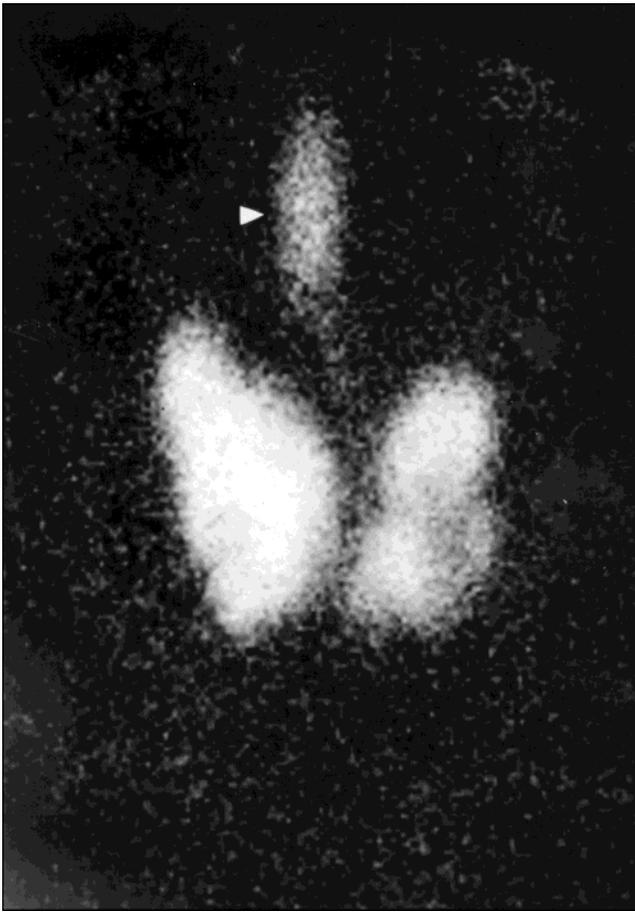


FIGURE 4. Technetium-99m thyroid scan shows a multinodular goiter and persistent activity along the course of the embryologic descent of the thyroid gland (arrowhead).

patient with an elevated TSH, thyroid dysgenesis should be considered. Most cases of euthyroidism with elevated TSH are likely to be caused by chronic lymphocytic thyroiditis (CLT), which is diagnosed by finding elevated thyroid antibodies. Occasionally, antibodies may be negative and an ^{123}I scan can be helpful in distinguishing cases of antibody negative CLT (15% of cases of CLT) from dysmorphogenesis. The pattern of ^{123}I uptake in cases of antibody negative CLT will be a rapid, early high uptake of iodine dischargeable with perchlorate, and a patchy, irregular scan of a diffusely enlarged gland (5).

Neonatal hypothyroidism usually is identified in newborn screening programs which are operational in all states in the US. Screening helps to avoid the mental deficiency caused by untreated hypothyroidism. Most cases of neonatal hypothyroidism are likely to be caused by CLT. However, when a negative thyroid antibody test is found, scintigraphy is indicated to exclude dysmorphogenesis (6).

Radioisotopes used in scanning the thyroid include ^{123}I and $^{99\text{m}}\text{Tc}$ -pertechnetate (7,8,9). These can be performed with an uptake measurement, scan or pharmacologic intervention with perchlorate. Although the uptake and organification of iodine by the thyroid gland is complex, involving multiple steps and multiple enzymes. We focus primarily on trapping and organifi-

cation since these steps are most important from the nuclear medicine perspective.

There are many studies comparing the relative merits of iodine and pertechnetate for thyroid imaging (10,11,12). In screening for thyroid disease in adults, radiolabeled $^{99\text{m}}\text{Tc}$ -pertechnetate is usually the radiopharmaceutical of choice since it can be imaged 20 min after intravenous administration. Technetium scanning demonstrates the avidity of the thyroid gland for trapping but is not representative of organification within the gland. Iodine-123 given orally demonstrates organification and trapping of iodine by the thyroid and often is preferred in children. An uptake can be performed at 4–6 h followed by imaging, making this a convenient 1-d study. The capsule form of ^{123}I is soluble in water, providing ease of administration in children.

The perchlorate discharge test is performed to detect the inability of the thyroid gland to properly organify iodine (13,14). Once the iodide is transported into the gland it is oxidized using the peroxidase enzymes and then organification occurs. When thyroid peroxidase is inhibited either by drugs (e.g., propylthiouracil), by autoimmune processes, or by inborn enzymatic defects, trapped iodide accumulates in the gland. In the standard test, the thyroid uptake of radioiodine is measured 1–2 h after dosing. Sodium perchlorate then is administered and the amount of thyroid radioiodine discharged during the ensuing 60 min is measured. In the normal gland less than 10% is discharged. Anything more than a 10% decrease indicates a block in organification, the fraction of iodine discharged being roughly proportional to the degree of block.

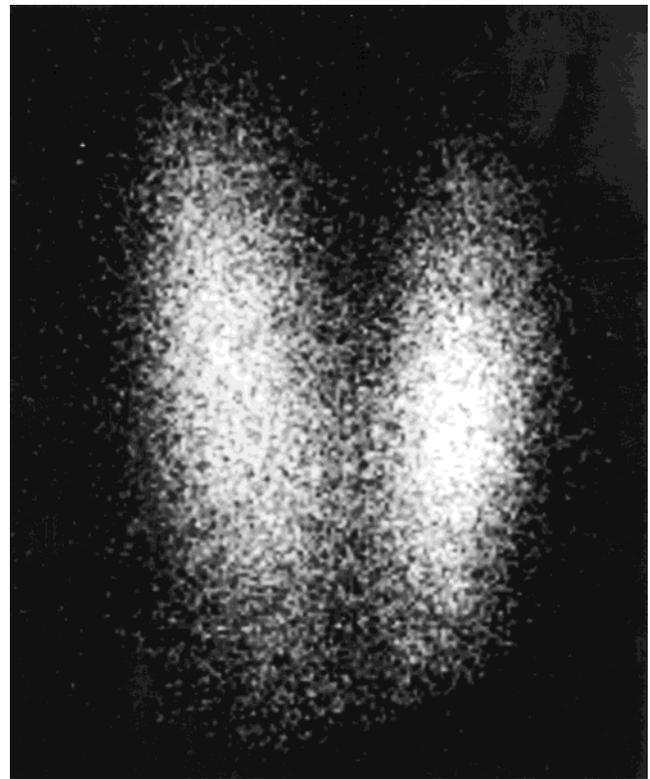


FIGURE 5. Six-hour ^{123}I scan shows symmetrically increased uptake in both lobes of the thyroid gland.

CONCLUSION

The use of nuclear medicine imaging with either ^{99m}Tc or ^{123}I is especially important as a diagnostic modality in children. The workup of children with thyroid disease using these radiotracers may avert invasive procedure, including biopsy, and provide both functional and anatomic information to the clinician.

These cases present a spectrum of thyroid dysgenesis. They show how the use of radioisotopes in scanning, uptake and pharmacologic intervention may aid in the elucidation of thyroid disease. Thyroid scintigraphy is useful in categorizing the causes of congenital hypothyroidism and is a valuable tool in the early assessment of infants indicated by thyroid screening.

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