Ultrasound for Primary Imaging of Congenital Hypothyroidism

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OBJECTIVE. The purpose of this study was to retrospectively evaluate the use of sonography as the primary imaging modality for congenital hypothyroidism (CH).

MATERIALS AND METHODS. From our regional registry, we reviewed the cases of patients for whom either sonography or 99mTc-pertechnetate scanning was performed for CH between 2003 and 2010. Ultrasound studies were reviewed for presence, size, echotexture, vascularity, and location of the thyroid gland. Technetium-99m-pertechnetate scans were evaluated for the presence and location of the thyroid gland. The ultrasound studies were compared with the 99mTc-pertechnetate scans. We assessed the use of ultrasound as the primary imaging modality for the evaluation of CH.

RESULTS. We identified the cases of 124 patients (89 girls, 35 boys). Ultrasound studies were available for 121 patients, and 99mTc-pertechnetate studies for 62 patients. Three patients were examined only by 99mTc-pertechnetate scanning. The final imaging results were normal location with normal size or diffuse enlargement of the thyroid gland (n = 47), sublingual thyroid gland (n = 49), agenesis (n = 18), hypoplasia (n = 8), and hemihypoplasia (n = 2). Compared with 99mTc-pertechnetate scanning, ultrasound had high (100%) specificity and low (44%) sensitivity for detection of sublingual thyroid gland.

CONCLUSION. We suggest using ultrasound as the primary imaging modality for guiding the treatment of children with CH, potentially decreasing radiation exposure and cost.

Keywords: 99mTc-pertechnetate, congenital hypothyroidism, organification defect, sublingual thyroid, ultrasound

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Examinations and thyroid ultrasound. Thyroid radionuclide studies with $^{99m}Tc$-pertechnetate or $^{123}I$ are considered the standard for imaging in the evaluation of thyroid dysgenesis. Although $^{99m}Tc$-pertechnetate is preferred because of lower thyroid and total body radiation dose ($\approx 0.04$ mSv compared with $0.35$ mSv) [7], both result in radiation exposure to the patient. In the case of eutopic location of the thyroid gland, an $^{123}I$ uptake followed by a $^{99m}Tc$-pertechnetate perchlorate discharge test is the definitive study for identifying an organization defect of the thyroid gland [8].

Sonography does not involve the risk of ionizing radiation and can be used to differentiate thyroid dysgenesis and other causes of CH in which the thyroid gland has normal morphologic features [9, 10]. Sonography, however, has lower sensitivity than $^{99m}Tc$-pertechnetate scintigraphy in the detection of sublingual thyroid. The use of color Doppler ultrasound (CDUS), however, has been found to increase the detection of sublingual ectopic thyroid [1, 2, 5, 11].

For several years at our facility, we have been using sonography as the primary screening imaging modality in the care of patients with CH and using $^{99m}Tc$-pertechnetate scintigraphy primarily for patients with thyroid dysgenesis. In this study, we summarize the experience with the use of ultrasound in CH that led us to recommend using an ultrasound-based imaging algorithm [12, 13].

Materials and Methods

Patients

A retrospective review was performed of the cases of all patients whose condition was diagnosed as CH at our institution between January 1, 2003, and December 31, 2010. Only patients whose thyroid ultrasound or $^{99m}Tc$-pertechnetate scans were available for review were included. Institutional review board approval was obtained with a waiver of informed consent for the study. All but three CH patients were initially imaged with thyroid ultrasound. The decision to order a $^{99m}Tc$-pertechnetate scan was then made by an endocrinologist on the basis of the ultrasound results. Typically $^{99m}Tc$-pertechnetate scanning was performed to evaluate or confirm ectopic sublingual thyroid when ultrasound showed thyroid dysgenesis.

Imaging Technique

For thyroid sonography, all patients were examined in the supine position with the neck hyperextended by placement of a folded towel beneath the scapula (Fig. 1). A 7–15 MHz linear transducer with a small footprint was used (Acuson Sequoia 512, Siemens Healthcare, or HDI 5000 IU 22, Philips Healthcare). Gray-scale transverse and longitudinal images were obtained from the base of the tongue. CDUS was performed in some patients to better depict ectopic sublingual thyroid.

For $^{99m}Tc$-pertechnetate scintigraphy, the scan was performed with 1–2 mCi of $^{99m}Tc$-pertechnetate IV (dose calculated on basis of patient’s weight). Images were obtained in the anterior and lateral views 15 minutes after administration.

Imaging Evaluation and Data Analysis

All of the imaging studies were reviewed at our standard clinical PACS workstation (Synapse, Fujiﬁlm). Both ultrasound and $^{99m}Tc$-pertechnetate scans were separately and independently reviewed by a pediatric radiologist (fellowship trained with 5 years of experience) and a nuclear medicine physician (30 years of experience).

Ultrasound studies were reviewed for the presence (eutopic, ectopic, or agenesis) of thyroid tissue, size (normal, hypoplastic, or hyperplastic) compared with the reference standard (Table 1) [14], echotexture (normal or increased echogenicity), and degree of thyroid vascularity (normal, increased, decreased). Technetium-99m-pertechnetate scans were evaluated for the presence (eutopic, ectopic or agenesis) of thyroid tissue and subjective degree (normal, increased, or decreased) of radiotracer uptake.

We used descriptive statistical analysis for each modality, divided into eutopic location, ectopic location, and agenesis of the thyroid gland. We also compared the sensitivity, specificity, and accuracy of the modalities using $^{99m}Tc$ scintigraphic results (when available) as the reference standard. On ultrasound images we evaluated the presence, location, size, echotexture, and vascularity of thyroid gland, and on the $^{99m}Tc$-pertechnetate studies—the reference standard for evaluation of sublingual thyroid—we evaluated presence, location, size, and uptake.

Results

All patients received thyroid hormone replacement before the first study. The time between date of birth and the first study (either ultrasound or scintigraphy) was 7 days–1 month. One hundred twenty-four patients (89 girls, 35 boys) were included in the study. All diagnoses were made and the patients’ cases followed by pediatric endocrinologists at our facility. One hundred twenty-one patients underwent ultrasound studies, 62 of whom also underwent $^{99m}Tc$-pertechnetate scanning. Three patients underwent only $^{99m}Tc$-pertechnetate scanning because of clinician order.

TABLE 1: Reference Standard for Thyroid Size (cm) by Age

<table>
<thead>
<tr>
<th>Plane</th>
<th>Infants and Young Children</th>
<th>Adolescents and Young Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse</td>
<td>1–1.5</td>
<td>2–4</td>
</tr>
<tr>
<td>Longitudinal</td>
<td>2–3</td>
<td>5–8</td>
</tr>
<tr>
<td>Anteroposterior</td>
<td>0.2–1.2</td>
<td>1–2.5</td>
</tr>
</tbody>
</table>

TABLE 2: Causes of Congenital Hypothyroidism in 124 Patients Between 2003 and 2010

<table>
<thead>
<tr>
<th>Cause</th>
<th>Girls</th>
<th>Boys</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysgenesis</td>
<td>62</td>
<td>15</td>
<td>77 (62)</td>
</tr>
<tr>
<td>Sublingual thyroid</td>
<td>41</td>
<td>8</td>
<td>49 (40)</td>
</tr>
<tr>
<td>Agenesis</td>
<td>16</td>
<td>2</td>
<td>18 (15)</td>
</tr>
<tr>
<td>Hypoplasia</td>
<td>4</td>
<td>4</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Hemiagenesis</td>
<td>1</td>
<td>1</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Normal location of thyroid gland</td>
<td>26</td>
<td>21</td>
<td>47 (38)</td>
</tr>
</tbody>
</table>

Note—Values in parentheses are percentages.
Seventy-seven of the 124 patients (62%) had dysgenesis of the thyroid gland. The causes of thyroid dysgenesis included ectopia \((n = 49, 40\%)\), agenesis \((n = 18, 15\%)\), hypoplasia \((n = 8, 6\%)\), and hemiagenesis \((n = 2, 1\%)\). All ectopic thyroid glands were sublingual in position. Forty-seven of 124 patients (38%) had a normal location of the thyroid gland (Table 2 and Figs. 2–6).

Thirty-eight of the patients had a normally sized thyroid gland, and eight patients had an enlarged thyroid gland. All these patients had homogeneous thyroid parenchymal echogenicity. Fourteen of the 38 patients (37%) with a normally sized gland had increased thyroid parenchymal vascularity, compared with six of the eight patients (75%) with an enlarged thyroid gland (Table 3).

Sonography depicted hypoplasia of the thyroid gland in nine patients. Only one of them had a 99mTc-pertechnetate study showing sublingual thyroid gland. Sonography showed hemiagenesis of the thyroid gland in two patients confirmed with 99mTc-pertechnetate scintigraphy. One of these patients also had sublingual thyroid gland.

Sixty-five patients underwent 99mTc-pertechnetate scanning. Forty-four of them had sublingual thyroid gland; 14, thyroid agenesis; five, normal location with poor uptake; one, hemiagenesis; and one, hemiagenesis with a sublingual thyroid gland. Of the three patients with only 99mTc-pertechnetate studies, one patient had eutopic thyroid gland with poor uptake, and the other two had sublingual thyroid gland (Table 4).

The conditions of 55 patients were diagnosed as either sublingual thyroid gland or...
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**Fig. 4**—7-day-old boy with thyroid hemiagenesis.
A, Transverse sonogram at level of thyroid bed shows hypoplastic right lobe of thyroid gland with normal size and echogenicity of left lobe.
B and C, Anterior (B) and lateral (C) $^{99}$Tc-pertechnetate scans 15 minutes after radiotracer administration show uptake in left lobe of thyroid.

**Fig. 5**—20-day-old girl with hemiagenesis and sublingual thyroid.
A and B, Transverse sonograms of thyroid show agenesis of right lobe of thyroid with normal size, echogenicity, and color flow of left lobe (arrowhead).
C and D, Anterior (C) and posterior (D) $^{99}$Tc-pertechnetate scans 15 minutes after radiotracer administration show uptake in left lobe of thyroid gland (arrowhead) and sublingual thyroid gland (arrow).
thyroid agenesis after an ultrasound examination, and then \(^{99m}\text{Tc}\)-pertechnetate scanning was performed (Table 5). The results of these scans confirmed that 18 ultrasound diagnoses of sublingual thyroid were sublingual thyroid (specificity, 100%). In 37 patients, thyroid agenesis was diagnosed with ultrasound, but in 23 of these patients, follow-up scintigraphy showed sublingual thyroid tissue. Therefore, the sensitivity of ultrasound for identifying sublingual thyroid was 44%. In 14 of the 37 patients, the agenesis diagnosed with ultrasound was confirmed at \(^{99m}\text{Tc}\)-pertechnetate scanning.

When we reviewed the cases of 23 patients whose condition was diagnosed as agenesis with ultrasound but was found to be sublingual thyroid tissue with scintigraphy, we found that 15 of the 23 patients (65%) did not undergo CDUS. One patient (4%) did not have a scan at the tongue base. Seven of 23 patients (31%) did not have ectopic thyroid gland detected, even with CDUS. Three studies (2%) showed discrepancy between the original report and retrospective review. In both cases, a small sublingual thyroid gland was retrospectively identified.

Cost comparison between ultrasound and \(^{99m}\text{Tc}\)-pertechnetate scanning is complex because costs vary among institutions. At our institution, an ultrasound study costs approximately $70 less than a \(^{99m}\text{Tc}\)-pertechnetate study.

**Discussion**

The treatment of CH patients is empiric and not guided by imaging findings. A neonate with a diagnosis of CH is immediately treated with thyroid hormone replacement [15]. Using a higher starting dose to more quickly normalize TSH levels to the target range within 2 weeks to normalized developmental IQ even in patients with severe CH is the main purpose of treatment. The initial thyroid hormone (levothyroxine) dose for ectopic thyroid gland is approximately 10 µg/kg/d, compared with 15 µg/kg/d for noneutopic thyroid gland [16].

Permanent CH can be assumed if ultrasound or radionuclide imaging shows the thyroid gland is absent or ectopic (together referred to as dysgenesis) or if at any time during the first year of life, the serum TSH concentration rises above 20 mU/L owing to undertreatment. The American Academy of Pediatrics and the European Society for Pediatric Endocrinology recommend that if permanent CH has not been established by 2–3 years of age, a 30-day trial without thyroid hormone be undertaken. If low serum T4 and elevated TSH concentrations are found, permanent CH is confirmed, and therapy is restarted [1]. If a patient has a eutopic thyroid gland, and the gland produces adequate thyroid hormone in the 30-day trial, a diagnosis of transient CH is established, and the patient needs no further thyroid hormone replacement.
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TABLE 3: Ultrasound Findings in Eutopic Thyroid Gland

<table>
<thead>
<tr>
<th>Finding</th>
<th>Normal Size (n=38)</th>
<th>Enlarged Gland (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>Increased</td>
<td>14</td>
<td>6</td>
</tr>
</tbody>
</table>

TABLE 4: 99mTc-Pertechnetate Findings in 44 Patients With Sublingual Thyroid Gland

<table>
<thead>
<tr>
<th>Finding</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>19</td>
</tr>
<tr>
<td>Moderate</td>
<td>19</td>
</tr>
<tr>
<td>Large</td>
<td>6</td>
</tr>
<tr>
<td>Uptake</td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
<td>10</td>
</tr>
<tr>
<td>Expected</td>
<td>26</td>
</tr>
<tr>
<td>Intense</td>
<td>8</td>
</tr>
</tbody>
</table>

Thyroid scintigraphy is considered the reference standard for the evaluation of CH. There are several reports, however, of limitations of scintigraphy in diagnosing eutopic thyroid gland. Perry et al. [3] and several other groups [5, 17, 18] reported that ultrasound shows thyroid tissue in 2–15% of patients who have none visualized at scintigraphy. These studies included patients with maternal thyrotropin receptor–blocking antibodies, exposure to maternal antithyroid medications, iodine deficiency, or iodine excess causing transient hypothyroidism [1, 5, 15, 17, 18]. These patients may have transient hypothyroidism and would likely not need thyroid hormone replacement for life. Therefore, in patients with a eutopic thyroid gland, no uptake at scintigraphy may be misleading.

In our 7-year cohort of patients with CH, we found a higher frequency of eutopic thyroid gland than reported in the literature. This finding may be related to a higher percentage (36%) of transient hypothyroidism in our screening program [8]. Regardless of the underlying cause, the initial treatment of CH is the same. However, patients with eutopic thyroid gland may need further investigation to differentiate between the permanent and transient forms of CH.

The main limitation of ultrasound is decreased sensitivity in the evaluation of ectopic thyroid gland. The ultrasound diagnosis of ectopic thyroid gland depends on technique and the experience of the sonographer. Marked variation in sensitivity (0–80%) has been reported among medical centers [1–3, 5, 11, 18, 19]. The sensitivity of sonography in the detection of ectopic thyroid gland in our series was 44%. Using CDUS increases the sensitivity of diagnosis of ectopic thyroid gland [1, 2, 5, 11]. In our series, in most cases of missed ectopic thyroid gland, CDUS was not used. The reported specificity of ultrasound in the detection of ectopic thyroid gland is high [1–3, 5, 11, 18, 19, 21]. In our series, the specificity of sonography was 100%.

Our experience showed that when ultrasound depicts ectopic or eutopic thyroid gland, the scintigraphic results will not change the initial management. For precise diagnosis of agenesis versus sublingual thyroid gland in all patients with ectopic thyroid gland, scintigraphy can be used selectively when ultrasound does not depict any thyroid tissue. In our series, that would have obviated scintigraphy for 54% of the patients.

For management guidance, it is important to differentiate patients with eutopic thyroid gland from those with thyroid dysgenesis. Patients with thyroid dysgenesis are being treated for life with thyroid hormone replacement. The ectopic thyroid gland eventually involutes owing to suppression of TSH. Differentiation between thyroid agenesis and ectopic thyroid gland does not change management. Scintigraphy can therefore be used selectively only in cases of equivocal ultrasound findings, such as hypoplastic thyroid gland.

In our series, we did not perform scintigraphy for most patients with eutopic thyroid gland and therefore do not have a correlation with thyroid size or parenchymal echotexture. With this management, we would remove the need for scintigraphy for 90% of patients. This approach will save both radiation and cost with no change in management.

Imaging of patients with CH has a role in the evaluation of the cause, in prognosis, and in guiding management. Ultrasound of the thyroid can be used to differentiate patients with thyroid dysgenesis from patients with eutopic thyroid. Thyroid dysgenesis is typically a sporadic disorder and carries no recurrence risk of CH with future pregnancies. Patients with eutopic thyroid gland are a heterogeneous group; some have a risk of recurrence in future pregnancies. Genetic consultation can be considered [1].

Our study had several limitations. First, our study was performed as a retrospective review of imaging findings, and there was inconsistent use of CDUS, possibly decreasing sensitivity in the detection of ectopic sublingual thyroid gland. Second, the ultrasound and 99mTc studies were reviewed by a single radiologist, possibly biasing interpretation of the studies. However, compared with original reports, in only two studies (3%) did the retrospective evaluations vary. Because the studies were reviewed by a single radiologist, we could not assess interobserver variability. Third, we imaged only patients who were evaluated prenatally at our institute. Fourth, the study did not include follow-up on euthyroid patients. However, the incidence of transient hypothyroidism in our institution (36%) had been published [8].

TABLE 5: Discrepancy Between Ultrasound and Scintigraphic Findings

<table>
<thead>
<tr>
<th>Finding</th>
<th>Ultrasound</th>
<th>99mTc Scintigraphy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agenesis</td>
<td>Sublingual Thyroid</td>
</tr>
<tr>
<td>Agenesis</td>
<td>37</td>
<td>14</td>
</tr>
<tr>
<td>Sublingual thyroid</td>
<td>18</td>
<td>23</td>
</tr>
</tbody>
</table>

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Conclusion
Ultrasound can be used as the primary imaging modality for guiding treatment of children with CH, potentially decreasing radiation exposure and cost. Scintigraphy can be reserved for the few patients with equivocal ultrasound findings, such as hypoplastic thyroid gland.

References
1. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis 2010; 5:17
6. Delange F. Screening for congenital hypothyroidism used as an indicator of the degree of iodine deficiency and of its control. Thyroid 1998; 8:1185–1192