Pediatr Radiol (2013) 43:1244–1253
DOI 10.1007/s00247-013-2735-9

REVIEW

Thyroid disease in children: part 1

State-of-the-art imaging in pediatric hypothyroidism

Jennifer L. Williams · David L. Paul · George Bisset III

Received: 17 January 2013 / Revised: 16 April 2013 / Accepted: 1 May 2013

Abstract Hypothyroidism, defined as inadequate production of thyroid hormone, can be secondary to various underlying abnormalities in the pediatric population. Most frequently, hypothyroidism is related to structural abnormalities of the gland (dysgenesis), particularly in the neonatal population. However, other etiologies including intrinsic biochemical (dyshormonogenesis) and autoimmune abnormalities, as well as other rare causes, must be considered. Imaging is required to differentiate among the various etiologies of hypothyroidism and can be helpful in guiding therapy. This review aims to present an organized approach to hypothyroidism in the pediatric population, and assist the imager in guiding patient care.

Keywords Pediatric hypothyroidism · Congenital hypothyroidism · Thyroid dysgenesis · Thyroid dyshormonogenesis · Children

Introduction

Hypothyroidism is a condition resulting from inadequate production of thyroid hormones; several underlying pathologies can produce this patho-physiological state. Hypothyroidism in the neonate and child presents a unique subset of problems, some of which can be severe and life-altering. A missed diagnosis of severe or complete hypothyroidism in the neonatal period is devastating, resulting in developmental disabilities. Undiagnosed hypothyroidism in the older child can result in stunted growth, pubertal abnormalities and other symptoms. For these reasons, understanding the various etiologies of hypothyroidism and their imaging findings is of critical importance.

The aim of this review article is to provide a structured approach to pediatric hypothyroidism related to imaging. We present an overview of the thyroid imaging modalities frequently used in children with hypothyroidism and discuss in depth the multiple etiologies of pediatric hypothyroidism and their imaging findings.

CME activity This article has been selected as the CME activity for the current month. Please visit the SPR Web site at http://www.pedrad.org on the Education page and follow the instructions to complete this CME activity.

J. L. Williams (✉) · G. Bisset III
The Edward B. Singleton Department of Pediatric Radiology, Texas Children's Hospital, 6701 Fannin St., Suite 470, Houston, TX 77030-2399, USA
e-mail: jlwilli1@texaschildrens.org

D. L. Paul
Department of Endocrinology, Texas Children's Hospital, Houston, TX, USA

Imaging modalities

The most useful imaging modalities in evaluating the thyroid in children with hypothyroidism are scintigraphy and ultrasonography. Nuclear medicine exams provide information on thyroid anatomy as well as function. US is useful in determining whether thyroid tissue is present and in characterizing thyroid disease. The remaining cross-sectional modalities (CT, MRI and PET) are typically not of much use in evaluating hypothyroidism.

Patient positioning is critical in both US and nuclear medicine exams, particularly in the neonatal period. Imaging of infants being evaluated for congenital hypothyroidism can be quite challenging given the short neck and potentially excess fat in the region of interest. As a consequence, patient positioning is crucial to success. Imaging the child with his neck extended can be helpful and can be accomplished by placing towels under the infant's shoulder [1].

Table 1 Physical characteristics of iodine (I)-123 and Tc99m

I-123	Tc99m
Low energy (159 keV)	Low energy (140 keV)
Short half-life (13 h)	Short half-life (6 h)
Dose: 6 μCi/kg; (25 μCi – 400 μCi)	Dose: 30 μCi/kg (200 μCi – 2 mCi)
Effective dose: 0.54 mSv/MBq	Effective dose: 0.04 mSv/MBq
Oral administration	IV administration
Image acquisition at 4 h and 24 h	Image acquisition in 30 min
- Continued uptake over 24 h	- Plateau 15–30 min after administration
- Moderate uptake of radiopharmaceutical by thyroid gland (20%)	- Low uptake of radiopharmaceutical by thyroid gland (1.2–7%)

Scintigraphy

Nuclear medicine imaging is based on capturing emitted energy utilizing gamma cameras. Two radiopharmaceuticals are used in evaluating the child with hypothyroidism: I-123 and Tc-99m (pertechnetate). These are both low-energy agents with short half-lives, resulting in relatively low radiation exposure. I-131 is avoided for routine imaging in children secondary to its high energy and long half-life. See Table 1 for further information regarding the physical properties of I-123 and Tc-99m.

I-123 is administered orally and can be used for focal thyroid imaging as well as whole-body screening. For focal thyroid imaging, a thyroid probe is used to obtain radioiodine uptake values at 4 h and 24 h (normal values 5–12% at 4 h, 10–30% at 24 h); see Fig. 1 for an example of a normal I-123 scan. At our institution, imaging of the thyroid gland occurs at 4 h, and anterior planar images as well as anterior, left anterior oblique (LAO) and right anterior oblique (RAO) pinhole views are obtained. Oblique views are used to ensure that small hot/cold defects are not missed and to better evaluate gland morphology and location.

Tc-99m (pertechnetate) is administered intravenously, and images are acquired sooner as compared to I-123; see Fig. 1 for an example of a normal Tc-99m scan [2]. Pertechnetate has lower energy and a shorter half-life than I-123; the effective dose is lower as well (see Table 1), and for this reason it has often been advocated in pediatric imaging. However, Tc-99m only reflects thyroid gland trapping capabilities. Thyroid follicular cells trap iodine and pertechnetate via a sodium iodine active transport pump; however, only I-123 uptake reflects the organification process (the enzymatic cascade that results in thyroid hormone production). This added information becomes useful in evaluating children with congenital hypothyroidism (see below). Finally, pertechnetate is taken up avidly by salivary glands, which can hinder interpretation (Fig. 2). Radioiodine uptake by the salivary glands is minimal, particularly at the doses employed in general thyroid imaging. I-123 does have some drawbacks; it can be less accessible than pertechnetate and is more expensive.

US imaging

Sonographic evaluation is also important in the workup of thyroid pathology. High-frequency (10- to 15-MHz) linear-array transducers provide detailed anatomical information regarding the thyroid gland [3]. Transverse and longitudinal views of the right and left lobes of the thyroid should be obtained, as well as evaluation of the isthmus. Length measurements and volumes should be obtained and compared to normal values [4]. Careful evaluation of the echotexture of the thyroid gland should be performed; the thyroid should be homogeneous in echotexture. In general, the gland is hyperechoic as compared to adjacent musculature [1]. Doppler interrogation is a frequent adjunct that can provide useful additional information. For instance, the normal thyroid gland has only moderate vascularity. Patients with Hashimoto thyroiditis and Graves disease have very similar gray-scale imaging; however, Doppler flow is increased in patients with Graves disease [1].

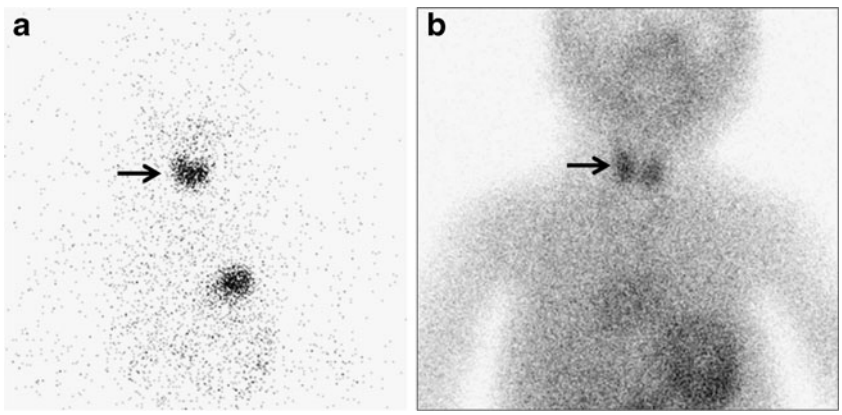

Fig. 1 Normal scintigraphy. **a** Normal I-123 scintigraphy of the thyroid gland (*arrow*) in a 1-month-old girl. Radioactive iodine uptake (RAIU) values were 9% at 4 h and 15% at 24 h. **b** Normal pertechnetate scintigraphy of the thyroid gland (*arrow*) in a 2-month-old boy

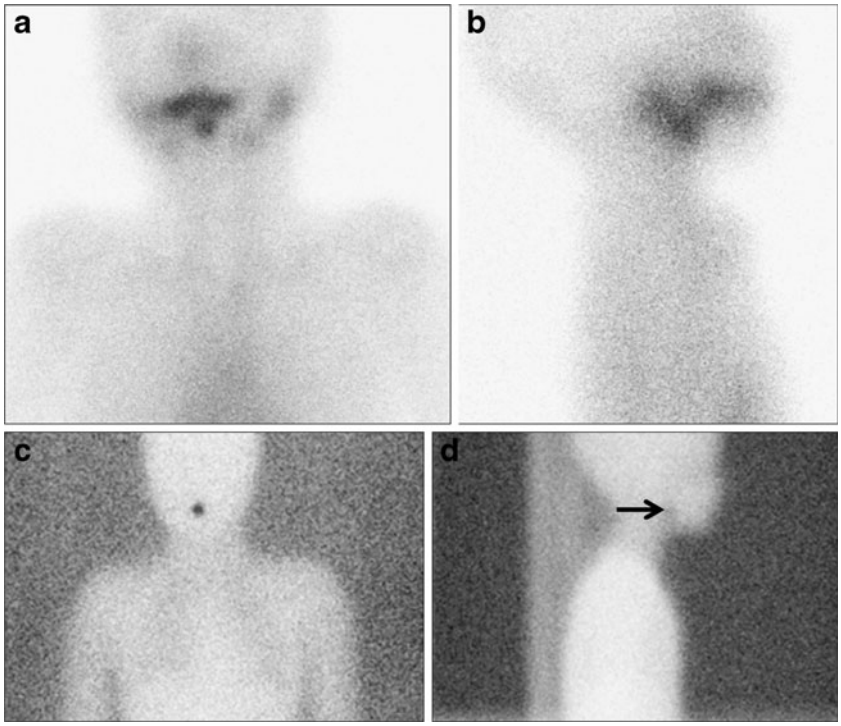

Fig. 2 Pertechnetate anterior (**a**) and lateral (**b**) planar transmission images of the neck in a 1-month-old girl with hypothyroidism. There is no radiotracer accumulation in the expected region of the thyroid gland. Extensive salivary gland uptake and nasolacrimal secretions obscure the pharyngeal region, making it difficult to evaluate for lingual thyroid tissue. I-123 anterior (**c**) and lateral (**d**) planar transmission images of the neck in the same infant demonstrate focal radiotracer accumulation in the oropharyngeal region (*arrow*), compatible with ectopic lingual thyroid tissue

Miscellaneous modalities

The remaining modalities, including CT, MRI and PET, are not utilized as primary imaging modalities in the evaluation of hypothyroidism. Cross-sectional imaging does occasionally demonstrate incidental abnormalities, in which case the child typically proceeds to US or scintigraphy for further characterization of the lesion. Cross-sectional imaging of the brain can also be useful for the rare child with central hypothyroidism.

Hypothyroidism

Typically two categories of children present for imaging. Most are neonates who were found to be hypothyroid following a perinatal screening exam (congenital hypothyroidism). The remaining children present later in childhood with symptoms eventually leading to the diagnosis of hypothyroidism. The etiology of congenital hypothyroidism falls into one of four categories: thyroid dysgenesis (abnormal structural development of the gland), thyroid dyshormonogenesis (abnormal function of the gland), transient hypothyroidism and, rarely, central hypothyroidism. Hypothyroidism presenting later in childhood can be caused by milder forms of congenital hypothyroidism as well as by autoimmune or subacute thyroiditis. The rare miscellaneous causes of hypothyroidism are discussed here as well. See Table 2 for a review of the etiologies of hypothyroidism in children.

Congenital hypothyroidism

Congenital hypothyroidism occurs in approximately 1 in 3,000–4,000 births and is twice as common in girls as boys [5, 6]. Hispanics and Native Americans are at higher risk than Caucasians; African-Americans have a low prevalence of this condition [1]. Diagnosing severe or complete hypothyroidism in neonates and children is crucial in preventing devastating developmental disabilities. For this reason,

Table 2 Etiology of hypothyroidism in the child

Congenital hypothyroidism	Childhood hypothyroidism
Thyroid dysgenesis	Mild thyroid dysgenesis
Agenesis	Mild thyroid dyshormonogenesis
Hemiagenesis	Autoimmune thyroiditis
Ectopia	Hashimoto thyroiditis
Hypoplasia	Subacute thyroiditis
Thyroglossal duct cyst	Iatrogenic
Thyroid dyshormonogenesis	Drugs
Transient	Radiation
Iodine deficiency	Surgery
Iodine excess	Central
Maternal autoimmune disease	Pituitary gland abnormality
Medication	Hypothalamic abnormality
Functional	
Central	
Pituitary gland abnormality	
Hypothalamic abnormality	

Table 3 Conditions associated with hypothyroidism

Condition
Down syndrome
Turner syndrome
Noonan syndrome
Infantile hepatic hemangiomas
Type 1 diabetes
Celiac disease
Williams syndrome
Prior thyroid surgery
Radiation
Medications (phenytoin, amiodarone)

newborn screening is performed in the United States as well as most developed countries. The American Academy of Pediatrics recommends that all neonates have both T4 and thyroid stimulating hormone (TSH) blood levels drawn; excluding either one of these tests can rarely lead to false-negatives. If hypothyroidism is established on a confirmatory test, levothyroxine therapy is initiated with plans for re-evaluation of hormone levels after early critical brain development has occurred (at approximately 3 years of age) [7].

Congenital hypothyroidism has an increased association with syndromes and extra-thyroidal congenital malformations as compared to the general public. There is an increased risk of structural cardiac malformations in these children (atrial septal defect, ventricular septal defect, pulmonary stenosis, tetralogy of Fallot, transposition of the great vessels, patent ductus arteriosus, and coarctation of the aorta have all been described). Multiple additional defects have been shown to have an increased association with congenital hypothyroidism including (but not limited to) central nervous system abnormalities, cataracts, clubfoot and cleft lip/palate. Children with Down syndrome are also known to have an increased incidence of congenital hypothyroidism [8, 9]. There is also an increased risk for hypothyroidism in children with infantile hepatic hemangiomas [10]. See Table 3 for additional conditions associated with hypothyroidism in the child.

Imaging of hypothyroidism in the neonate is aimed at detecting the presence of thyroid tissue and diagnosing the various forms of thyroid dysgenesis (discussed below). Understanding the underlying etiology for a child's hypothyroid state is useful in treatment-planning and potential genetic counseling. Figure 3 presents a diagnostic approach to congenital hypothyroidism.

Thyroid dysgenesis

Thyroid dysgenesis is the most common etiology of congenital hypothyroidism [11, 12] and can be defined as any structural abnormality of the thyroid gland that results in hormonal deficiencies. Variations of dysgenetic thyroid tissue include agenesis, hemiagenesis, hypoplasia, ectopia and thyroglossal duct cysts.

Imaging evaluation of the thyroid gland of the neonate with suspected congenital thyroid abnormality is useful in treatment planning and prognosticating and includes nuclear medicine thyroid scan and US. Scintigraphic evaluation of the thyroid can be performed for several days after initiation of

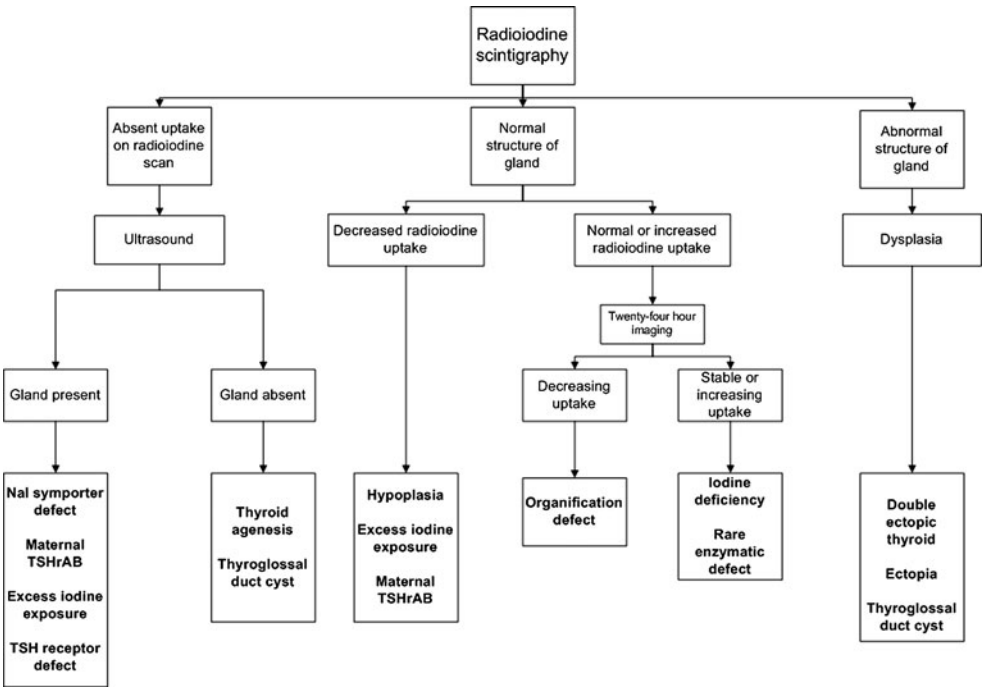

Fig. 3 Diagnostic approach to congenital hypothyroidism

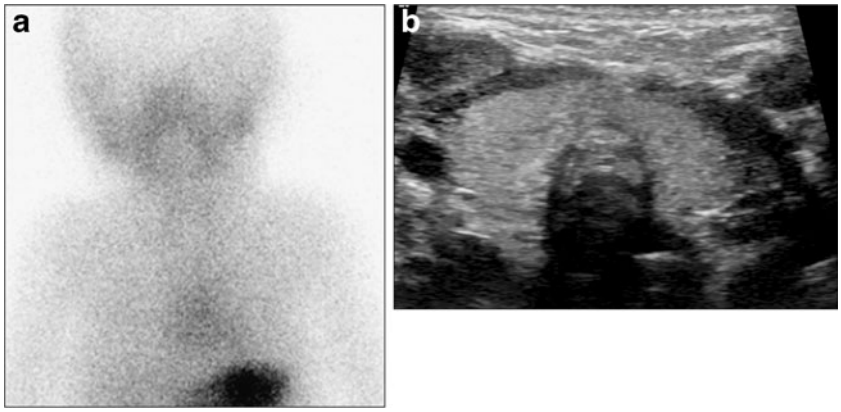

Fig. 4 Dyshormonogenesis in a 2-month-old boy. **a** Anterior planar image obtained after pertechnetate administration does not show uptake within the expected region of the thyroid gland. **b** Transverse US image confirms the presence of a thyroid gland. This boy most likely has dyshormonogenesis (specifically an NaI transporter defect); given the boy's age, transient hypothyroidism is less likely

hormone replacement therapy because thyroid stimulating hormone levels do not drop immediately. Elevation of the TSH levels ensures that (if present and functioning) thyroid tissue will be visualized with scintigraphy [7]. Following administration of I-123, nonvisualization of the thyroid gland suggests agenesis; however, other etiologies including thyroglossal duct cyst without functioning thyroid tissue, transient hypothyroidism and some forms of dyshormonogenesis remain as considerations. US is required to confirm this diagnosis; if there is no uptake on scintigraphy but a structurally normal or small gland is seen on US, the child has transient hypothyroidism or dyshormonogenesis (Fig. 4) [6].

Scintigraphy is especially useful in demonstrating ectopic thyroid tissue. US can also detect ectopic thyroid; however, the results are highly variable and dependent on the sonographer's experience. Moreover, even with careful US evaluation, ectopic tissue can be missed. Again I-123 can be beneficial over pertechnetate because pertechnetate can sometimes produce confusing results secondary to salivary glandular uptake and salivary secretions [11]. Ectopia is further categorized as lingual, suprahyoid (Fig. 5), hyoid, infrahyoid and double ectopic [6, 13]. Of note, lingual thyroid tissue can be more problematic than the remaining forms of ectopia because it can result in airway obstruction or hemorrhage (Fig. 6) [14].

Other forms of thyroid dysgenesis include hypoplastic glands, hemiagenesis and thyroglossal duct cysts [6, 15]. Hypoplasia is self-explanatory; the gland is smaller in size or volume than expected for age and as such might not produce sufficient thyroid hormone. These glands typically have an unusual shape (round/blunted) as well as decreased uptake on thyroid scintigraphy. The findings can be more difficult to diagnose on US. Careful attention to thyroid volume measurement, however, can lead to the diagnosis [11].

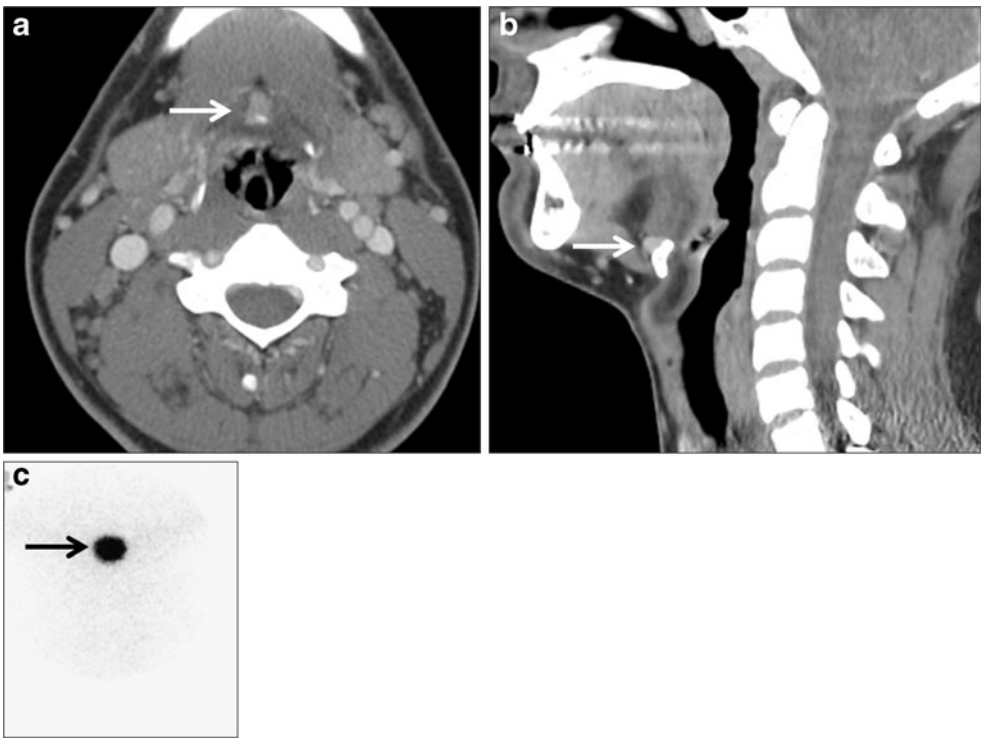

Fig. 5 Ectopic suprahyoid tissue. **a** Axial and (**b**) sagittal CT images demonstrate enhancing tissue in the suprahyoid region (*arrows*) in this 4-year-old boy. **c** I-123 anterior planar scintigraphy confirmed this to be ectopic functioning suprahyoid thyroid tissue (*arrow*)

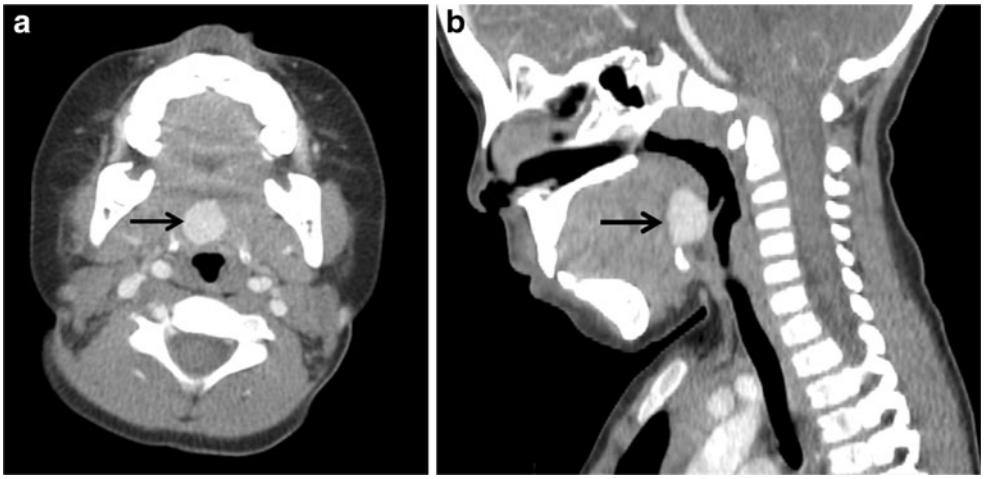

Fig. 6 Lingual thyroid tissue. **a** Axial and (**b**) sagittal CT images demonstrate enhancing tissue in the lingual region (*arrows*) in this 3-year-old boy

Thyroid hemiagenesis is a rare entity occurring in 0.05% of the population. The left lobe is absent in 80% of cases [11]. These patients typically present later in life because thyroid hormone values are normal or only minimally decreased. US imaging and scintigraphy reveal a solitary thyroid lobe (Fig. 7). The isthmus is absent as well in approximately 50% of cases [11].

Thyroglossal duct cysts are epithelial remnants of the thyroglossal duct. Typically these occur in conjunction with normal thyroid tissue [16]. Children often present later in life with a palpable midline neck mass [17]. US is frequently performed for initial evaluation, and thyroglossal duct cysts can have variable appearances; lesions can be solid, cystic, homogeneous or heterogeneous (Fig. 8). Scintigraphy can be performed if a normal thyroid is not detected on sonography; in these cases it is important to determine whether the thyroglossal duct cyst contains functioning thyroid tissue and to locate any potential site of ectopic thyroid tissue. It should be noted that typically thyroglossal duct cysts do not have normally functioning thyroid tissue. Thus these lesions do not classically have uptake following radioisotope administration.

Transient hypothyroidism

Transient hypothyroidism is a condition of the neonate that can be caused by iodine deficiency, iodine excess, exposure to maternal thyrotropin-receptor-blocking IgG antibodies (i.e. TSH receptor antibodies) and antithyroid drugs [18]. Prematurity can also result in hypothyroidism secondary to functional immaturity of the hypothalamic-pituitary axis. Functional immaturity is typically considered separately from the aforementioned etiologies because it has a less predictable clinical course. In general, transient hypothyroidism should resolve within 2 months, while functional immaturity has a variable time course until resolution [18, 19]. The diagnosis of transient hypothyroidism is typically based on clinical and laboratory data.

Brief discussion of iodine states in the neonate is warranted to fully understand transient hypothyroidism caused by iodine excess or deficiency. Neonates exposed to excessive iodine loads (typically related to a betadine sterilization procedure during delivery) can become hypothyroid secondary to the Wolff-Chaikoff effect. This refers to an autoregulatory process in which the high plasma concentrations of iodine lead to a decreased production of thyroid hormone, and it typically lasts approximately 10 days [20]. Scintigraphy is not frequently performed because this condition is usually diagnosed clinically; if performed, a radioiodine scan would show decreased radioiodine uptake (and in severe cases absence of uptake) secondary to generalized down-regulation of the thyroid gland. US would demonstrate a normal gland.

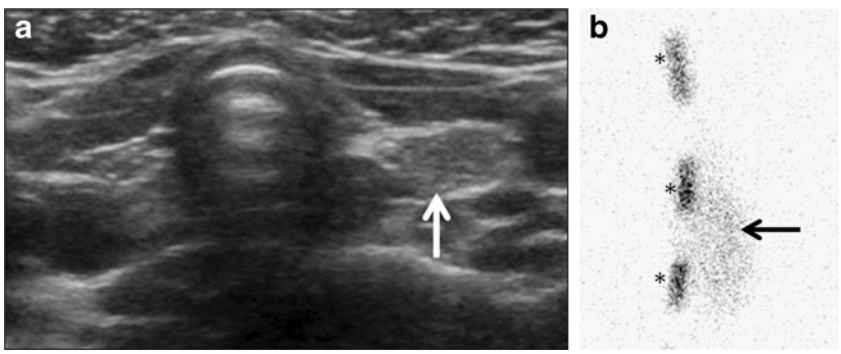

Fig. 7 Hemiagenesis. **a** Transverse US image shows only a left lobe thyroid lobe (*arrow*), consistent with hemiagenesis in this 4-year-old boy. **b** I-123 anterior planar image in an 8-year-old girl shows uptake in only the left lobe (*arrow*), consistent with hemiagenesis. Asterisks are adjacent to a midline marker

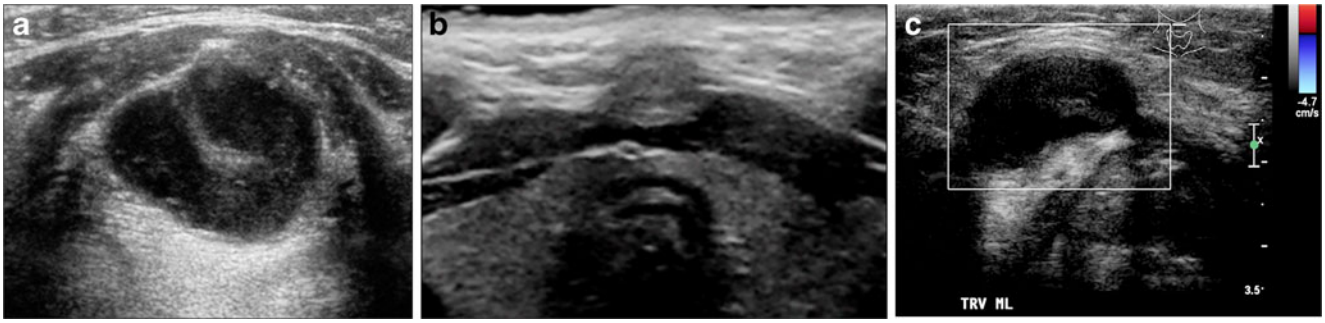

Fig. 8 Variable imaging of thyroglossal duct cyst on US. The lesions can appear as (**a**) complex cysts, as in this 4-year-old girl; (**b**) solid masses, as in this 4-year-old girl, or (**c**) simple cysts, as in this 6-year-old boy

Iodine deficiency can also result in hypothyroidism, because without iodine, thyroid hormone cannot be produced [18]. However, these children would have avid increased uptake on radioiodine scan secondary to up-regulation of the thyroid gland (i.e. these children have elevated TSH, which would result in increased radioiodine uptake within the gland). Again, US typically does not show any distinguishing abnormality.

The final two categories of transient hypothyroidism are typically diagnosed clinically. In children with transient hypothyroidism secondary to TSH receptor blocking antibodies, scintigraphy shows absent or decreased uptake. Neonates exposed to maternal antithyroid medications have scintigraphic findings similar to children with dyshormonogenesis; early uptake is present because of intact trapping capabilities, but delayed imaging shows some degree of radioiodine washout.

In cases where transient hypothyroidism cannot be distinguished between dyshormonogenesis and dysgenesis, the neonate is placed on hormone replacement therapy until approximately 3 years of age to ensure proper neuronal development. At that time thyroid replacement therapy can be temporarily discontinued for re-evaluation [7]. Transient hypothyroidism will have resolved by this time; thus if there is persistent abnormality on scintigraphy in the setting of a normal thyroid US exam, the underlying etiology is dyshormonogenesis. Confirming a diagnosis of transient hypothyroidism is important because it saves the child from years of needless thyroid hormone replacement therapy.

Thyroid dyshormonogenesis

Thyroid dyshormonogenesis is a much less frequent etiology of congenital hypothyroidism, accounting for approximately 10–15% of cases [11, 18, 21]. This refers to a defect in any of the multiple steps in thyroid hormone synthesis including abnormalities in the NaI transporter (i.e. the iodine trapping mechanism), thyroid peroxidase enzyme (the organification enzyme) or any of the remaining enzymatic steps. Evaluation of dyshormonogenesis is particularly dependent on the use of I-123 versus pertechnetate because I-123 allows for narrowing of the differential diagnosis (see below).

Children with thyroid dyshormonogenesis might begin their evaluation with US, which can be normal or show an enlarged gland. Scintigraphy can help in further classifying the underlying pathology. One form of dyshormonogenesis is a nonfunctioning NaI transporter. Patients with this defect have no uptake on scintigraphy regardless of which radiotracer is used; neither pertechnetate nor I-123 can be taken into thyroid follicular cells when the NaI transporter is nonfunctioning, and thus no gland is visualized on scintigraphy.

Organification defects can also be detected using I-123. In healthy children there is I-123 uptake at both 4 h and 24 h. Typically the radioactive iodine uptake (RAIU) value is stable or slightly increased at 24 h as compared to 4 h [22]. In children with an organification defect, 4-h images show a normal scintigraphic appearance of the thyroid (secondary to an intact trapping mechanism), but 24-h images typically reveal decreased RAIU values because iodine that is not organified is lost from the thyroid cell (Fig. 9). Pertechnetate scans cannot demonstrate an organification defect; this radioisotope is trapped by thyroid follicular cells, but (because

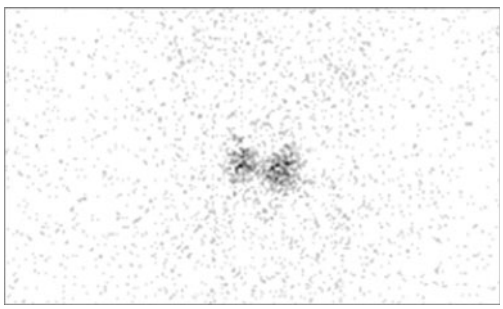

Fig. 9 Anterior planar I-123 image in a 1-month-old girl with hypothyroidism demonstrates appropriate uptake in the thyroid gland. The RAIU value at 4 h was 7% and at 24 h had dropped to 4%. These findings are most consistent with an underlying organification defect

it is not iodine) there is no potential for organification. Thus 24-h delayed imaging to evaluate for radiotracer washout cannot be performed.

The perchlorate washout test can be utilized to aid in diagnosing organification defects. Potassium perchlorate ($KClO_4^-$) competes with iodine at the level of the NaI transporter. Children with a suspected organification defect undergo thyroid scintigraphy using I-123 as described above. Following this, perchlorate is administered at concentrations that saturate the NaI transporter. This prevents further iodine from entering the cell. Follow-up imaging is then performed; in children with a functioning organification mechanism, the administered radioiodine is organified. Thus RAIU levels remain stable on follow-up images. However, in children with a defective organification mechanism, the (non-organified) iodine diffuses out of the cell. This results in washout of radiotracer on scintigraphy and decreased RAIU values [21].

Hypothyroidism in the older child

Hypothyroidism that presents later in childhood can still be caused by less severe cases of thyroid dysgenesis or dyshormonogenesis. However, other etiologies should be considered, including autoimmune etiologies, subacute thyroiditis and, rarely, disorders of the hypothalamus or pituitary.

Autoimmune thyroiditis

Autoimmune thyroiditis resulting in hypothyroidism is either goiterous (Hashimoto disease) or agoiterous (atrophic thyroiditis). This disease is caused by an autoimmune reaction to the thyroid gland. These children often have antibodies to thyroglobulin and thyroid peroxidase enzyme. There is a resultant lymphocytic infiltration of the thyroid gland with subsequent destruction of the gland [23]. The disease has been reported to occur in approximately 2% of school-age children but remains the most common etiology for acquired hypothyroidism in the pediatric patient [1, 11]. The clinical effects can be quite significant, including poor growth, pubertal abnormalities and bone maturation delays, in addition to classic findings of hypothyroidism encountered in adults (Table 4) [24].

The appearance of the thyroid gland in children with Hashimoto thyroiditis depends on the stage of the disease. Early in the disease process, thyroid function is typically normal secondary to an intact pituitary-thyroid axis. Thus, although there is a mild decrease in the production of thyroid hormones, TSH levels increase allowing for temporary maintenance of normal hormone levels. However, this increased TSH stimulation does result in increased radioiodine uptake on scintigraphy [25]. US can be normal or show mild heterogeneity in echotexture. Similarly, Doppler flow can be normal or increased [24].

Occasionally children present with Hashitoxicosis, in which there is rapid damage to the thyroid gland. These children present clinically in a fashion similar to those with Graves disease. On scintigraphy, these children have significantly elevated radioiodine uptake. US classically demonstrates heterogeneity in echotexture as well as increased Doppler flow [25]. Specific laboratory data (TSH receptor antibodies) can help to differentiate between Hashitoxicosis and Graves disease (see Thyroid Disease in Children: Part 2 in this issue for further details on this).

As the disease progresses, increasing fibrosis of the thyroid gland occurs. This results in an enlarged, goiterous gland. US examination of these children typically shows a heterogeneous echotexture, often with scattered tiny hypodense micronodules (Fig. 10); occasionally larger nodules are detected, and further evaluation (i.e. fine-needle aspiration/biopsy) might be required because some studies suggest an increased risk of malignancy in children with Hashimoto disease [26]. Doppler evaluation classically shows normal to diffuse decreased flow of the gland (Fig. 10) [1, 23]. Scintigraphic findings can be variable; often the gland is nodular with some regions containing more

Table 4 Signs and symptoms of hypothyroidism

General	Physical signs	Specific to children
Poor growth	Bradycardia	Delayed bone maturation
Constipation	Dry skin	Delayed puberty
Cold intolerance	Increased body hair	Poor school performance
Fatigue	Delayed relaxation of deep tendon reflexes	Delayed neuronal development
Irregular menses	Goiter	
	Fluid retention/puffiness	
	Weight gain	

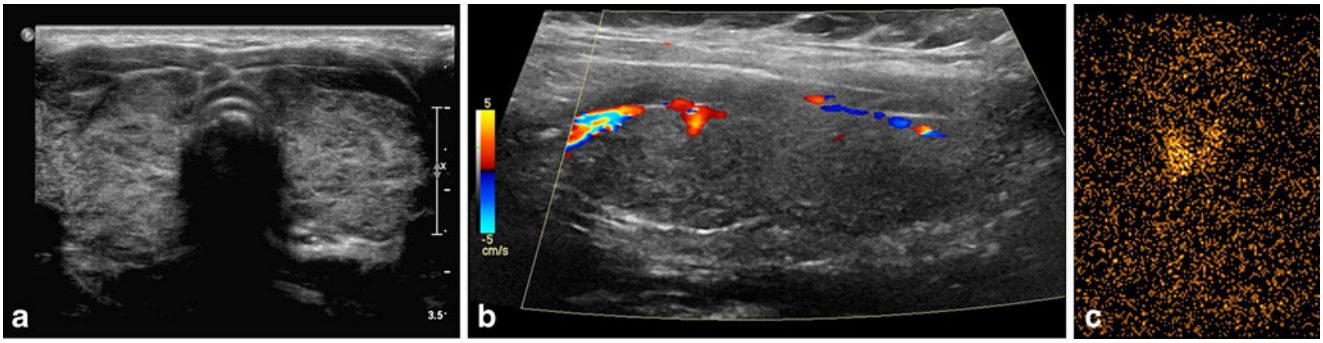

Fig. 10 Gray-scale US demonstrates classic findings of Hashimoto thyroiditis in a 13-year-old girl. **a** Transverse US image demonstrates the gland to be enlarged and heterogeneous, with multiple small hypoechoic nodules. **b** Longitudinal Doppler image demonstrates decreased flow throughout the gland. **c** Anterior planar I-123 scintigraphy demonstrates global decreased radiotracer uptake

functioning thyroid cells than others. On scintigraphy, this results in a gland with variable regions of increased and decreased uptake [23]. With disease progression there is eventually diffuse decreased radioiodine uptake on scintigraphy (Fig. 10).

Subacute thyroiditis

Subacute thyroiditis is typically clinically encountered during the hyperthyroid phase secondary to symptomology, and is thus fully discussed in Thyroid Disease in Children: Part 2. These children undergo a hypothyroid phase, but typically this is short-lived. Moreover, classically the diagnosis is known secondary to the clinical presentation (i.e. the immediate prior episode of hyperthyroidism). Although rare in children, this condition should be considered in the hypothyroid child. US and scintigraphic findings are fully discussed in Thyroid Disease in Children: Part 2 please refer to this review for full details.

Miscellaneous causes of hypothyroidism

The remaining etiologies for hypothyroidism are rare. Central (or secondary) hypothyroidism occurs when there is an underlying abnormality in the pituitary gland or hypothalamus resulting in decreased or absent production of their respective stimulating hormones (TSH from the pituitary gland, thyrotropin releasing hormone from the hypothalamus) [27]. Peripheral defects in thyroid hormone metabolism (such as resistance to thyroid hormone secondary to a mutation in the peripheral receptor site) are also very rare etiologies for hypothyroidism. Other conditions associated with hypothyroidism are listed in Table 3.

Conclusion

Hypothyroidism in the child has various etiologies. It is crucial to make an early diagnosis to prevent both mental and physical developmental abnormalities. Imaging can be of significant benefit in distinguishing between possible etiologies and establishing the underlying pathology. An organized approach can help the imager to distinguish between the possibilities and guide patient care.

Conflicts of interest None

References

1. Babcock DS (2006) Thyroid disease in the pediatric patient: emphasizing imaging with sonography. Pediatr Radiol 36:299–308, quiz 372–373
2. Sfakianakis GN, Ezuddin SH, Sanchez JE et al (1999) Pertechnetate scintigraphy in primary congenital hypothyroidism. J Nucl Med 40:799–804
3. Lyshchik A, Drozd V, Demidchik Y et al (2005) Diagnosis of thyroid cancer in children: value of gray-scale and power Doppler US. Radiology 235:604–613
4. Zimmermann MB, Hess SY, Molinari L et al (2004) New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. Am J Clin Nutr 79:231–237
5. Schoen EJ, Clapp W, To TT et al (2004) The key role of newborn thyroid scintigraphy with isotopic iodide (123I) in defining and managing congenital hypothyroidism. Pediatrics 114:e683–e688
6. LaFranchi SH (2011) Approach to the diagnosis and treatment of neonatal hypothyroidism. J Clin Endocrinol Metab 96:2959–2967
7. American Academy of Pediatrics, Rose SR, Section on Endocrinology and Committee on Genetics, American Thyroid Association et al (2006) Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 117:2290–2303

8. Olivieri A, Stazi MA, Mastroiacovo P et al (2002) A population-based study on the frequency of additional congenital malformations in infants with congenital hypothyroidism: data from the Italian Registry for Congenital Hypothyroidism (1991-1998). J Clin Endocrinol Metab 87:557–562
9. Razavi Z, Yavarikia A, Torabian S (2012) Congenital anomalies in infant with congenital hypothyroidism. Oman Med J 27:364–367
10. Bessho K, Etani Y, Ichimori H et al (2009) Increased type 3 iodothyronine deiodinase activity in a regrown hepatic hemangioma with consumptive hypothyroidism. Eur J Pediatr 169:215–221
11. Clerc J, Monpeyssen H, Chevalier A et al (2008) Scintigraphic imaging of paediatric thyroid dysfunction. Horm Res 70:1–13
12. Lobo G, Ladrón de Guevara D, Arnello F et al (2003) Tc99m-pertechnetate thyroid scintigraphy in newborns with congenital hypothyroidism. Rev Med Chil 131:283–289
13. Wildi-Runge S, Stoppa-Vaucher S, Lambert R et al (2012) A high prevalence of dual thyroid ectopy in congenital hypothyroidism: evidence for insufficient signaling gradients during embryonic thyroid migration or for the polyclonal nature of the thyroid gland? J Clin Endocrinol Metab 97:E978–E981
14. Rahbar R, Yoon MJ, Connolly LP et al (2008) Lingual thyroid in children: a rare clinical entity. Laryngoscope 118:1174–1179
15. Ruchała M, Szczepanek E, Sowiński J (2011) Diagnostic value of radionuclide scanning and ultrasonography in thyroid developmental anomaly imaging. Nucl Med Rev Cent East Eur 14:21–28
16. Manohar K, Bhattacharya A, Kashyap R et al (2010) Concurrent sublingual thyroid and thyroglossal cyst with functioning thyroid tissue in the absence of an orthotopic thyroid gland. Jpn J Radiol 28:552–554
17. Ren W, Zhi K, Zhao L et al (2011) Presentations and management of thyroglossal duct cyst in children versus adults: a review of 106 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 111:e1–e6
18. Parks JS, Lin M, Grosse SD et al (2010) The impact of transient hypothyroidism on the increasing rate of congenital hypothyroidism in the United States. Pediatrics 125:S54–S63
19. Eugster EA, LeMay D, Zerin JM et al (2004) Definitive diagnosis in children with congenital hypothyroidism. J Pediatr 144:643–647
20. El-Shirbiny AM, Stavrou SS, Dnistrian A et al (1997) Jod-Basedow syndrome following oral iodine and radioiodinated-antibody administration. J Nucl Med 38:1816
21. Fugazzola L, Persani L, Vannucchi G et al (2007) Thyroid scintigraphy and perchlorate test after recombinant human TSH: a new tool for the differential diagnosis of congenital hypothyroidism during infancy. Eur J Nucl Med Mol Imaging 34:1498–1503
22. Keeling DH, Williams ES (1972) Changes in the normal range of thyroidal radioiodine uptake. J Clin Pathol 25:863–866
23. Intenzo CM, Capuzzi DM, Jabbour S et al (2001) Scintigraphic features of autoimmune thyroiditis. Radiographics 21:957–964
24. Cappa M, Bizzarri C, Crea F (2010) Autoimmune thyroid diseases in children. J Thyroid Res 2011:675703
25. Intenzo CM, dePapp AE, Jabbour S et al (2003) Scintigraphic manifestations of thyrotoxicosis. Radiographics 23:857–869
26. Kangelaris GT, Kim TB, Orloff LA (2012) Role of ultrasound in thyroid disorders. Ultrasound Clinics 7:197–210
27. Rastogi MV, LaFranchi SH (2010) Congenital hypothyroidism. Orphanet J Rare Dis 5:17