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REVIEW

Thyroid disease in children: part 2

State-of-the-art imaging in pediatric hyperthyroidism

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Abstract Hyperthyroidism occurs secondary to overproduction of thyroid hormone by the thyroid gland. This condition can have rather serious effects on children, and thus timely diagnosis and treatment are of utmost importance. Imaging is quite useful in the management of children with hyperthyroidism. In addition to determining the underlying pathology, radiologic exams are crucial for therapy. This article describes the underlying etiologies of pediatric hyperthyroidism and provides general information on treatment.

Keywords Hyperthyroidism · Pediatric hyperthyroidism · Pediatric Graves disease · Neonatal hyperthyroidism

Introduction

Hyperthyroidism is defined as any condition of the thyroid gland that results in overproduction of thyroid hormone. This is distinct from thyrotoxicosis, which is a hypermetabolic state produced when thyroid hormone levels are elevated; thus thyrotoxicosis can occur in the presence of a normally functioning thyroid gland [1, 2]. Hyperthyroidism is relatively uncommon in children [3] but can have a significant deleterious impact on development if not diagnosed early. In addition to the classic symptoms of hyperthyroidism (weight loss, heat intolerance, tachycardia, hypertension, palpitations, diarrhea, goiter, exophthalmos, etc.), children can have accelerated bone growth and maturation, premature puberty, and poor school performance (Table 1).

Routine laboratory evaluation in children suspected of having hyperthyroidism includes TSH (thyroid-stimulating hormone), T3 (triiodiothyrine) and T4 (thyroxine) levels; several additional lab values are also utilized. A brief summary of the major thyroid blood studies and their utility in managing hyperthyroidism can be found in Table 2. Integration of laboratory and clinical data is critical in assessing and treating the thyrotoxic child and must be utilized in conjunction with imaging to provide appropriate care.

Multiple etiologies exist for hyperthyroidism in children. Graves disease is the most common pathology [4–6], but other autoimmune conditions can occur. Less frequently, children have hyperthyroidism as a result of thyroiditis, underlying genetic conditions or syndromes, toxic nodules, exposure to excessive amounts of iodine or pituitary adenomas. Specific etiologies for hyperthyroidism exist in the neonatal period and are described here.

Modalities

A brief review of the various imaging modalities is required prior to discussion of the various etiologies for pediatric hyperthyroidism.

Scintigraphy

Nuclear medicine imaging is based on capturing emitted energy utilizing gamma cameras. Three radiopharmaceuticals are used in evaluating the thyroid gland: I-123, Tc-99m, and I-131. The first two (I-123 and Tc-99m) are the primary agents employed for imaging. These are both low-energy agents with short half-lives as compared to I-131, thus lowering radiation exposure. A more extensive review of the physical properties

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Table 1 Signs and symptoms of hyperthyroidism

General	Physical signs	Specific to children
Poly-phagia/dipsia/uria	Exophthalmos	Accelerated bone maturation
Diarrhea	Tachycardia/Palpitations	Poor school performance
Heat intolerance	Hypertension	Often misdiagnosed with attention deficit hyperactivity disorder (ADHD)
Irritability/hyperactivity	Goiter	
Tremor	Weight loss	
Menstrual irregularity	Increased perspiration	
	Shortened deep tendon reflexes	

of these radiopharmaceuticals is presented elsewhere in this issue in "Thyroid Disease in Children: Part 1."

I-123 is administered orally and is used for thyroid imaging of the hyperthyroid patient at our institution. A thyroid probe is used to obtain radioactive iodine uptake (RAIU) values at 4 and 24 h, and images of the thyroid gland are obtained at 4 h. Images acquired include anterior planar, and pinhole anterior, left anterior oblique, and right anterior oblique views. Oblique views are needed to ensure that overlying tissue does not obscure small hot and cold defects. Anterior planar radioiodine uptake patterns are extremely important in formulating an accurate differential diagnosis (Fig. 1).

Graves disease is the most common etiology for pediatric hyperthyroidism. Radioiodine ablation is frequently required for the therapy of Graves disease, and thus the 24-h radioiodine uptake data are critical because they are utilized in dose determination. Pertechnetate is not utilized in evaluation of the hyperthyroid patient at our institution because this radiotracer is indicative only of thyroid trapping capabilities. Because pertechnetate is not an iodine compound, organification cannot occur; thus 24-h data could not be acquired for ablation planning if pertechnetate were used.

Ultrasound

Sonographic evaluation can be important in the workup of pediatric hyperthyroidism but typically is performed as a result of scintigraphic findings; in particular, US is required if a nodule (hot or cold) is detected on scintigraphy. Because most cases of hyperthyroidism are attributable to Graves

Table 2 Pertinent laboratory tests and selected values in hyperthyroidism

Laboratory value	Description	Normal value[a]
Thyroid-stimulating hormone (TSH, thyrotropin)	Hormone produced by pituitary gland; binds to TSH receptor on thyroid follicular cell; results in increased production/release of thyroid hormones	0.5–4.0 μIU/mL
Thyroxine (T4)	Thyroid hormone; lab value includes bound and unbound forms; contains four iodine atoms	4.5–10.0 μg/dL
Triiodiothyrine (T3)	Thyroid hormone; contains 3 iodine atoms; more potent thyroid hormone that can be derived from T4	90–260 ng/mL
Free T4	More accurate measurement of T4 levels; not affected by protein levels (as opposed to T4)	0.8–2.0 ng/dL
Thyrotropin releasing hormone (TRH, thyroid releasing factor—TRF)	Hormone produced by hypothalamus; acts on pituitary to induce release of TSH	Values vary significantly according to child's age
Thyroxine binding globulin	Primary protein that transports/binds thyroid hormone in blood	13.0–30.0 μg/mL
Thyroid peroxidase antibody (TPO)	Antibody against thyroid follicular cell enzyme that is used in multiple steps of thyroid hormone synthesis; present in several autoimmune conditions (e.g., Hashimoto, Graves)	0.0–9.0 IU/mL
Thyroglobulin antibody	Antibody against thyroglobulin molecule	0–4.0 IU/mL
TSH receptor antibodies (TRAb)	Laboratory tests used to evaluate for stimulating or inhibitory antibodies	TSI: < or = 122% basal activity
	Stimulating: thyroid-stimulating immunoglobulin (TSI), thyroid-stimulating antibody (TSAb); specific for Graves but lower sensitivity	TBII: < or = 1.75 IU/L
	Inhibitory antibodies (TSH receptor binding inhibitor immunoglobulin—TBII) less specific, but more sensitive for Graves	

[a] The laboratory ranges provided above apply to the broadest pediatric age range. Most of these values vary slightly throughout childhood and more significantly in the neonatal and infant period. Thus these values should be used as a general reference range, but for specific values the imager must refer to the laboratory data references used at his or her institution

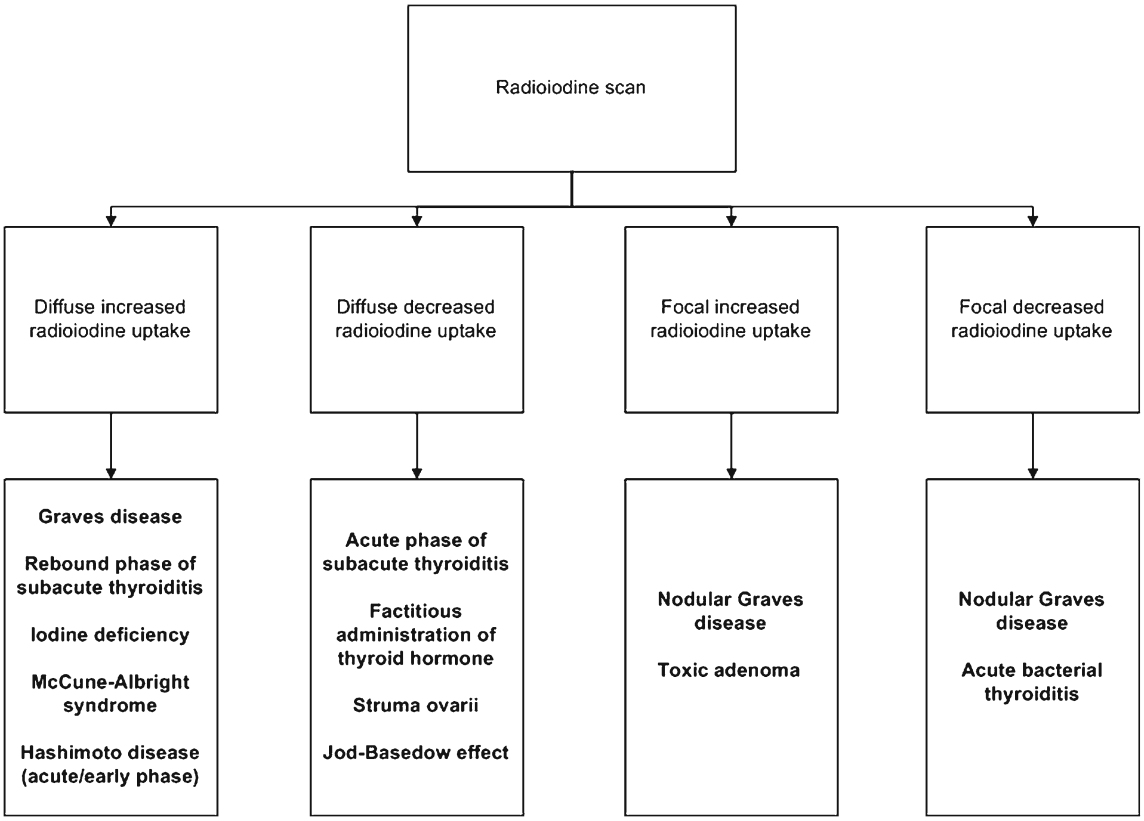

Fig. 1 Diagnostic approach to hyperthyroidism using radioiodine scintigraphy

disease (for which US findings are fairly nonspecific), US is not as useful as a primary imaging modality. Appropriately performed sonography includes the use of high-frequency (10–15 MHz) linear-array transducers, which provide detailed anatomical information [7]. 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 standards [8]. 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 [9].

Doppler interrogation can provide useful additional information. The normal thyroid gland has only moderate vascularity. Increased Doppler flow is suggestive of Graves disease in the correct clinical setting. Doppler US is also used in the evaluation of thyroid nodules and masses [9].

Miscellaneous modalities

The remaining modalities, including fluoroscopy, CT, MRI and positron emission tomography (PET), are not utilized as frequently in thyroid imaging. Fluoroscopy is occasionally required in the evaluation of remnants of the pyriform sinus. CT and MRI are not utilized regularly for primary evaluation of the thyroid gland but do occasionally detect abnormalities incidentally. Often these patients proceed to sonography or scintigraphy for further characterization. PET can occasionally demonstrate incidental thyroid uptake, both diffusely and focally. Again, this finding often necessitates sonography or nuclear medicine for further evaluation. Cross-sectional imaging of the brain is also useful for the rare patient with central hyperthyroidism.

Thyroid disease in children

Hyperthyroidism can occasionally occur in neonates; however, the majority of cases in the pediatric population are in older children. We will describe pediatric etiologies of hyperthyroidism including autoimmune and non-autoimmune conditions as well as toxic adenomas, pituitary adenomas and miscellaneous pathologies. We also present a brief discussion on neonatal causes of hyperthyroidism.

Autoimmune thyroiditis

Graves disease

Graves disease is the most common etiology for hyperthyroidism in children [3–6] and is characterized by the clinical triad of diffuse goiter, ophthalmopathy and hyperthyroidism. This

condition occurs secondary to auto-production of stimulating antibodies against the thyroid cell TSH receptor site, with resultant increased production and release of thyroid hormone.

Several conditions are associated with Graves disease, including other autoimmune conditions such as lupus, rheumatoid arthritis and Sjogren syndrome [10]. There is also an increased incidence of Graves disease in children with type I diabetes and celiac disease [3, 10]. Children with Down syndrome also have an increased risk for thyroid disease [10]; these children can present with hyperthyroidism secondary to Graves disease or with hypothyroidism. Children with Down syndrome and Graves disease might require radioiodine ablation and can be treated successfully with the cooperation of the child's parents or care providers and the nuclear medicine staff (see discussion below on Graves therapy).

Diagnosis of Graves disease in children can be challenging; children often initially present with nonspecific behavioral symptoms such as attention difficulties, hyperactivity and poor school performance [3]. However, recognition of classic physical signs and symptoms can usually facilitate the diagnosis. These children are frequently tachycardic, often requiring beta-blockade for control. Other symptoms of hyperthyroidism are variably present (Table 1). Children with Graves disease have decreased TSH levels and increased T3 and T4 levels. In unclear cases other laboratory data can be acquired. Thyroid peroxidase (TPO) antibodies are frequently elevated in autoimmune thyroid disease but are nonspecific and can be abnormal in hyper- and hypothyroid autoimmune conditions. TSH receptor antibodies (TRAb), specifically thyroid-stimulating antibody (TSAb) and thyroid-stimulating immunoglobulin (TSI), are specific for Graves disease (Table 2) [11].

In many children Graves disease can be diagnosed confidently with clinical presentation and laboratory data alone. However, the classic clinical triad might not be present and other etiologies for hyperthyroidism must then be considered. In these cases nuclear medicine studies are of critical importance for diagnosis; moreover, RAIU values are necessary for radioiodine therapy planning. For these reasons, radioiodine scintigraphy is typically performed. Graves disease has a classic scintigraphic appearance, with an enlarged thyroid gland and a prominent pyramidal lobe (Fig. 2) [12]. RAIU values at 4 h and 24 h are both elevated, with 24-h uptakes typically ranging between 50% and 80% (normal RAIU values are 5–12% at 4 h, 10–30% at 24 h) [13]. Of note, the etiology for diffuse increased radioiodine uptake in a nontoxic patient is quite different from that of the toxic patient, and thus it is of critical importance to interpret scintigraphy studies in combination with laboratory and clinical data.

The gray-scale US findings of Graves disease are nonspecific, and include glandular enlargement and heterogeneity in echotexture (Fig. 3). Doppler evaluation typically

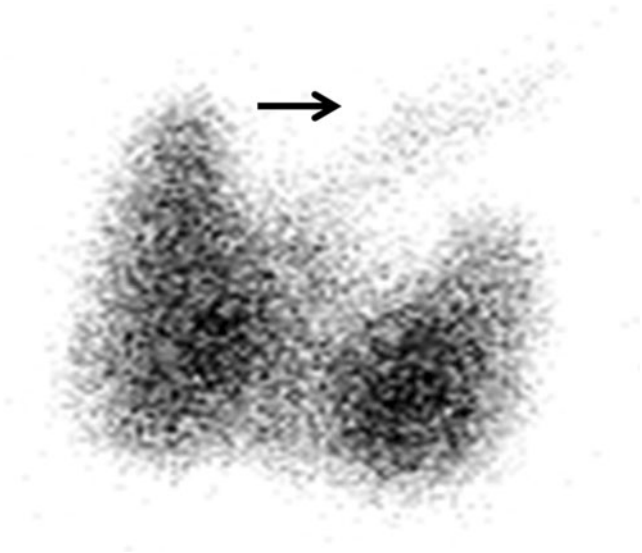

Fig. 2 Planar I-123 scintigraphy images obtained at 4 h show an enlarged thyroid gland with a prominent pyramidal lobe (*arrow*) in a 14-year-old girl with Graves disease

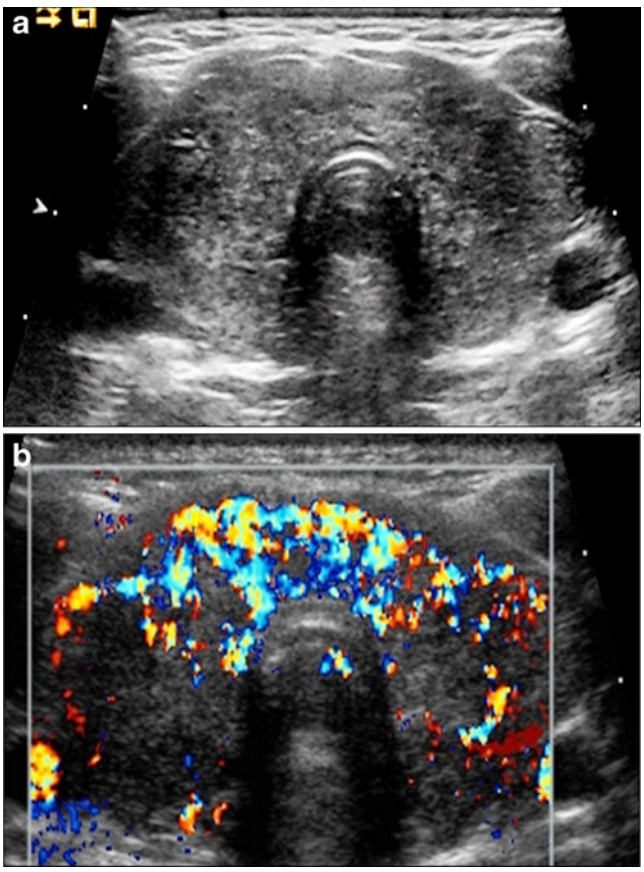

Fig. 3 Graves disease in a 14-year-old girl. **a** Gray-scale transverse US of the thyroid shows an enlarged and markedly heterogeneous gland. **b** Doppler US reveals increased flow throughout the gland

demonstrates hypervascularity (Fig. 3), producing a so-called thyroid inferno [9, 14]. Although US findings are often nonspecific, they can be quite useful in certain cases such as when a palpable nodule is detected (i.e. nodular Graves disease or Marine-Lenhart syndrome).

Therapy for Graves disease remains an area of controversy, particularly in children. Antithyroid medications, including propylthiouracil and methimazole, act by inhibiting thyroid hormone synthesis [6]. However, long-term remission rates in children receiving these medications are less than 30% after 2 years [6, 15]. Both medications have an increased risk of agranulocytosis. Moreover, recent studies have found that patients treated with propylthiouracil can have up to a 25% risk of severe hepatotoxicity, with several reported cases of end-stage liver disease requiring transplantation [6]. Thus this medication is rarely used in children [4]. Methimazole has less risk of serious complications; however, reports suggest that therapy with either medication can decrease sensitivity of the thyroid to I-131 therapy (which is often required secondary to low spontaneous remission rates) [15]. Subtotal or total thyroidectomy is utilized at some institutions, with high success rates (particularly for total thyroidectomy). However, the risk of transient or partial hypoparathyroidism, hemorrhage, and vocal cord paralysis [5] often results in the recommendation by many endocrinologists for medical management.

I-131 therapy in children has been found to be efficacious and safe [4, 16] in the treatment of Graves disease. In radioiodine ablation, thyroid destruction occurs primarily via I-131 beta emission. Dose administration must be performed by an authorized user; some institutions give uniform fixed doses; however, many (particularly in the pediatric population) calculate the dose based on RAIU values at 24 h and thyroid mass to minimize radiation exposure. The standard formula determines dose as follows: Dose (mCi) = (uCi I-131/g thyroid tissue × tyroid weight × 100)/24 – h RAIU. Thyroid mass estimates classically are determined clinically, via physical exam; typically physicians attempt to administer 100–250 μCi I-131 per gram of thyroid tissue [4].

Nodular Graves disease

Nodular Graves disease, or Graves disease with coexistent nodules, presents in an identical fashion to Graves disease but is rare in children [17]. TSH levels are suppressed and thyroid hormone levels are elevated. In distinction to classic Graves disease, patients with nodular Graves disease typically have palpable nodules. On scintigraphy, occasional nodules will be hot (increased radioiodine uptake). However, most nodules present as regions of decreased radioiodine uptake (Fig. 4). The cold nodules actually represent regions of normally functioning thyroid tissue that are responding appropriately to the severely depressed TSH levels (Fig. 4) [12]. This

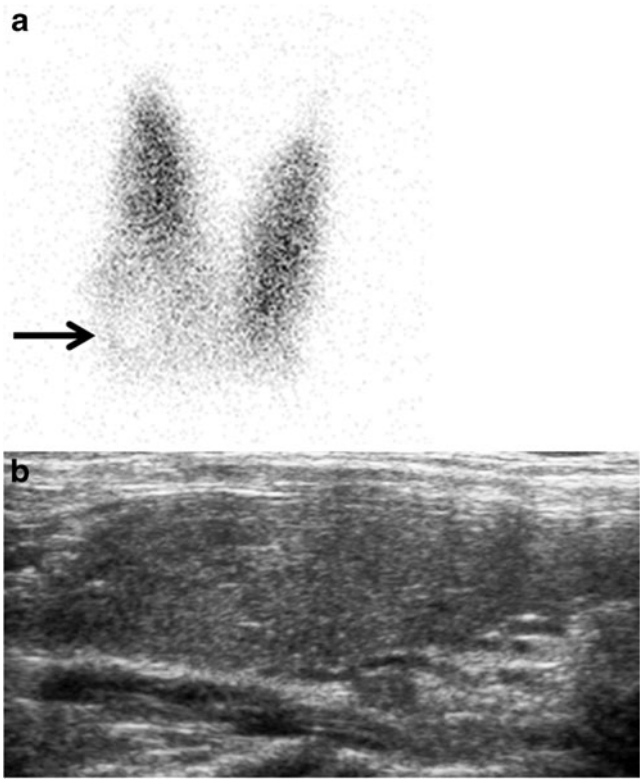

Fig. 4 Images in an 18-year-old woman with laboratory and clinical parameters of Graves disease. **a** Scintigraphy reveals a cold nodule in the inferior right lobe of the thyroid (*arrow*). **b** US performed to further evaluate the cold nodule shows no abnormality. The cold nodule in this case is compatible with a region of normally functioning thyroid-stimulating hormone (TSH)-dependent thyroid tissue; the findings are consistent with Marine-Lenhart syndrome

constellation of findings was first described by Marine and Lenhart and thus this is often referred to as Marine-Lenhart syndrome [18]. US imaging should be performed when a cold nodule is detected on scintigraphy to evaluate for underlying mass lesion. When a diagnosis of nodular Graves disease is confirmed, radioiodine therapy can be performed (as described above in patients with classic Graves disease).

Hashimoto disease

Hashimoto disease occurs secondary to autoimmune lymphocytic infiltration of the thyroid gland. Most patients are euthyroid or hypothyroid but occasionally children present with hyperthyroidism or toxicosis [17]. This occurs after rapid release of thyroid hormones secondary to acute lymphocytic infiltration and apoptosis of the follicular cells. This can occur after rapid release of thyroid hormone secondary to acute immune-mediated apoptosis of follicular cells (thyrotoxicosis without hyperthyroidism) or it can be from humoral immune mediated receptor activation similar to Graves disease. Several underlying medical conditions are associated with Hashimoto disease, including type I diabetes, celiac disease, Down

syndrome, Turner syndrome, Noonan syndrome, Williams syndrome and treated Hodgkin disease [3, 9].

On gray-scale US, Hashimoto disease can appear similar to Graves disease. The gland is enlarged and heterogeneous or coarse in echotexture [9]. There can be multiple small hypoechoic nodules (Fig. 5) [3, 9]. Unlike in Graves disease, Doppler imaging typically demonstrates normal or decreased flow in the thyroid gland of a patient with Hashimoto disease (Fig. 5). Unless they are in the acute thyrotoxic phase, children with Hashimoto have normal or decreased uptake on thyroid scintigraphy (Fig. 6).

Non-autoimmune thyroiditis

Thyroiditis refers to any inflammatory condition of the thyroid gland. In childhood, this includes acute bacterial or microbial thyroiditis, subacute thyroiditis and the previously described autoimmune conditions. The autoimmune etiologies are discussed separately because they are by far the most frequent causes of hyperthyroidism in children. Acute and subacute thyroiditis are rare in children [9, 17]. Scintigraphy is of utmost importance in differentiating the forms of thyroiditis and subsequent therapy planning.

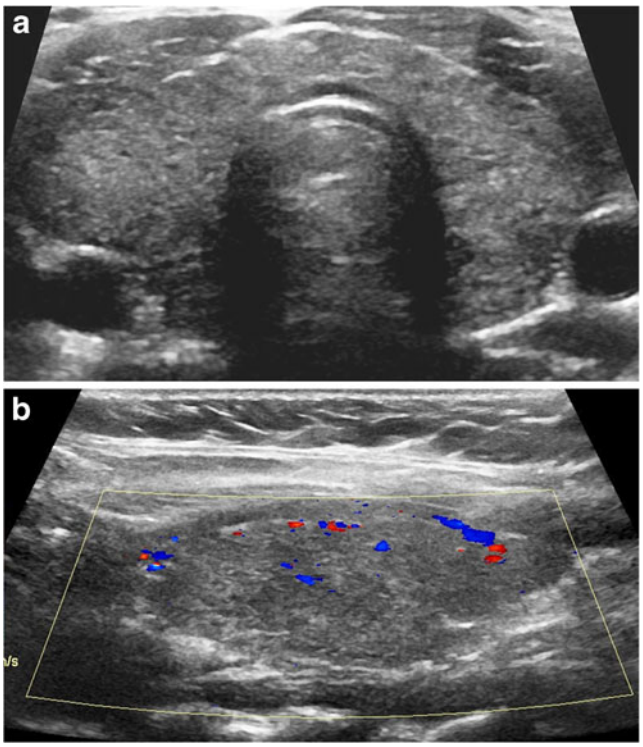

Fig. 5 Hashimoto disease in a 13-year-old girl. **a** Transverse gray-scale US shows enlargement and heterogeneity in the echotexture of the thyroid gland. **b** Doppler longitudinal imaging of the right lobe of the thyroid shows normal flow—a finding that favors Hashimoto disease over Graves

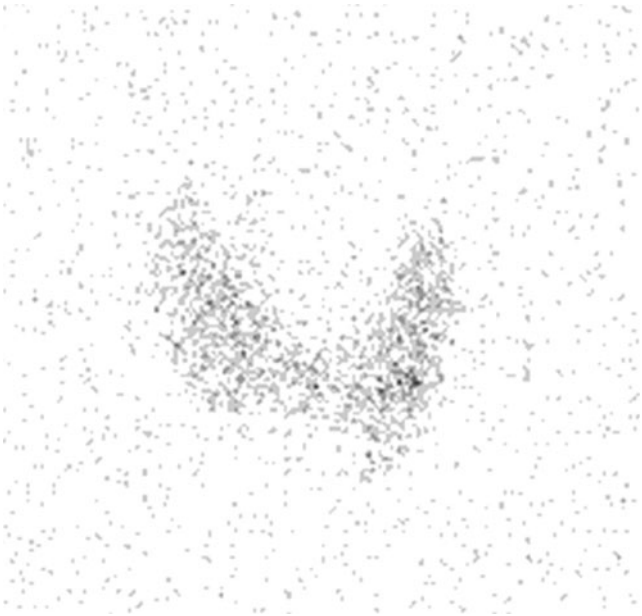

Fig. 6 Anterior planar I-123 scintigraphy in an 11-year-old boy with Hashimoto disease demonstrates diffuse decreased radioiodine accumulation throughout the gland

Acute bacterial thyroiditis

In acute bacterial thyroiditis, children present with fever, painful thyroid and sore throat [9, 17]. Destruction of the follicular cells results in release of thyroid hormone, rendering the patient thyrotoxic. These children do not typically undergo scintigraphy but would have decreased RAIU in the region of involved thyroid tissue. US imaging can demonstrate a focal region of abnormal heterogeneous echotexture or potentially an abscess (Fig. 7) [9]. Occasionally CT is obtained, often because the lesion is concerning for a mass (Fig. 7). Careful evaluation for a pyriform sinus remnant (using esophagram with focused frontal views of the pyriform sinus) should be performed because these are detected in greater than 90% of children with acute bacterial thyroiditis [17].

Subacute thyroiditis

Subacute thyroiditis can be classified according to its etiology as either granulomatous (DeQuervain disease) or lymphocytic. Granulomatous (subacute) thyroiditis is a post-viral inflammation of the thyroid gland that classically occurs in women ages 30–50 and is infrequent in children. Patients often present with neck pain and elevated erythrocyte sedimentation rate (ESR). Lymphocytic (subacute) thyroiditis is an autoimmune condition that, like Hashimoto disease, occurs secondary to lymphocytic infiltration of thyroid follicular cells [19]. In contrast to Hashimoto thyroiditis, this condition is transient. Lymphocytic thyroiditis

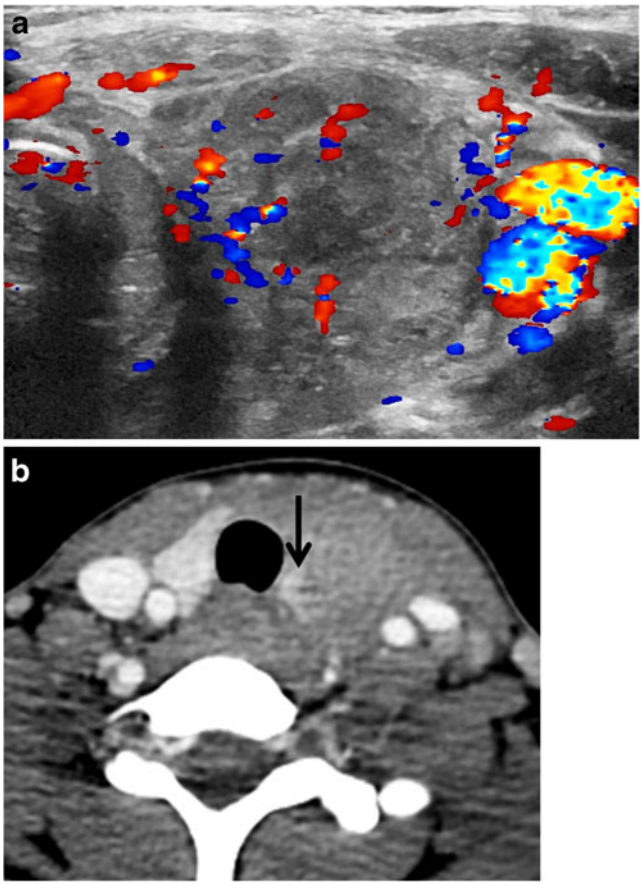

Fig. 7 Fever, neck pain and sore throat in a 13-year-old girl. **a** Transverse Doppler US of the left lobe of the thyroid demonstrates a heterogeneous phlegmonous mass with increased vascularity. **b** Contrast-enhanced axial CT image shows the lesion to be arising from the thyroid; note the minimal remaining normal enhancing thyroid tissue on the left (*arrow*)

is further classified as post-partum or painless/silent thyroiditis; post-partum cases are infrequent in children.

Laboratory and radiologic findings of subacute thyroiditis depend on the stage of disease. Laboratory values during the acute phase of the disease are identical to those of patients with Graves disease; T3/T4 are elevated, thyroid peroxidase antibodies are elevated and thyroid-stimulating hormone is markedly depressed [20]. Differentiation from Graves disease can be difficult because both have identical laboratory values and clinical presentations. Scintigraphy is crucial in diagnosing subacute thyroiditis (and thus avoiding inappropriate therapy). During the acute active inflammatory portions of the disease, children have extremely low RAIU values (typically <5%). On planar imaging, the thyroid gland is faint and difficult to distinguish from background activity (Fig. 8) [20]. This is in stark contrast to children with Graves disease, who have significantly elevated RAIU values. US imaging is not significantly helpful in distinguishing Graves disease from subacute thyroiditis. Imaging findings are nonspecific, with heterogeneity of the thyroid gland and normal vascularity (similar to Hashimoto disease).

During the beginning of the recovery/rebound phase of subacute thyroiditis, laboratory values can normalize or the patient can become mildly hypothyroid. Scintigraphy continues to show mildly depressed or potentially normal RAIU values. However, as the recovery phase progresses, the patient typically experiences worsening hypothyroidism. RAIU values elevate and can mimic values of Graves disease. Fortunately, laboratory analysis allows for differentiation between these entities; patients in the recovery phase of subacute thyroiditis are typically hypothyroid (or potentially euthyroid) in contrast to those with Graves disease, who are hyperthyroid [20]. See Table 3 for a review of subacute thyroiditis.

Differentiating between Graves disease and the acute phase of subacute thyroiditis is crucial because the two entities require significantly different therapies. The acute phase of subacute thyroiditis is a transient condition, although it can occasionally recur [1]. Although these children might require supportive management during the thyrotoxicosis (i.e. beta blockade) and hypothyroid (i.e. levothyroxine) phases, they eventually return to a euthyroid state. It is crucial to differentiate between silent thyroiditis and Graves disease to avoid the inappropriate administration of I-131 radioiodine therapy to children who are thyrotoxic secondary to subacute thyroiditis. This again emphasizes the importance of diagnostic nuclear medicine scintigraphy.

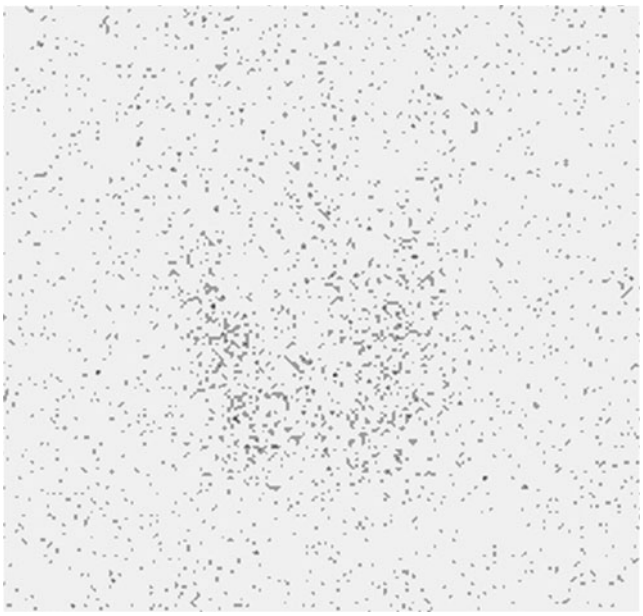

Fig. 8 Minimal I-123 uptake in an 11-year-old boy who presented with hyperthyroidism (3% and 2% RAIU values at 4 h and 24 h, respectively). The boy was negative for thyroid antibodies; the combined laboratory and imaging findings are most consistent with the acute phase of subacute thyroiditis

Table 3 Diagnostic approach to the phases of subacute thyroiditis using laboratory data and RAIU values. *RAIU* Radioactive iodine uptake, *T3/T4* triiodiothyrine/thyroxine, *TSH* thyroid-stimulating hormone

	Acute phase	Active/chronic phase	Recovery/rebound phase
T3/T4	Markedly elevated	Normal to mildly depressed	Depressed
TSH	Markedly depressed	Normal to mildly elevated	Elevated
RAIU	Markedly depressed	Normal to mildly depressed	Markedly elevated

Toxic adenoma

Toxic adenoma is a hyperfunctioning nodule that results in hyperthyroidism. This entity is also frequently referred to as toxic autonomous nodule, or Plummer disease, and is thought to occur when an adenoma undergoes gene mutations resulting in continuous production of thyroid hormone [12]. These children have suppressed TSH values, and elevated T3/T4 values similar to children with Graves disease. Antibodies against the TSH receptor are not present, which can help in distinguishing these entities. Imaging is quite useful in differentiating the two; children with toxic adenomas show a solitary nodule with significant radioiodine uptake. The remainder of the gland has diminished uptake secondary to appropriate response to a generalized lack of TSH (Fig. 9). US imaging shows a mass lesion, which can have variable features (Fig. 9). Echogenicity can be increased or decreased, homogeneous or heterogeneous; they can have a hypoechoic halo and are classically described as hypovascular [9]. These lesions can be treated with radioiodine but often require higher doses. Surgery is also a potential modality for therapy.

Pituitary adenoma

TSH-secreting adenomas infrequently cause hyperthyroidism in children. Pituitary adenomas in children are more likely to be macroadenomas than microadenomas. These can present with visual symptoms secondary to compressive effects on the optic nerve from the mass. In addition to thyroid-stimulating hormone, these masses also frequently secrete growth hormone and prolactin [17]. MR is most useful in diagnosing pituitary tumors; microadenomas (<1 cm) are typically hypointense with delayed enhancement following contrast agent administration. Macroadenomas (Fig. 10) tend to have uniform enhancement following contrast agent administration.

Miscellaneous causes of hyperthyroidism in children

Several infrequent etiologies for hyperthyroidism require brief discussion. In children, hyperthyroidism can be caused by medication overdose, e.g., accidental ingestion of excessive amounts of levothyroxine by a toddler or young child. History classically leads to diagnosis, and imaging is not usually required. Most often these children can be treated symptomatically with no long-term sequelae [21]. Factitious thyrotoxicosis, caused by intentional overuse or misuse of levothyroxine, can occur in teenagers. Scintigraphy is useful in these children; they are thyrotoxic, but have markedly depressed 24-h uptake levels. If these findings exist following exclusion of subacute thyroiditis, factitious thyrotoxicosis should be considered.

Ectopic thyroid production can occur in struma ovarii/ovarian teratoma but is exceedingly rare [2]. These patients are hyperthyroid but have markedly decreased or absent uptake on 24-h thyroid scintigraphy. Whole-body I-123 imaging can demonstrate abnormal uptake at the tumor site.

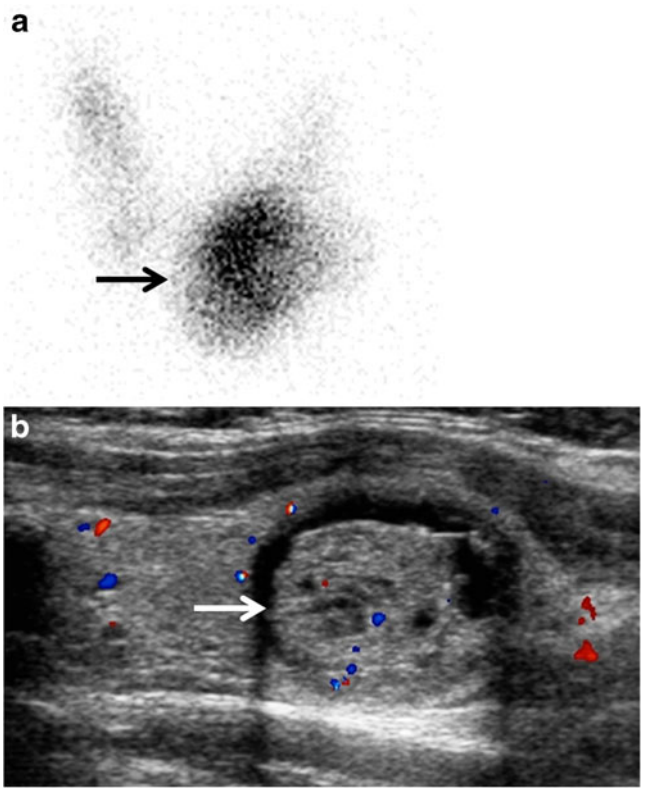

Fig. 9 Images in an 18-year-old woman who presented with hyperthyroidism. **a** I-123 planar scintigraphy demonstrates a solitary hot nodule (*arrow*) in the left lobe of the thyroid. The remainder of the gland has mildly suppressed uptake. **b** Longitudinal Doppler US of the left lobe thyroid nodule (*arrow*) shows a hypovascular and heterogeneous nodule. The findings are compatible with a toxic adenoma

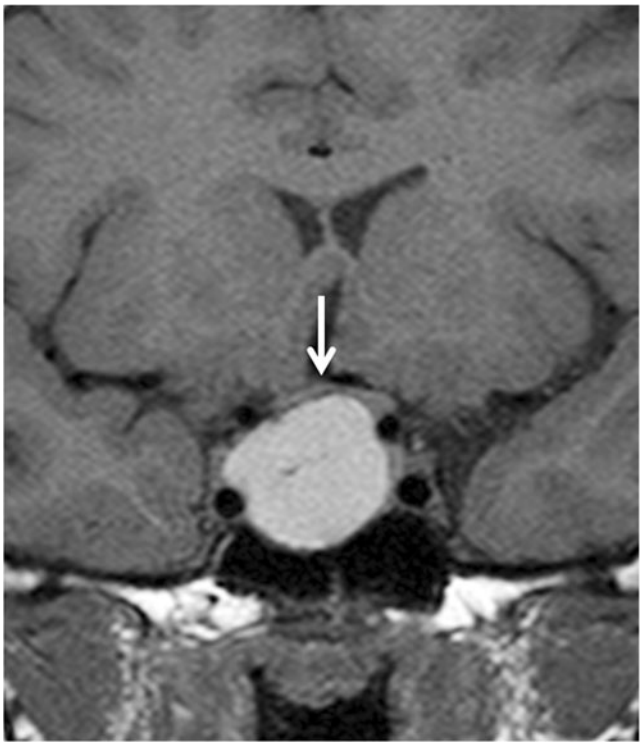

Fig. 10 Images in a 15-year-old girl who presented with visual disturbances. Coronal postcontrast T1-W MR image through the pituitary gland reveals a homogeneously enhancing macroadenoma displacing the optic chiasm (*arrow*)

The Jod-Basedow effect is a rare phenomenon that occurs secondary to exposure to large amounts of iodine in hypothyroid patients. These children are classically hypothyroid secondary to iodine deficiency and thus are not frequently encountered in industrialized nations. If exposed to large amounts of iodine, these children produce and secrete large amounts of thyroid hormone (secondary to large amounts of circulating TSH). This can lead to thyrotoxicosis. This condition can be differentiated from Graves disease by RAIU values, which are diffusely decreased or absent. Jod-Basedow results from absence of the Wolff-Chaikoff effect (Table 4) [22].

Neonatal hyperthyroidism

A brief discussion of neonatal hyperthyroidism is being presented to complete the review of pediatric hyperthyroidism. Because most neonates with hyperthyroidism have a self-limiting process, imaging (and particularly radioiodine scintigraphy) is not indicated. General knowledge of these processes can be useful in the guiding of care of these children.

Neonatal Graves disease

Neonatal Graves disease, also termed neonatal hyperthyroidism, occurs in approximately 1% of fetuses born to women with Graves disease. In these women, maternal thyroid-stimulating IgG antibodies (TSAb) cross the placenta and result in stimulation of the fetal thyroid gland. Women who have been previously treated for Graves disease with ablation still carry thyroid-stimulating immunoglobulins (TSIs), and thus their fetuses are at risk for this condition as well. Fetal hyperthyroidism is diagnosed when there is fetal goiter, tachycardia and intrauterine growth retardation. Often the goiter can be detected on prenatal US. Close monitoring pre- and post-delivery is required. Neonates can be treated with methimazole, saturated solution of potassium iodide and beta blockers, as needed. The half-life of thyroid-stimulating immunoglobulins is roughly 14 days, thus most cases of neonatal Graves disease resolve in 3–12 weeks [3].

Miscellaneous causes of neonatal hyperthyroidism

When neonatal hyperthyroidism persists beyond 3 months of age, other etiologies must be considered, including McCune-Albright syndrome, an activating mutation of the TSH receptor, and thyroid hormone resistance syndrome. McCune-Albright syndrome is classically characterized by polyostic fibrous dysplasia, café au lait spots and precocious puberty [23]. Children with McCune-Albright syndrome

Table 4 Eponyms in thyroid disease

Eponym	Description
Jod-Basedow effect	Inappropriate autoregulation occurring in patients with prolonged hypothyroidism; inhibitory feedback mechanism nonresponsive resulting in continued production/release of thyroid hormone following iodine exposure
Wolff-Chaikoff effect	Induction of hypothyroidism following iodine exposure secondary to functioning thyroid feedback mechanism
Graves disease	Autoimmune disease resulting in excess thyroid hormone production/release
Hashimoto disease	Autoimmune disease resulting in decreased thyroid hormone production/release
DeQuervain thyroiditis	Granulomatous post-viral form of thyroiditis
Marine-Lenhart syndrome	Nodular Graves disease/Graves disease with coexistant multinodular goiter

can become thyrotoxic and might require treatment or radioablation (Fig. 11).

In children with mutations of the TSH receptor, there is enhanced function of the TSH receptor; activation of the TSH receptor results in overproduction of thyroid hormones [24, 25]. These children often require radioablation as well.

Finally, children with thyroid hormone resistance syndrome have end-target tissues that do not respond to thyroid hormone (i.e. ineffective feedback loop). As such, these children have continued production of excess thyroid hormone. Radioablation is rarely used in these children; occasionally children with severe cardiac symptoms are considered for therapy [25].

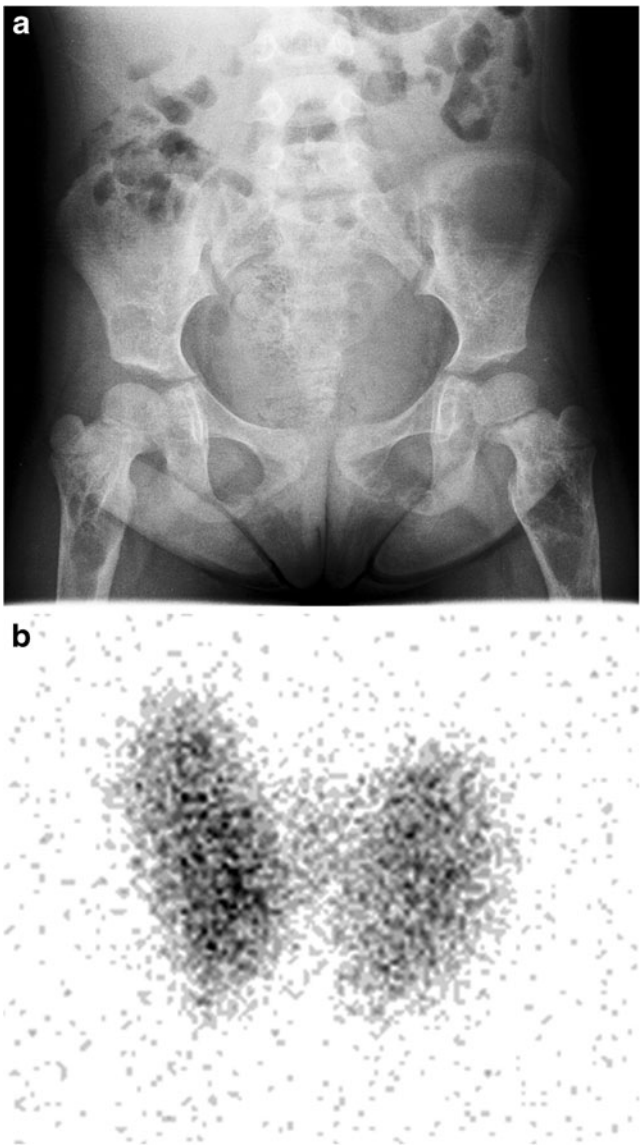

Fig. 11 McCune-Albright syndrome in a 3-year-old girl. This girl presented with precocious puberty, which led to a skeletal survey. **a** A select radiograph of the pelvis from the skeletal survey demonstrates multiple expansile lucent lesions involving the iliac wings, superior and inferior pubic rami and proximal metaphyseal portions of the bilateral femurs. The girl was subsequently found to have thyrotoxicosis. **b** Anterior planar I-123 scintigraphy demonstrates diffuse increased radiotracer accumulation throughout the gland, in a pattern identical to what would be seen in Graves disease

Conclusion

Hyperthyroidism in the pediatric patient is most commonly secondary to Graves disease; however, there are multiple other etiologies to consider. Understanding the various pathologies, along with the proper imaging techniques used to elucidate the underlying disease processes, allows for accurate diagnosis and treatment. This in turn can prevent problematic lifelong sequelae. An organized approach can help the imager in determining the correct diagnosis and in guiding care.

Conflicts of interest None

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