



Pearls and Pitfalls in Pediatric Thyroid Imaging

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This article discusses the role of imaging of the thyroid gland in children, highlighting pearls and pitfalls. In the pediatric age group, thyroid imaging is mainly performed for the evaluation of congenital hypothyroidism, diffuse thyroid enlargement, and thyroid nodules. Permanent congenital hypothyroidism is most often caused by thyroid dysgenesis. Diffuse thyroid enlargement is mainly seen in teenage girls, and most often caused by Hashimoto disease, nodular hyperplasia, Graves disease, or diffuse papillary carcinoma. Thyroid nodules are less common in children than they are in adults, but more likely to be malignant; TI-RADS criteria may underestimate the risk of malignancy in children, and lead to erroneous classification downgrading. Knowledge of unique features of thyroid imaging in the pediatric population is critical for accurate diagnosis and management recommendations.

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Introduction

The normal thyroid gland has similar appearances at all ages, with homogeneous echotexture and echogenicity slightly greater than that of adjacent muscles¹ (Fig. 1). In the pediatric population, imaging evaluation of the thyroid gland is mainly performed in 1 of 3 different scenarios: congenital hypothyroidism, diffuse thyroid enlargement, and presence of thyroid nodule.² This article will discuss the role of imaging in these 3 scenarios, highlighting pearls and pitfalls.

Congenital Hypothyroidism

Deficiency of thyroid hormone at birth, which may be transient or permanent.³ Transient causes include maternal thyroid-blocking antibodies, maternal antithyroid medication, maternal iodine deficiency, and iodine overload (such as from iodine-based antiseptics). These do not require imaging due to their temporary nature. Permanent causes include thyroid dysgenesis (responsible for about 80% of cases of permanent hypothyroidism), dyshormonogenesis (about 20% of cases of permanent hypothyroidism), and hypopituitarism

(very rare). Thyroid dysgenesis is further divided into agenesis, hemiagenesis, hypoplasia, and ectopia.

The need for imaging in congenital hypothyroidism is controversial. Those in favor argue that imaging evaluates the cause, clarifies prognosis, and guides management. Those against imaging contend that management is not changed.⁴ When imaging is used, radionuclide scintigraphy is traditionally considered the reference standard for anatomical diagnosis. However, scintigraphy involves ionizing radiation exposure. Furthermore, transient hypothyroidism may be misdiagnosed as thyroid agenesis by scintigraphy.⁴

Ultrasound is an ionizing-radiation-free alternative to radionuclide scintigraphy. However, thyroid ectopia may be misdiagnosed as agenesis by ultrasound³ (Fig. 2).

Thyroid Agenesis

Absence of the thyroid gland is diagnosed when no thyroid tissue is identified on ultrasound or radionuclide scanning³ (Fig. 3). On ultrasound, in the absence of visible thyroid tissue in its expected location, it is imperative to look for ectopic thyroid tissue before entertaining the diagnosis of thyroid agenesis. This requires meticulous scanning along the midline neck from the thyroid cartilage up to the base of the tongue.³

Thyroid Hemiagenesis

Failure of formation of one of the thyroid lobes (usually the left). While often asymptomatic and found incidentally

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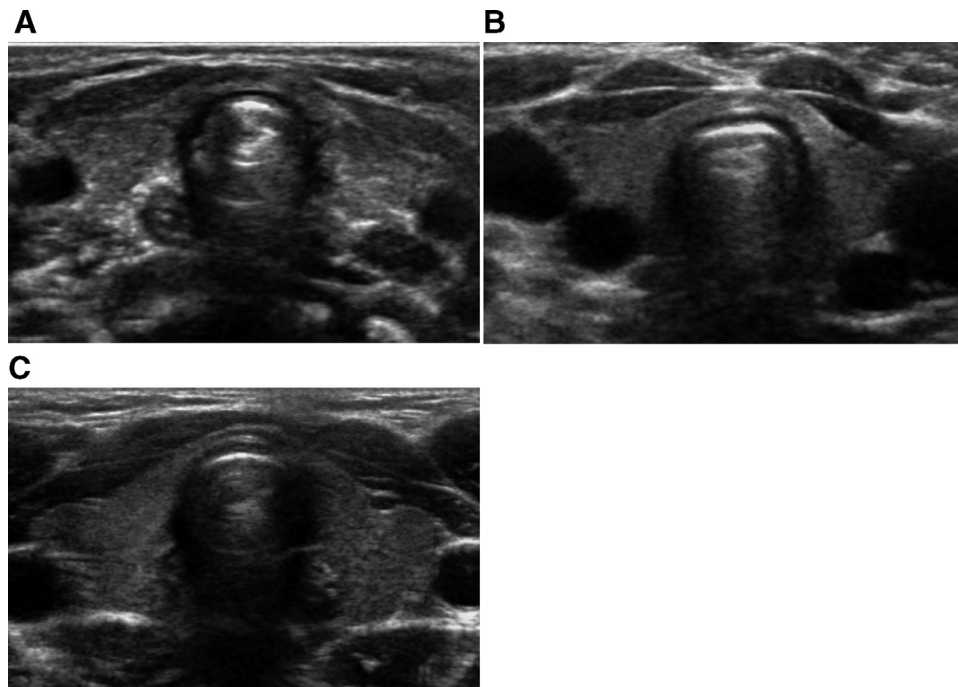


Figure 1 Transverse gray scale ultrasound images of normal thyroid glands show similar appearances in children of different ages. A. One-month-old boy. B. One-year-old girl. C. 10-year-old girl.

(Fig. 4), thyroid hemiagenesis may lead to congenital hypothyroidism in some patients.^{3,5}

Thyroid Ectopia

Thyroid tissue absent from orthotopic location and present anywhere along the course of thyroid descent from the base of the tongue to the level of the thyroid cartilage⁴ (Fig. 5).

Scintigraphy is considered more sensitive than ultrasound on finding ectopic thyroid tissue.

Dyshormonogenesis

Inborn errors of thyroid hormone metabolism. The thyroid gland is normally located but enlarged on ultrasound and with increased uptake on scintigraphy (Fig. 6).

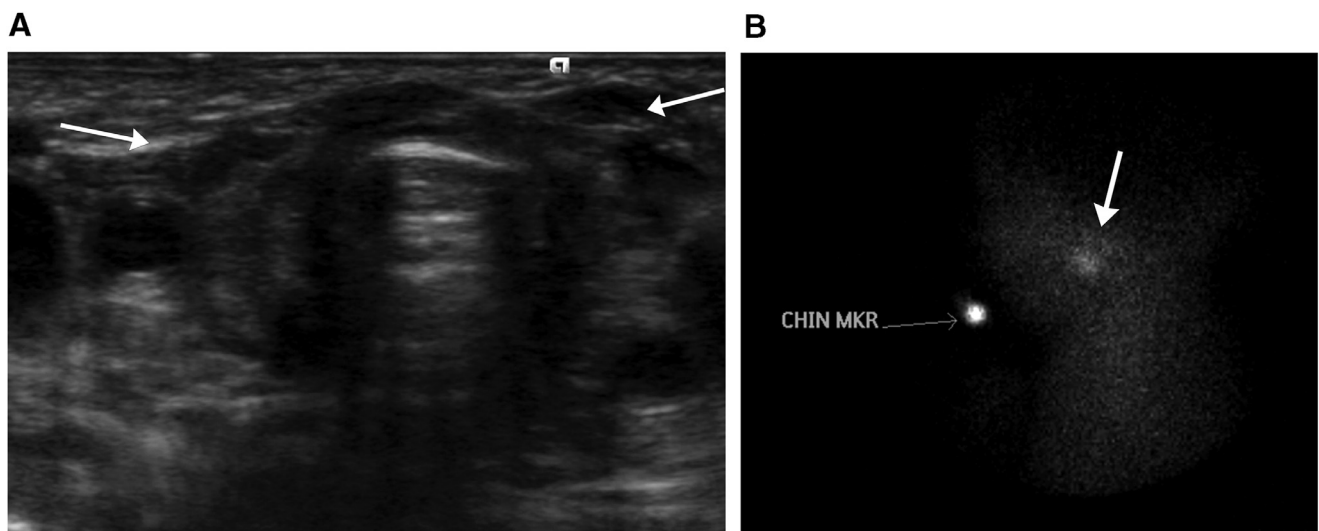


Figure 2 Ectopic thyroid misdiagnosed as thyroid agenesis by ultrasound. Four-day-old girl with abnormal congenital blood spot screening. A. Transverse gray scale ultrasound image of the anterior neck failed to show the thyroid on its usual position wrapping around the anterior aspect of the trachea (arrows). B. Tc99m pertechnetate scintigraphy performed 4 days later. Left lateral projection shows uptake at the inferior portion of the mouth posteriorly (arrow), in keeping with ectopic lingual thyroid.

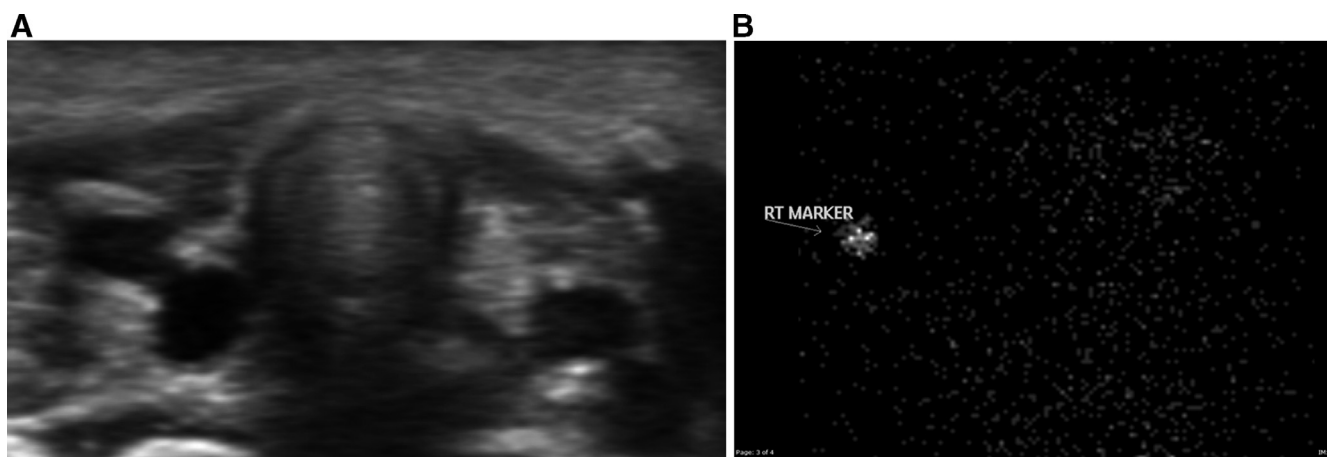


Figure 3 Thyroid agenesis. Eight-day-old girl with abnormal congenital blood spot screening. A. Transverse gray scale ultrasound image of the anterior neck along the thyroid bed shows no thyroid tissue. B. Iodine 123 scintigraphy performed 5 days later. Frontal projection shows no thyroid uptake.



Figure 4 Thyroid hemiagenesis. Six-year-old boy with suspected mass over the right of the thyroid. Transverse gray scale ultrasound image shows absence of the left thyroid lobe. The right lobe is prominent in size accounting for the suspected palpable mass and contains small colloid cysts.

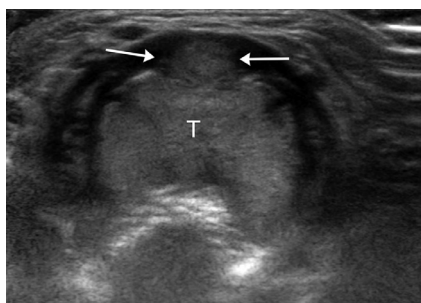


Figure 5 Ectopic thyroid. 22-day-old girl with abnormal congenital blood spot screening. Transverse gray scale ultrasound image at the floor of the mouth shows the thyroid gland as a solid nodule (between arrows), isoechoic to the tongue (T).

Diffuse Thyroid Enlargement

Most cases of diffuse enlargement of the thyroid gland in children are due to one of the following 4 conditions: chronic lymphocytic thyroiditis (Hashimoto disease); nodular hyperplasia; diffuse hyperplasia (Graves disease); and diffuse papillary carcinoma.² Regardless of the cause, diffuse thyroid enlargement has a female predominance and is most commonly seen in early teenage years.²

Hashimoto Disease

Hashimoto disease is an autoimmune disorder characterized by lymphocytic infiltration of the thyroid and is the most

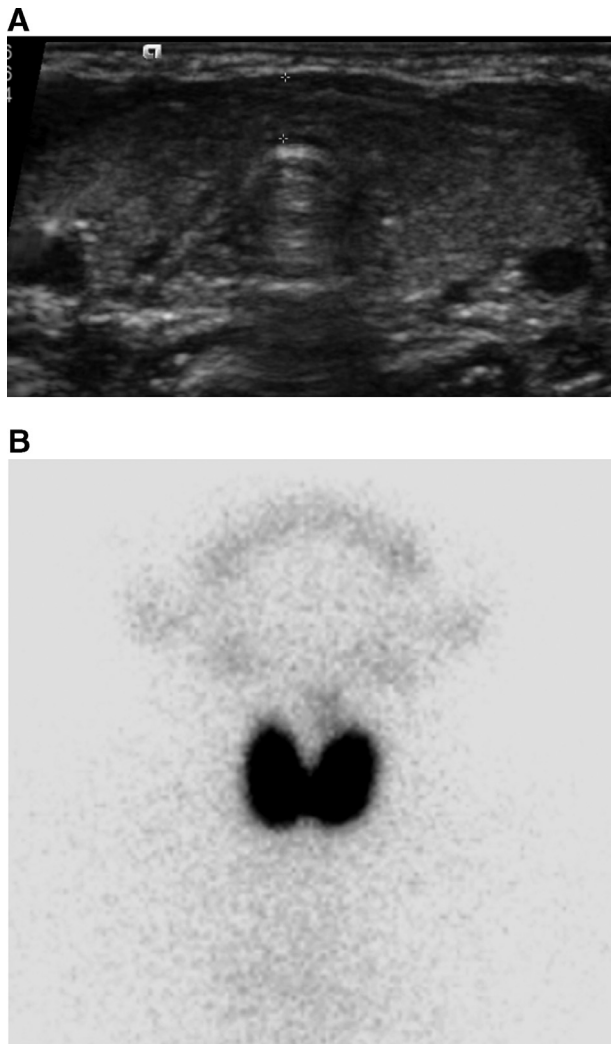


Figure 6 Thyroid dysmorphogenesis in 2 patients with abnormal congenital blood spot screening. A. Transverse gray scale ultrasound image in a 12-day-old girl shows an enlarged thyroid gland. B. Tc99m pertechnetate radionuclide scintigraphy on frontal projection in a 6-week-old girl shows increased thyroid uptake.

common cause of hypothyroidism in children and adolescents. It is 50 times more common than Graves disease in childhood, with an incidence of about 1/100 patients. Although on clinical examination the gland might appear enlarged on initial stages of the disease, such enlargement may be at times illusive, secondary to increased stiffness, with normal volumes on ultrasound. On later stages the gland atrophies. Echogenicity is normal initially, and becomes decreased in later stages. There are different patterns of echotexture including heterogeneous thyroid with fibrotic septa, a diffuse pseudo-nodular pattern, and less common with presence of discrete nodules. The thyroid borders are often lobulated. Vascularity is initially normal, subsequently increased (at which stage it might be difficult to

differentiate from Graves disease by ultrasound), and decreased on later stages^{2,6} (Fig. 7).

Nodular Hyperplasia

Seen in 2 different subset of patients: those with dietary iodine deficiency (most common cause worldwide), and those with congenital defect in hormonal synthesis. On ultrasound, there is diffuse enlargement of the gland, heterogeneous echotexture with nodules (some with liquefaction, at times with colloid signature). Although the nodules may be hypervascular on color Doppler, the overall gland vascularity is usually normal^{2,6,7} (Fig. 8).

Graves Disease

Graves disease is an autoimmune disorder characterized by circulating autoantibodies that stimulate thyroid growth resulting in hyperthyroidism. Graves disease is rare in children, with an incidence of about 1/5000. On ultrasound, there is diffuse gland enlargement, heterogeneous echotexture, and increased vascularity on color Doppler (Fig. 9). With advanced disease one may find hyperechoic and coarse skeletal muscles, as well as enlarged extraocular muscles resulting in thyroid ophthalmopathy (Fig. 10). Colloid cysts are rare, seen in patients who do not comply with treatment.^{2,6}

Papillary Carcinoma

The rare diffuse sclerosing variant of papillary carcinoma may present on ultrasound as a widespread irregular or nodular gland enlargement, which may spare parts of the gland. Microcalcifications may be present. Cervical lymphadenopathy usually indicates extra-thyroid spread⁸⁻¹⁰ (Fig. 11).

Nodule

Thyroid nodules may be palpable or found incidentally by imaging. They are less common in children than they are in adults, but more likely to be malignant.^{8,11,12} The most common benign thyroid nodules are hyperplastic nodules, colloid nodules, adenomas, and focal chronic lymphocytic (Hashimoto) thyroiditis^{8,11,12} (Fig. 12). Their differentiation from malignant nodules can sometimes be difficult on ultrasound.

The vast majority of malignant nodules are due to papillary carcinoma, followed by follicular carcinoma, and much less commonly medullary and anaplastic carcinoma. Malignant thyroid nodules peak in teenage years and have a female predominance. Their incidence seems to be increasing, perhaps secondary to incidental detection due to increased

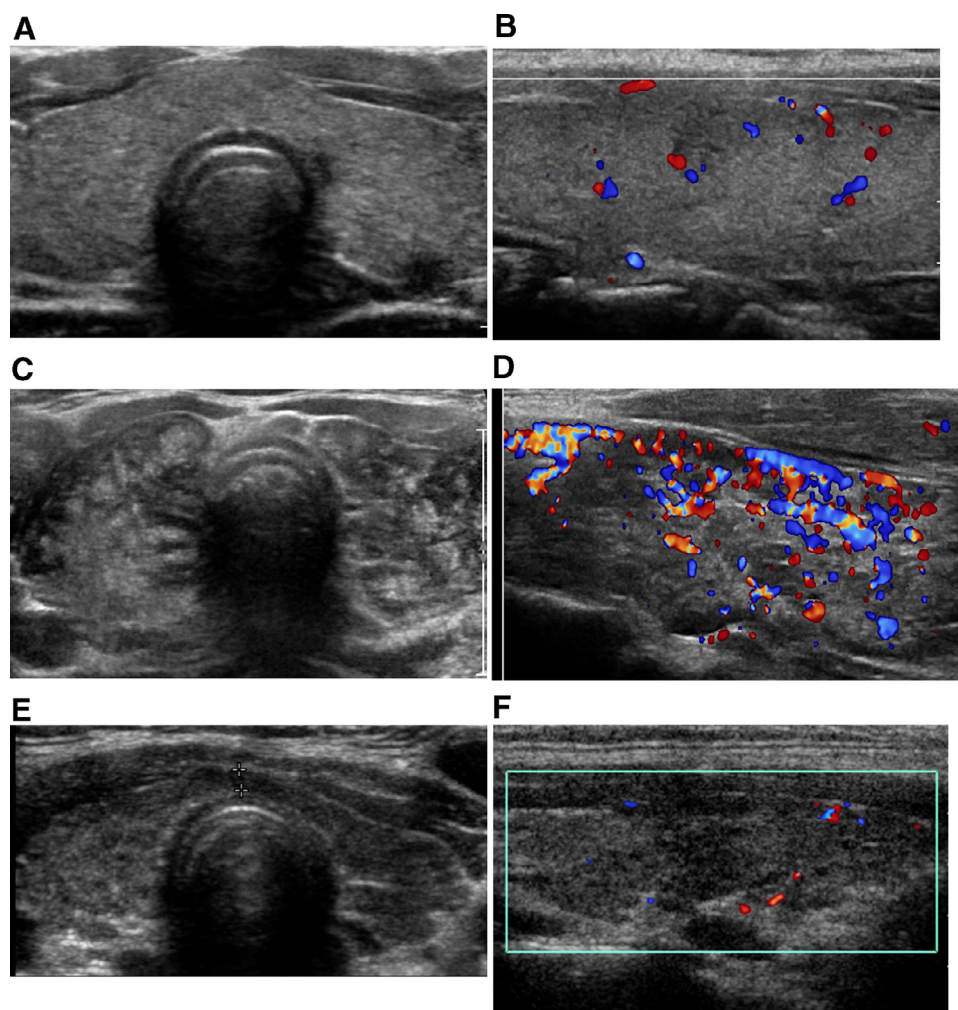


Figure 7 Hashimoto disease. Time progression of imaging findings on gray-scale and color Doppler ultrasound. On initial stages the gland is normal in size or enlarged, retains normal echogenicity but with heterogeneous echotexture (A). Vascularity on color Doppler is normal (B). Subsequently, the echogenicity of the gland becomes heterogeneous (C), and vascularity increases (D). On later stages, the gland atrophies (E) and vascularity is scant (F).

thyroid imaging. The prognosis of malignant thyroid nodules in children is much better than in adults.⁸

Papillary Carcinoma

Most papillary carcinomas of the thyroid gland present as palpable nodules. The main risk factor is radiation exposure. These lesions are often multifocal and bilateral. In children, there is a high rate of lymph node metastases, underscoring the importance of systematic evaluation for neck lymphadenopathy. However, these lesions are indolent, with a high long-term survival rate.^{7,8}

Follicular Carcinoma

These lesions have iodine deficiency as a major risk factor. They are usually unifocal, and less aggressive than papillary

carcinomas. When metastases do occur, they most often involve the lungs and bones. Metastases to lymph nodes are uncommon.⁸

Sonographic Evaluation

Rationale

In the setting of a palpable thyroid nodule, ultrasound evaluation is performed to stratify the risk of malignancy and guide fine-needle aspiration (FNA) recommendations. There are several published guidelines for the adult population,^{8,13-18} many of which^{8,16-18} have been evaluated for diagnostic performance in children.¹⁹⁻²³

Suspicious Nodule Findings

Published guidelines revolve around the concept of suspicious findings, which are features in the nodule that increase

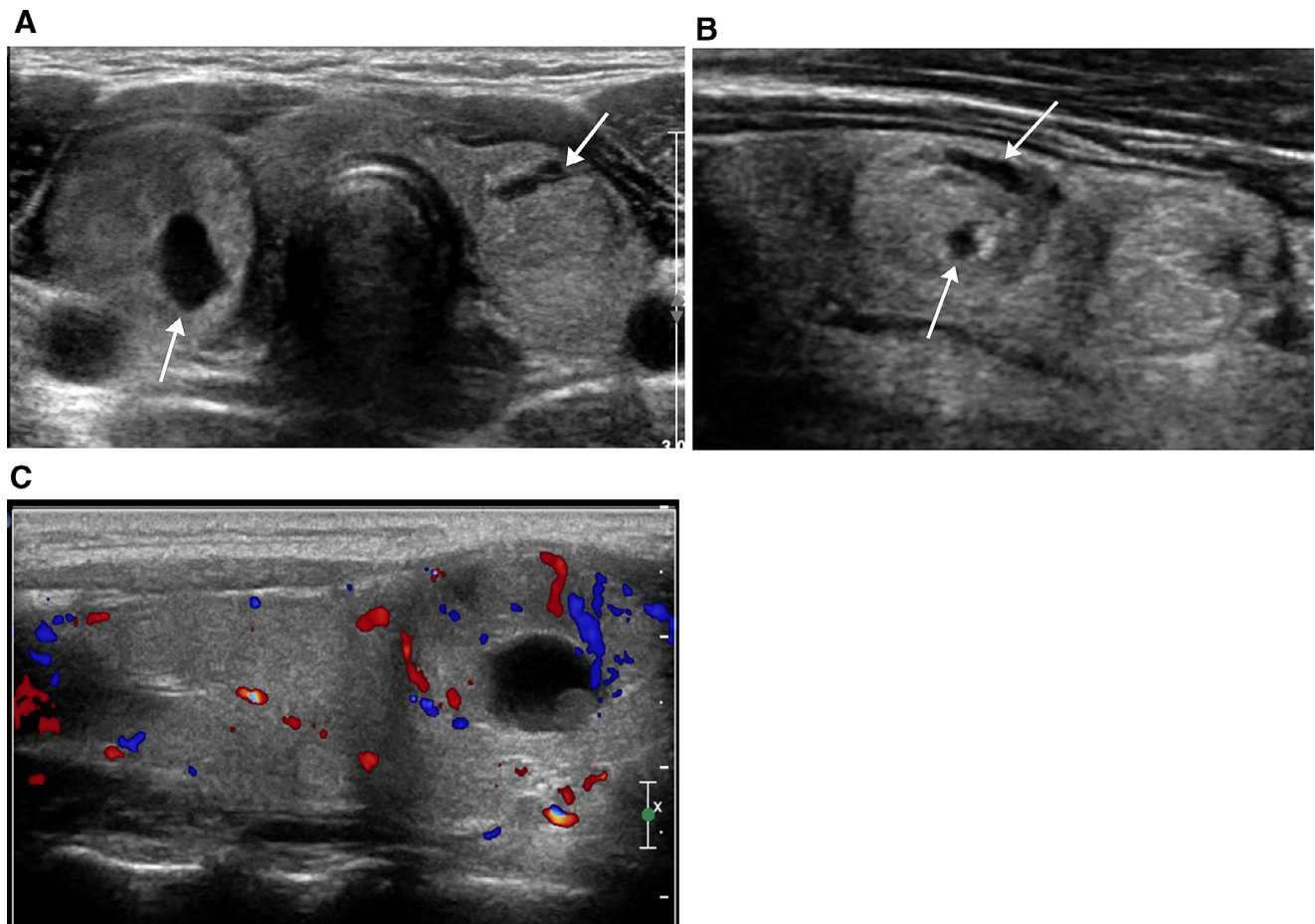


Figure 8 Nodular hyperplasia. Eleven-year-old girl with thyroid enlargement on physical examination. Transverse (A) and sagittal (B, C) gray scale ultrasound images show an enlarged gland with numerous slightly echogenic nodules that contain areas of presumed liquefaction (arrows). The nodules have increased flow on color Doppler, but overall parenchymal vascularity is normal (C). Fine-needle aspiration of the largest lesions in each thyroid lobe revealed hyperplastic nodules.

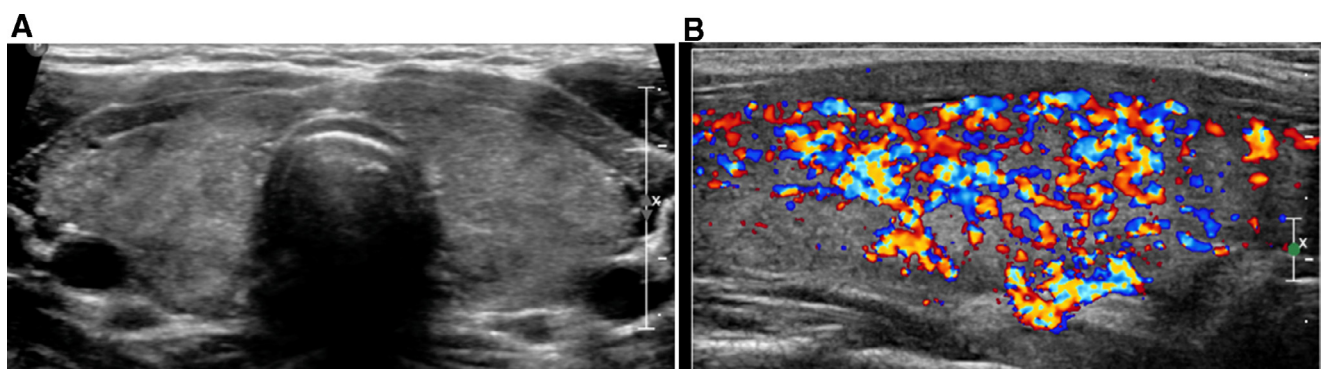


Figure 9 Graves disease. Fourteen-year-old girl presenting with weight loss, fatigue, elevated thyroid hormone levels, and TSH suppression. A. Transverse gray scale ultrasound image shows an enlarged and heterogeneous gland. B. Sagittal color Doppler ultrasound image demonstrates increased vascularity.

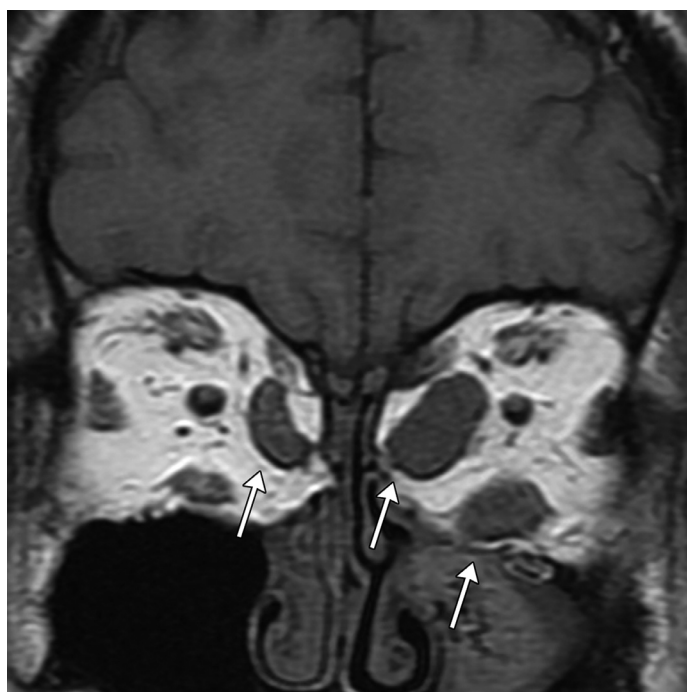


Figure 10 Advanced Graves disease with thyroid ophthalmopathy. Coronal T1-weighted MR image of the orbits shows enlargement of extraocular muscles (arrows) as well as increase of the intraorbital fatty tissue.

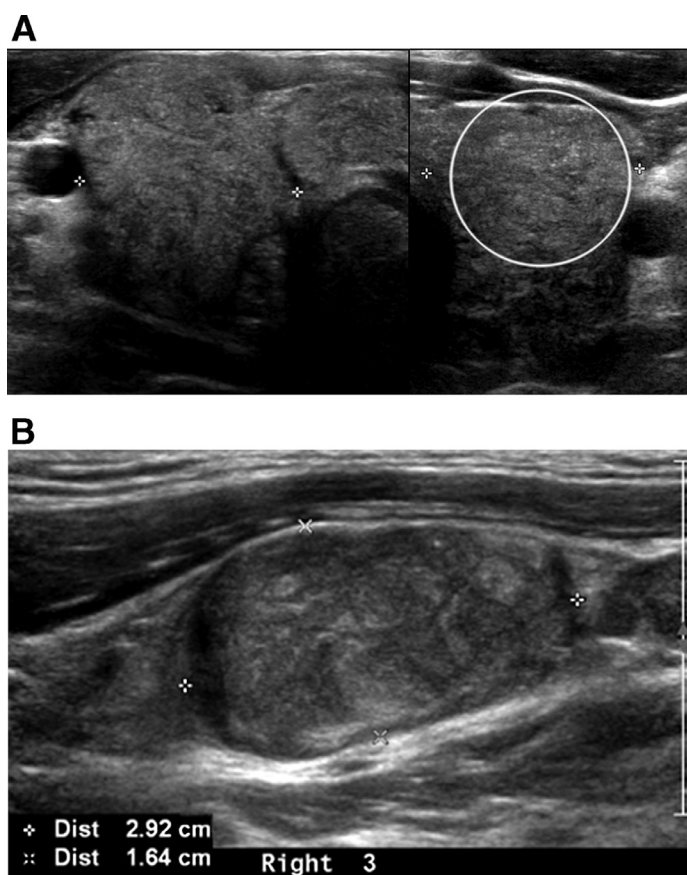


Figure 11 Papillary carcinoma of the thyroid, diffuse sclerosing variant. Eighteen-year-old male with an anterior neck mass. A. Transverse gray scale composite ultrasound image shows multinodular enlargement of the thyroid gland, as well as hyperechoic punctate foci in keeping with microcalcifications (within circle). B. Sagittal gray scale ultrasound image at level III in the right side of the neck shows an enlarged and heterogeneous lymph node. Fine-needle aspiration revealed papillary carcinoma. The patient underwent total thyroidectomy and neck dissection. Histology revealed papillary carcinoma of the thyroid, diffuse sclerosing variant, metastatic to multiple lymph nodes.

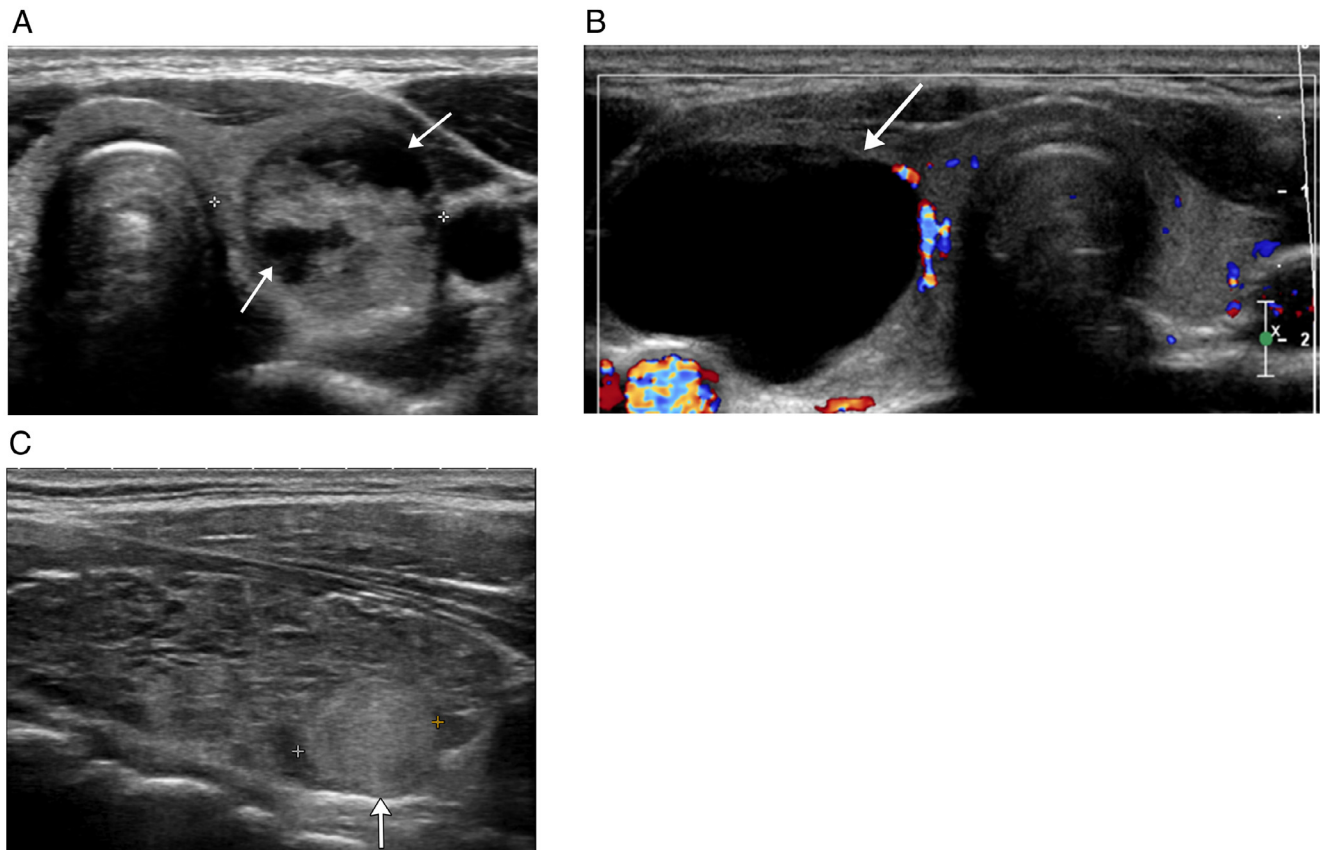


Figure 12 Benign thyroid nodules depicted on ultrasound. A. Hyperplastic nodule (proved on fine-needle aspiration) in an 11-year-old girl. The nodule is composed of echogenic areas interspaced with anechoic foci of presumed liquefaction (arrows). B. Presumed colloid cyst in a 14-year-old girl. The nodule (arrow) is entirely anechoic, with no solid components. C. Hashimoto disease in a 17-year-old boy. Well-defined diffusely hyperechoic nodule (arrow) in the lower pole of the left lobe in a background of diffusely heterogeneous thyroid parenchyma. A diffusely hyperechoic nodule in the setting of thyroiditis is invariably benign, commonly representing a regenerative nodule.

the suspicion of malignancy. These are illustrated in [Figure 13](#) and include:

- Presence of a solid component^{8,13,14,16,17}
- Echogenicity of a solid component lesser than that of the unaffected thyroid parenchyma or (even more suspicious) lesser than that of the strap muscles^{8,13,14,16,17}
- “Taller than wide” shape^{8,13,14,16,17}
- Margins that are microlobulated, irregular, or invasive (the latter extending out of the thyroid gland invading surrounding structures)^{8,13-17}
- Presence of calcifications, especially if smaller than 1 mm (so called microcalcifications)^{8,13-17}
- Increased vascularity of the solid component^{8,13}
- Increased stiffness on elastography²⁴
- Suspicious cervical lymph nodes^{8,11,14,25}

Pitfall in the evaluation of thyroid nodules: intrathyroid ectopic thymus

Ectopic thymic tissue can be present in the thyroid and may be identified on ultrasound incidentally or in patients with suspected thyroid disease. These foci of ectopic thymus are usually sharply marginated hypoechoic nodules with speckled echogenicity that

may mimic the appearance of microcalcifications^{26,27} ([Fig. 14](#)). With this sonographic appearance, they can be erroneously considered suspicious for malignancy. Clues in recognizing these nodules as ectopic thymic tissue include its similar echogenicity as compared to normal orthotopic thymus ([Fig. 14](#)) and that tend to be seen at a younger age than malignant nodules.²⁶

Suspicious lymph node findings

Although thyroid cancer in children has a high rate of lymph node metastases, to our knowledge there are no pediatric-specific sonographic criteria for suspicious lymph node findings, and nodal evaluation is based on adult criteria. The following are findings that are suspicious for lymph node metastases in adults^{8,25,28} ([Fig. 15](#)):

- Round shape
- Loss of the central hilum
- Short axis greater than 5 mm (possibly 8 mm for level II lymph nodes)
- Cystic appearance
- Presence of microcalcifications
- Peripheral vascularity

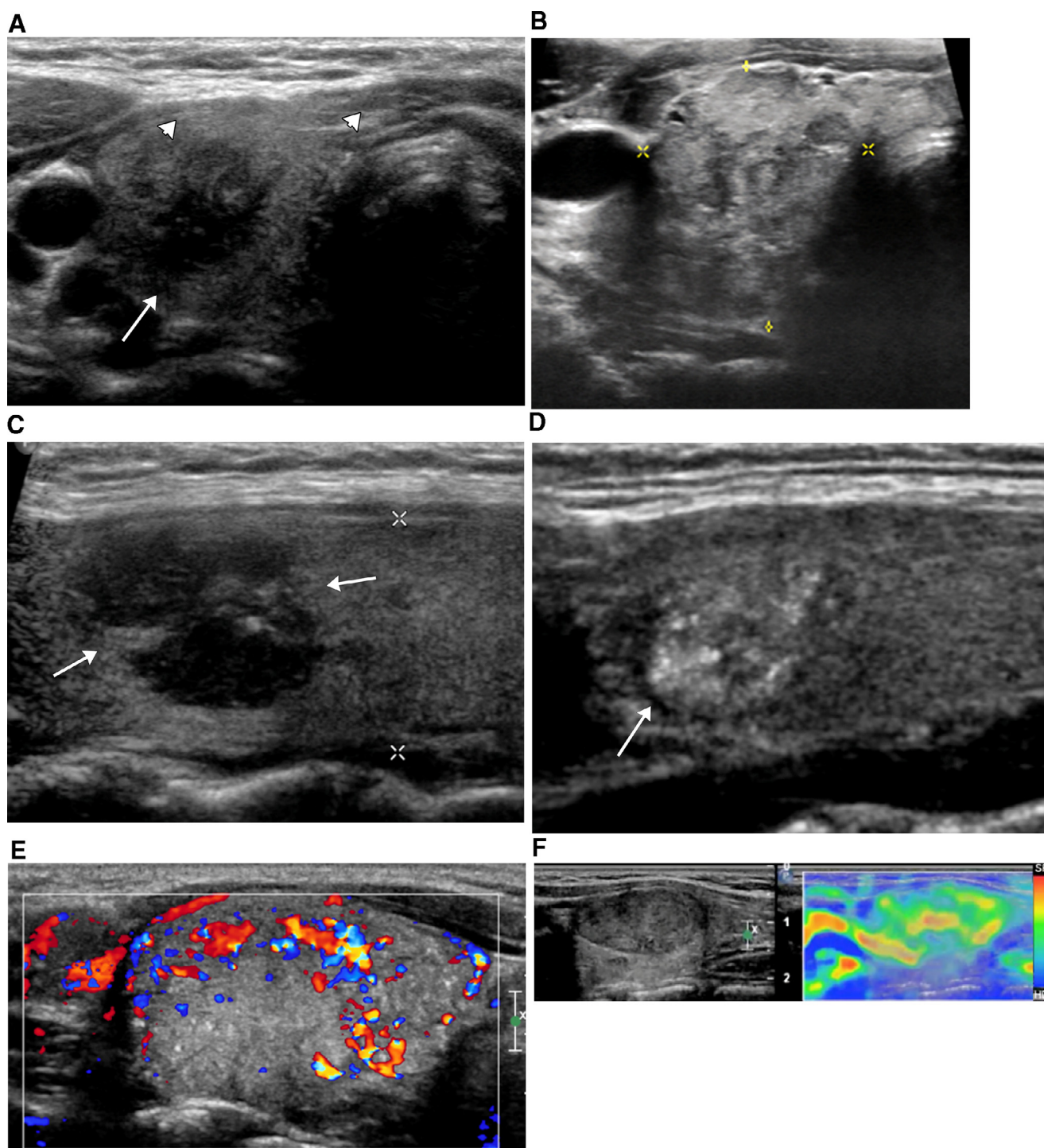


Figure 13 Suspicious nodule findings on ultrasound. Histology-proven papillary carcinomas in multiple patients. A. Hypoechoic solid component. Transverse gray scale ultrasound image in an 18-year-old girl shows a hypoechoic solid nodule (arrow), more hypoechoic than the strap muscles (arrowheads). B. “Taller than wide” shape. Transverse gray scale ultrasound image in a 16-year-old girl shows a nodule (between calipers) that is larger on the anteroposterior than on the transverse dimension. C. Irregular margins. Transverse gray scale ultrasound image in an 18-year-old girl (same patient as in A) shows a nodule with margins that interdigitate with the adjacent normal thyroid parenchyma (arrows). D. Microcalcifications. Sagittal gray scale ultrasound image in a 14-year-old girl shows a nodule (arrow) containing multiple microcalcifications, depicted as punctate hyperechoic foci. E. Increased vascularity of the solid component. Sagittal color Doppler ultrasound image in a 6-year-old boy shows substantial vascularity within the nodule. F. Increased stiffness on elastography. Dual gray scale (left) and shear-wave elastography (right) ultrasound images in a 16-year-old girl show a nodule with mostly stiff parenchyma. Image courtesy of Monica Epelman, MD.

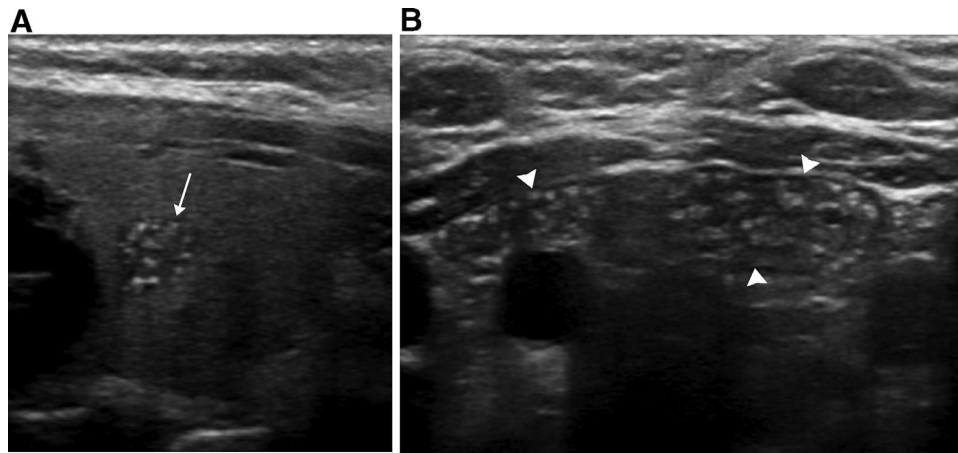


Figure 14 Ectopic intrathyroidal thymic tissue in a 4-year-old girl. A. Sagittal gray scale ultrasound image shows a small, relatively well-defined hypoechoic nodule (arrows) in the left lobe of the thyroid, which contains multiple punctate hyperechoic foci that can be misinterpreted as microcalcifications. B. Transverse gray scale ultrasound image of the midline upper chest shows normal orthotopic thymus (arrowheads) with similar echogenicity as the thyroid nodule suggesting that the nodule represents ectopic thymic tissue.

A preliminary report by Navallas Irujo et al²⁹ indicate that at presentation, most lymph nodes with histology-proven metastatic involvement from differentiated thyroid carcinoma in children are round in shape and have abnormal echogenicity and vascularity. However, these authors emphasize that metastatic nodes may be normal in size and shape and the diagnosis of metastatic involvement may be based solely on the identification of abnormal echogenicity and vascularity.

Stratification of Risk for Malignancy

Following the sonographic evaluation and description of any suspicious findings of a nodule, one may attempt to stratify its risk of malignancy, preferably by using one of the guidelines that have been evaluated in the pediatric population, such as the Kwak TI-RADS,¹⁶ the American Thyroid Association (ATA),^{8,17} or the American College of Radiology Thyroid Imaging, Reporting and Data System (ACR-TIRADS).¹⁸ However, one should be cognizant of the limitations of adult-oriented guidelines when applied in the pediatric population. For instance, although papillary carcinoma is more often metastatic to cervical lymph nodes in children than adults, neither the Kwak TI-RADS nor the ACR-TIRADS take into consideration the appearances of cervical lymph nodes on their risk stratification schemes (although the ACR-TIRADS recommends FNA of suspicious lymph nodes). Moreover, recent studies suggest that the use of the ATA, ACR-TIRADS, or Kwak TI-RADS criteria in the pediatric population may underestimate the risk of malignancy and lead to erroneous classification downgrading.²⁰⁻²³

Management Recommendations

- Recommendation for FNA and ultrasound follow-up

Subsequent to malignant risk stratification, one may offer advice in regards to the appropriateness of ultrasound follow-up and/or further evaluation with FNA. Although a few of the above mentioned guidelines also include management recommendations,^{13,17,18} one should be mindful not only of the risk of erroneous classification downgrading described in the section above, but also of the different epidemiology and biology of malignant thyroid nodules in children. As an example, utilization of size criteria for management recommendation, as is suggested in those guidelines, may not be pertinent in children.^{8,22} Specifically, contrary to adults, in the pediatric population nodules which contain suspicious features but measure less than 1 cm should still be considered for FNA.⁸ Similarly, the ACR-TIRADS does not recommend ultrasound follow-up on nodules classified as “benign” or “not suspicious.” Such recommendation, if followed in children, might halt follow-up of 3% of malignant nodules, which would have been misclassified on the initial ultrasound.²³

- Post-FNA recommendations⁸

The ATA guidelines for nodules with benign cytology on FNA suggest ultrasound follow-up, initially in 6-12 months, and subsequently every 1-2 years. FNA should be repeated if a new suspicious feature arises, or if there is continued growth (more than 50% in volume or more than 20% increase in size in at least 2 dimensions). Lobectomy should be considered if there is substantial growth or if the nodule is larger than 4 cm.

ATA guidelines for nodules with suspicious, indeterminate, or malignant cytology on FNA suggest surgical resection (lobectomy or thyroidectomy), followed by ultrasound surveillance, initially at 6 months, and subsequently every 6-12 months for at least 5 years. Ultrasound follow-up seems less important in follicular carcinoma.

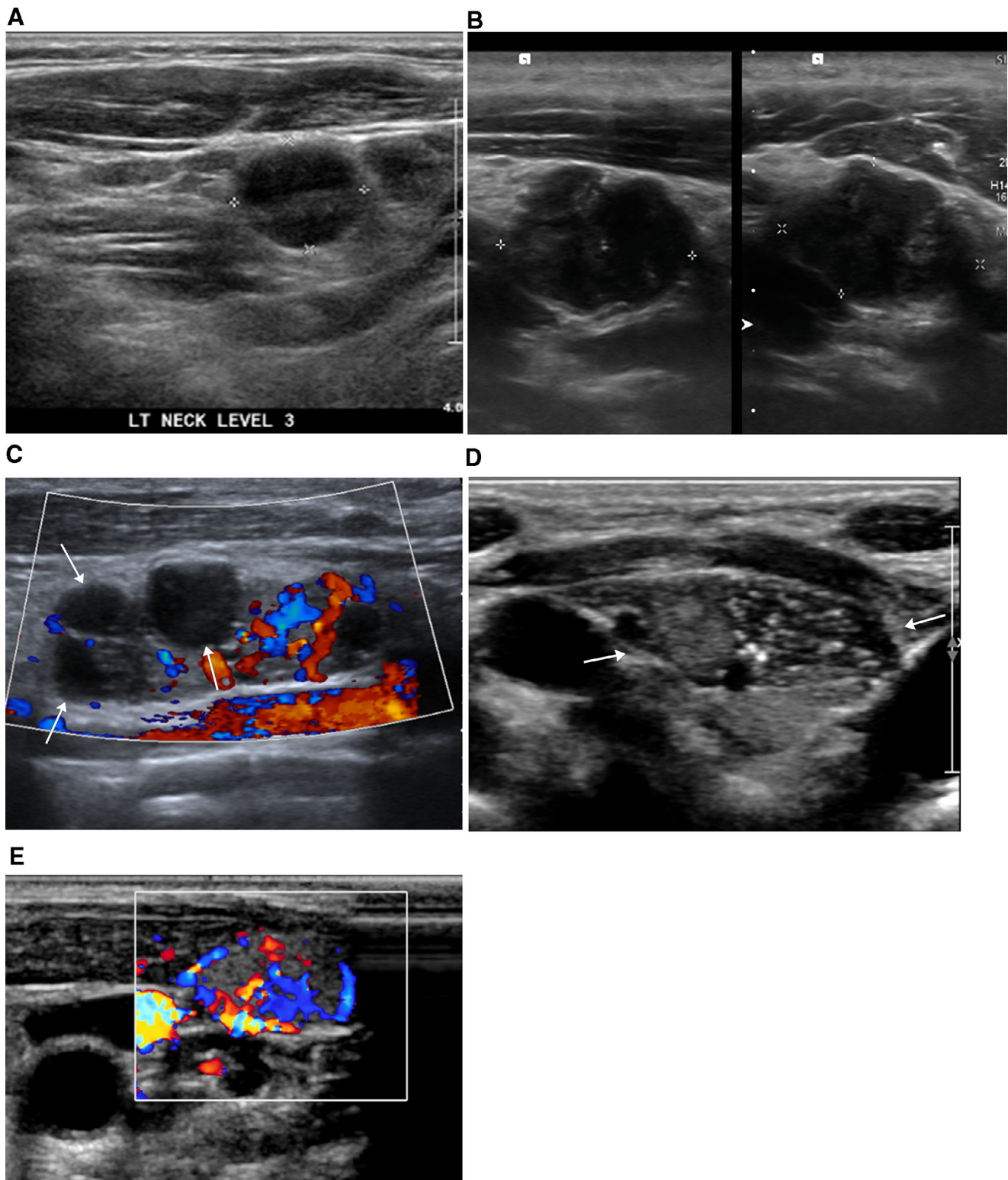


Figure 15 Suspicious lymph node findings on ultrasound in different patients with histology-proven metastases from papillary carcinomas. A. Round shape. Transverse gray scale ultrasound image in a 17-year-old girl shows a level III lymph node (between calipers) that has lost its normal oblong shape. B. Loss of central hilum. Transverse and coronal gray scale ultrasound images in a 17-year-old boy show a level IV lymph node (between calipers) with architectural distortion including loss of the central hilum. C. Cystic appearance. Transverse gray scale ultrasound image in a 17-year-old girl shows a level IV lymph node containing anechoic cystic-appearing areas (arrows). D. Presence of microcalcifications. Transverse gray scale ultrasound image in a 6-year-old boy shows a level IV lymph node (arrows) that contains multiple punctate hyperechoic foci, in keeping with microcalcifications. E. Peripheral vascularity. Transverse Color Doppler ultrasound image in a 6-year-old boy (same patient as in D) shows a level IV lymph node with abundant peripheral vascularity.

Conclusion

Knowledge of unique features of thyroid imaging in the pediatric population is critical for accurate diagnosis and management recommendations.

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