Ultrasound Findings in Thyroid Nodules: a Diagnostic Challenge in Pediatrics

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Abstract
Thyroid nodules are rare in pediatrics, but one in four nodules is malignant. Ultrasound is the method of choice for detecting these nodules because it provides information that often allows determining the probability of malignancy. The characteristics to be defined in a thyroid nodule are: composition, margins, echogenicity, calcifications, vascularity, stiffness and the presence of abnormal cervical lymph nodes. Composition includes cystic, solid or mixed appearance (the latter contains the spongiform subtype). Margins are described as smooth, irregular, ill-defined or lobulated. Echogenicity is defined as hyper-, hypo- or isoechoic to the adjacent thyroid parenchyma. For heterogeneous nodules, the predominant pattern is described. Calcifications are described as microcalcifications and macrocalcifications. Vascularity is classified as normal, centrally or peripherally increased, and mixed on color Doppler examination. Elastography measures the stiffness of the nodule being evaluated relative to that of adjacent thyroid tissue. Finally, cervical lymph nodes should be evaluated for echotexture abnormalities. Recognition of benign and malignant features of these lesions is crucial for guiding specialists in decision-making.

Keywords: *Thyroid nodule. Pediatrics. Thyroid. Ultrasound*

Introduction

Thyroid nodules in the pediatric population are rare findings that, in general, cause some uncertainty among pediatric radiologists about how to describe their appearance and which approach to suggest. The incidence of pediatric thyroid nodules ranges between 0.05% and 5.1%, but their rate of malignancy is high, with one in four nodules being malignant[1,2], in contrast to the adult population, in which the likelihood of malignancy is considerably lower (5-10%).[2,3]

Thyroid nodules of benign etiology include, but are not limited to, simple cyst, follicular adenoma, intrathyroid abscess, intrathyroidal ectopic thymus and nodular goiter.[4-7] As regards malignant thyroid nodular disease, papillary thyroid carcinoma (PTC) accounts for 90% of cases, with its histological variants being classic, solid, follicular and diffuse sclerosing.[1] PTC is followed, in order of frequency, by follicular thyroid carcinoma, while medullary thyroid cancer, poorly differentiated tumors, anaplastic carcinomas, lymphoma and metastasis occur more rarely.[1] Thyroid nodules may present as an incidental finding after a study performed for an unrelated condition or clinically as a palpable lesion and, less frequently, with thyroid dysfunction or compressive symptoms.[8]

Ultrasound (US) is the most sensitive method for detecting thyroid nodules because it provides information that often allows determining the probability of malignancy.[2] Furthermore, it is useful for the assessment of cervical lymph nodes. The aim of this article is to describe the sonographic findings in thyroid nodules in the pediatric population and to differentiate features of benignity from those of malignancy, suggesting a checklist for an adequate recognition of these features.

Technique

For ultrasound examination of the thyroid gland, the patient must be in a supine position with fully extended neck. The transducer placed over the anterior neck should be slid the entire embryological path of the thyroid from the mandible to the sternal notch. The thyroid must be fully scanned including both lobes and the isthmus in transverse and longitudinal planes. It is also important to evaluate cervical lymph nodes, the common carotid artery and the internal jugular vein.

High-frequency linear-array (7-18 MHz) or hockey-stick-shape transducers should be used to obtain more detailed anatomical information about the structures evaluated. Adjustments include focal zone placement in the thyroid region with adequate depth and gain. It is important to use color Doppler and elastography when available, as these tools will provide information on vascularity and elasticity of the structure evaluated, respectively.[9-11]

Sonographic features

There is a standardized system for risk stratification of thyroid nodules in adults known as Thyroid Imaging Reporting and Data System (TI-RADS) that was proposed by Horvath et al. in 2009 on the basis of sonographic findings, and which has been modified throughout the years. One of such modifications is the one proposed by the American College of Radiology (ACR), ACR TI-RADS, which establishes a scoring system for the various sonographic findings, thus defining risk, which serves as guidance to recommend either fine-needle aspiration (FNA) or ultrasound follow-up.[12] To date, none of the systems has been accepted for the pediatric population. For this reason, it is important to evaluate and describe the sonographic features summarized in Table 1 and detailed below.

Composition

Composition describes the internal components of the nodule, identifying the presence of solid (Fig. 1) or cystic content (Fig. 2), and in cases of mixed nodules (Fig. 3), the proportions of each (predominantly solid/predominantly cystic). When evaluating a partially cystic nodule, it is important to characterize the solid component, indicating if it is centrally or peripherally located (peripheral location might be associated with an increased risk of malignancy).[13]

Entirely cystic nodules are considered as benign[2,14,15] and solid nodules are mostly associated with malignancy[15,16]. However, benign solid nodules have been described, and cases of nodules confirmed as PTC with mixed components have also been reported.[2,15,17]

There is another subtype of nodule, spongiform, of mixed pattern and with multiple internal small cysts, which has a very low risk of malignancy.[2,13,14,18]

Margins

The margin is the border between the nodule and the adjacent thyroid parenchyma or adjacent extrathyroid structures. Margins are classified as "smooth" (Fig. 4) when they are well-defined, curvilinear, forming a spherical or elliptical shape and uninterrupted; as "irregular" (Fig. 5) when they are spiculated or jagged and the entire contour can be clearly

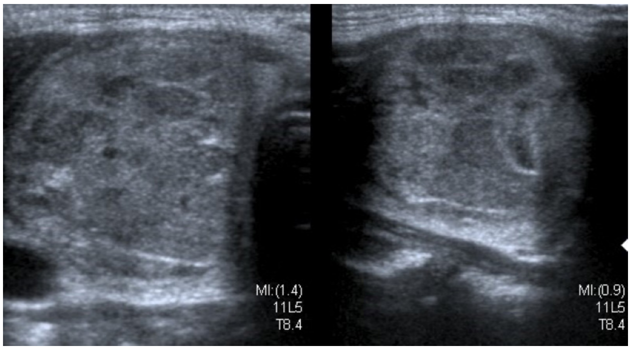

Figure 1. Follicular carcinoma in a 10-year-old patient. Gray-scale transverse US scan of the right thyroid lobe shows a heterogeneous lesion of solid appearance involving nearly the entire lobe and laterally displacing the carotid artery.

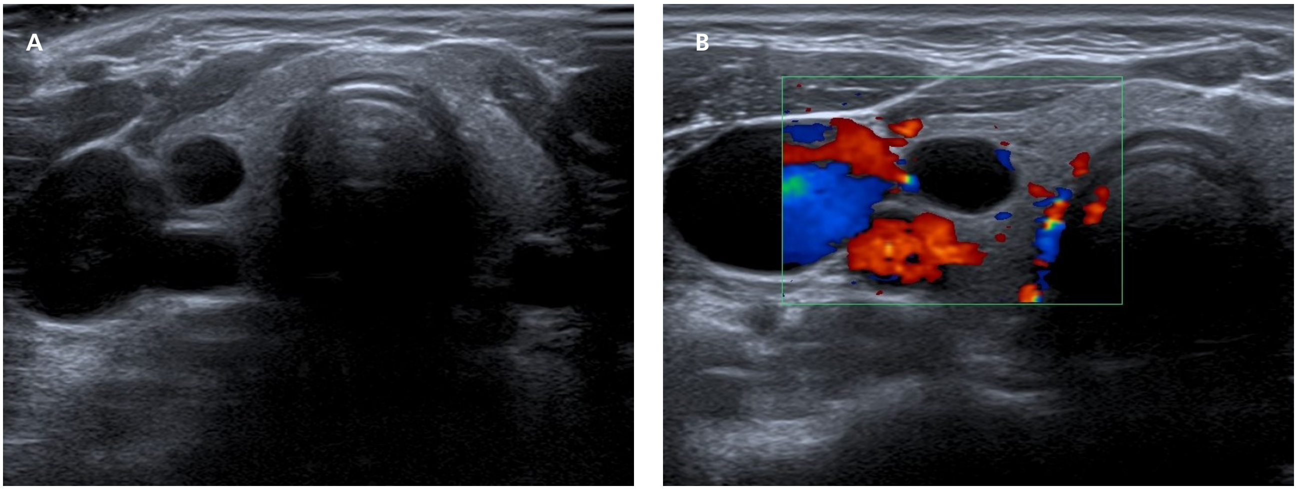

Figure 2. Simple cyst in a 16-year-old patient. Gray-scale transverse US scan of the right thyroid lobe shows (A) a rounded lesion of well-defined margins with anechoic (cystic) content, (B), without vascularity on color Doppler examination.

demarcated, which differentiates them from "ill-defined" margins (fig. 6), which are difficult to distinguish from thyroid parenchyma. Margins are described as "lobulated" (Fig. 7) when they have rounded protrusions that vary in size. The "halo" (Fig. 8) is a hypoechoic ring that may completely or partially encircle the nodule. It is considered as a fibrous capsule that is most commonly seen in benign nodules, although it may also be present in some malignant nodules.[2,18] In the published literature, most authors report that irregular margins are the ones most commonly associated with malignancy[1,2,12,15,19-22], while other authors report ill-defined margins as a feature of malignancy[16,23].

Table 1: Sonographic features of thyroid nodules

Feature	Description
Composition	
Cystic	Fluid-filled
Solid	Similar to soft tissue
Mixed	Cystic areas and solid areas
Margins	
Smooth	Well-defined, uninterrupted
Irregular	Spiculated, with sharp angles
Ill-defined	Difficult to distinguish from adjacent parenchyma
Lobulated	Rounded, of different sizes
Halo	Hypoechoic border encircling the nodule; it may be complete or incomplete
Echogenicity	
Hyperechoic	Increased echogenicity relative to thyroid tissue
Isoechoic	Similar echogenicity relative to thyroid tissue
Hypoechoic	Decreased echogenicity relative to thyroid tissue
Very Hypoechoic	Decreased echogenicity relative to muscular tissue
Calcifications	
Microcalcifications	Smaller than 1 mm, with no posterior acoustic shadowing
Macrocalcifications	Larger than 1 mm, with posterior acoustic shadowing
Comet-tail artifacts	Triangular reverberation artifact that may mimic microcalcifications
Vascularity	
Absent	
Central	
Peripheral	
Elastography	
Normal	
Increased	
Cervical lymph nodes	
Normal	
Abnormal	

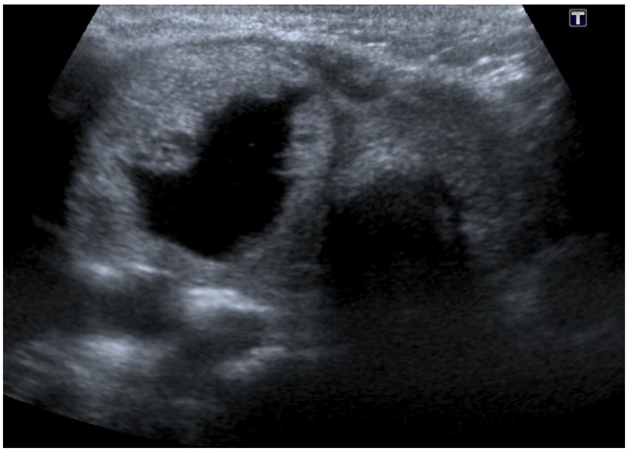

Figure 3. Follicular adenoma in an 8-year-old patient. Gray-scale transverse US scan of the right thyroid lobe shows a nodular lesion of mixed composition with peripheral solid area and central cystic area.

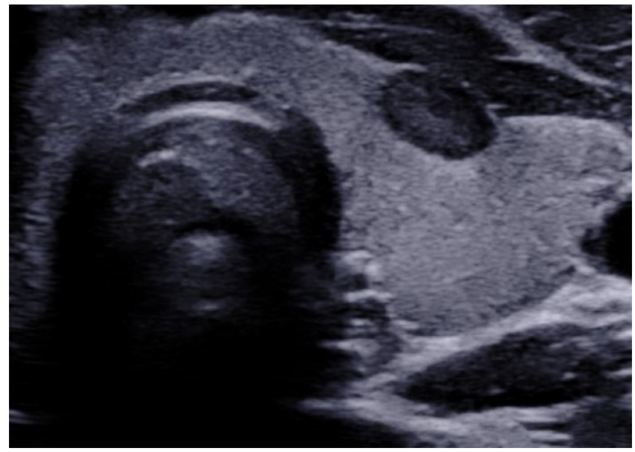

Figure 4. Nodular hyperplasia in a 15-year-old male patient. Transverse US scan of the thyroid gland shows a homogeneous, hypoechoic nodular lesion of smooth and well-defined margins in the anterior left lobe.

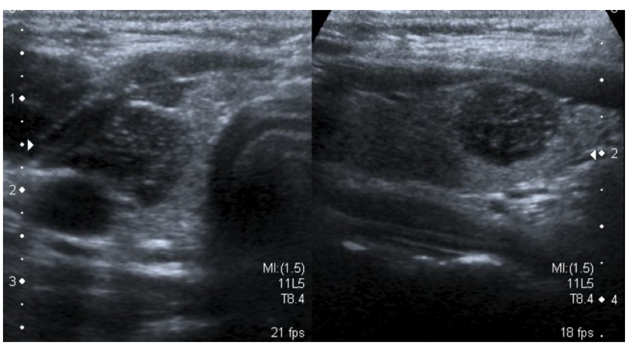

Figure 5. Papillary carcinoma in a 9-year-old boy. Gray-scale transverse and longitudinal US scan of the right thyroid lobe shows nodular hypoechoic lesion with microcalcifications and irregular margins.

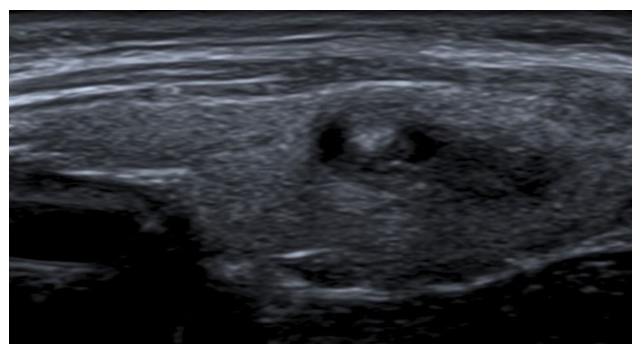

Figure 6. Papillary carcinoma in a 9-year-old girl. Gray-scale longitudinal US scan of the right thyroid lobe shows a nodular heterogeneous lesion, predominantly hypoechoic, of ill-defined margins.

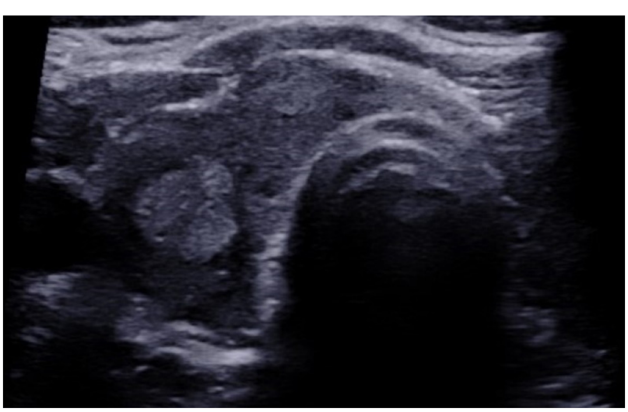

Figure 7. Gray-scale transverse US scan of the right thyroid lobe shows a nodular lesion that appears hyperechoic relative to the adjacent parenchyma, with borders with a soft or rounded protrusion, known as lobulated margins.

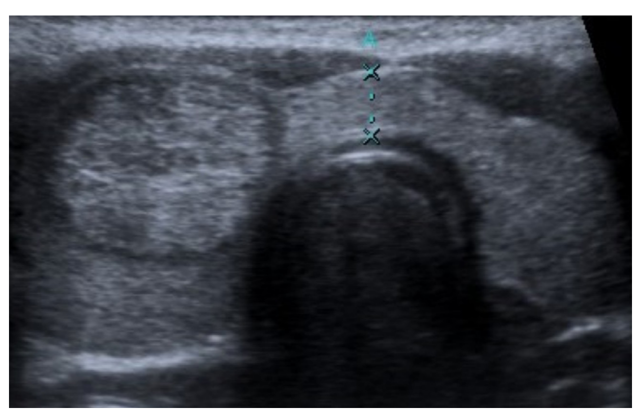

Figure 8. Adenomatoid nodule in multinodular hyperplasia in a 5-year-old boy. Gray-scale transverse US scan of the thyroid gland shows a hyperechogenic heterogeneous nodular lesion of well-defined margins, with a complete and well-defined hypoechoic peripheral halo.

Echogenicity

This feature refers to the level of echogenicity (non-calcified and non-cystic) of a nodule relative to the thyroid parenchyma: hyperechoic (Fig. 9), Isoechoic (Fig. 10) and hypoechoic (Fig. 11). In the case of very hypoechoic nodules (Fig. 12), echogenicity is compared with that of adjacent muscles.

Even if malignant nodules are more commonly hypoechoic, many histologically benign nodules are also hypoechoic.[20] According to the literature, very hypoechoic nodules have an increased risk of malignancy[2,13,16], but this feature has been reported only in the adult population.

In nodules with solid and cystic components, echogenicity must be described relative to the solid portion, so as not to confuse the term heterogeneous with the mixed solid and cystic component.

Nodules may also be characterized as homogeneous (Fig. 13) or heterogeneous (Fig. 14). Heterogeneous nodules have areas with different echogenicity, and in order to provide more descriptive information, the predominant pattern should be mentioned.

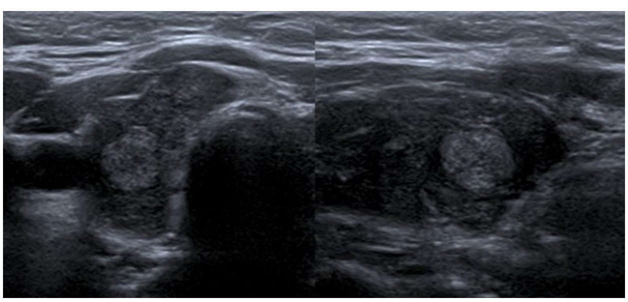

Figure 9. Papillary carcinoma in an 11-year-old patient. Gray-scale transverse and longitudinal US scan of the right thyroid lobe shows a hyperechoic nodular lesion of lobulated margins.

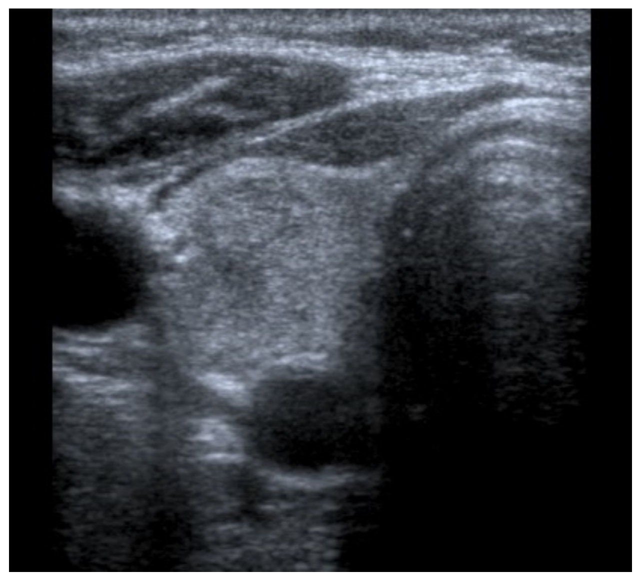

Figure 10. Follicular carcinoma in a 14-year-old patient. Gray-scale transverse US scan of the right thyroid lobe shows a nodular lesion that appears Isoechoic relative to the adjacent thyroid parenchyma and appears to involve nearly the entire lobe.

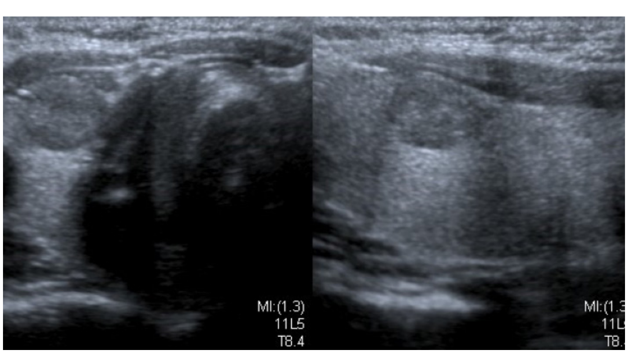

Figure 11. Oncocytic variant of follicular carcinoma in an 8-year-old patient. Gray-scale transverse and longitudinal US scan of the right thyroid lobe shows a nodular lesion of well-defined and irregular margins that appears hypoechoic relative to the adjacent thyroid parenchyma.

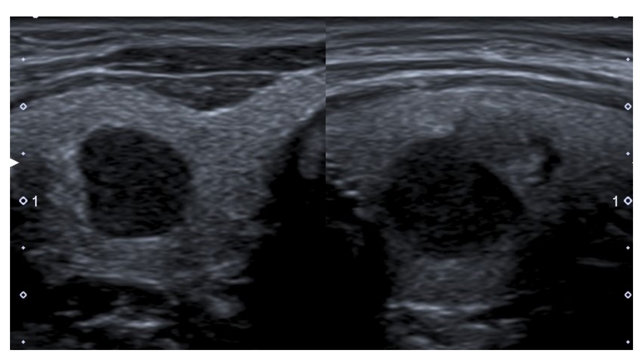

Figure 12. Papillary carcinoma in a 9-year-old patient. Gray-scale transverse and longitudinal US scan of the right thyroid lobe shows a nodular lesion of very hypoechoic echotexture with an area of increased echogenicity in the anterior-inferior region. Margins are well defined in the upper portion and ill-defined in the lower portion of the nodule.

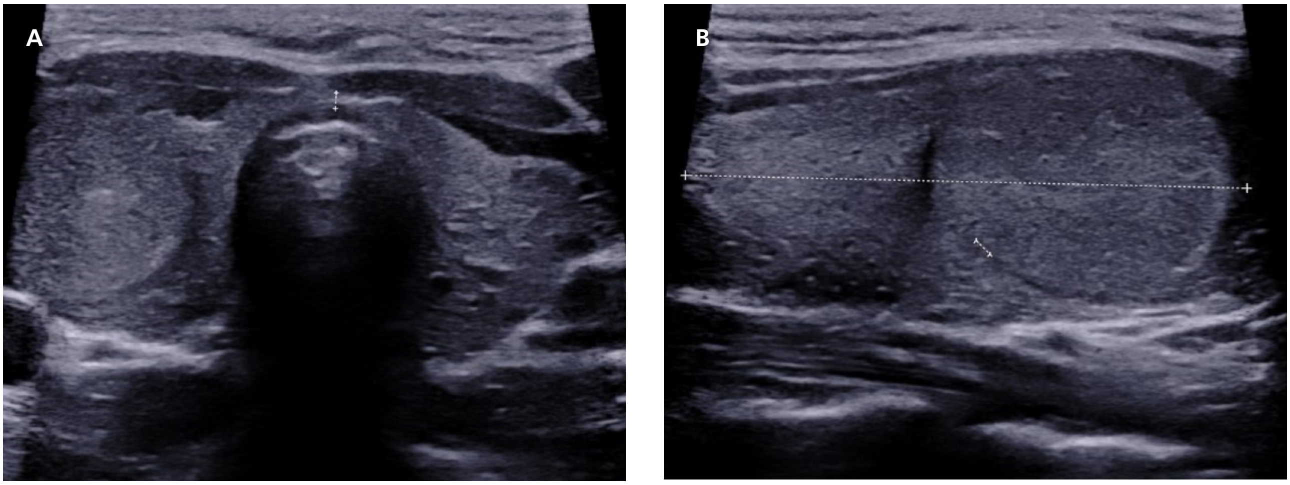

Figure 13. Gray-scale transverse and longitudinal US scan of the right thyroid lobe shows a well-defined, Isoechoic and homogeneous nodular lesion with a thin peripheral hypoechoic halo.

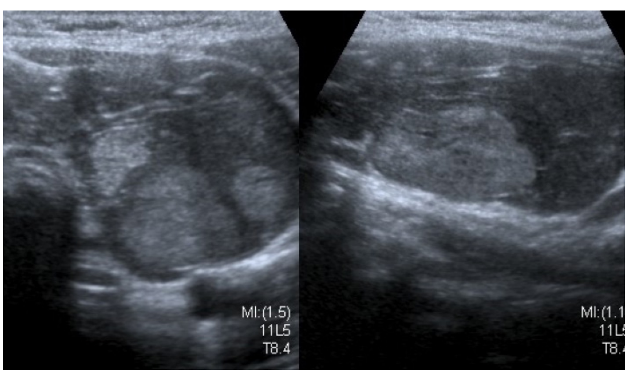

Figure 14. Gray-scale transverse and longitudinal US scan of the left thyroid lobe shows an enlarged thyroid gland of heterogeneous echotexture, with a heterogeneous nodular lesion occupying nearly the entire left lobe. The lesion contains lobulated nodular areas of increased echogenicity within a predominantly hypoechoic component.

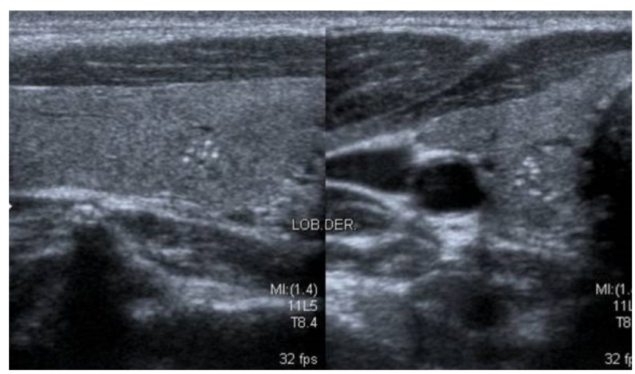

Figure 15. Gray-scale transverse and longitudinal US scan of the thyroid shows an Isoechoic nodule of poorly defined margins located in the right lobe, with punctate echogenic foci consistent with microcalcifications.

Calcifications

Echogenic foci that may be classified as microcalcifications (Fig. 15) and macrocalcifications (Fig. 16) depending on their size. Microcalcifications are less than 1 mm in size and have no posterior acoustic shadowing, while macrocalcifications are larger than 1 mm, with posterior acoustic shadowing.

Microcalcifications are associated with a high risk of malignancy. In fact, some authors consider that microcalcifications are by themselves predictors of malignancy[20] and others suggest that the presence of microcalcifications combined with increased central vascularity and abnormal lymph nodes warrants fine-needle aspiration.[23]

Comet-tail artifact (Fig. 17) is caused by reverberation in colloid cysts and may mimic microcalcifications. Unlike microcalcifications, the comet-tail artifact appears as a bright echogenic line with an echogenic triangle or lines reverberating posterior to it, and is usually associated with benignity.[2]

Vascularity

Vascularity is evaluated with color Doppler ultrasound to determine whether it is absent (Fig. 18) or increased in the nodule relative to the thyroid parenchyma. Increased vascularity may exhibit two patterns: central (Fig. 19) and peripheral (Fig. 20), with the pattern of increased chaotic central vascularity being associated with a higher risk of malignancy.[2,14,19,22,24] A pattern of peripheral vascularity is mostly associated with benignity[15,18], although some authors have described vascularity as a non-significant feature for differentiating benign from malignant nodules[2,3.14,16].

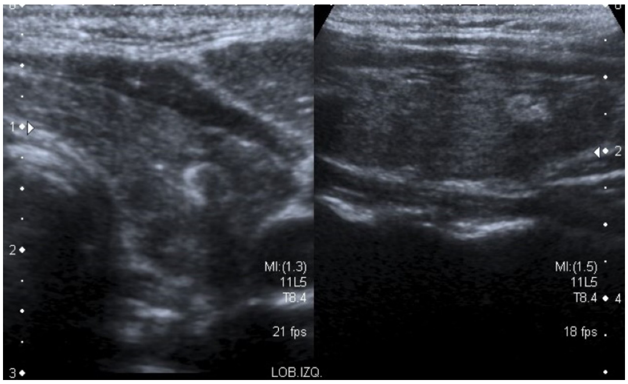

Figure 16. . Gray-scale transverse and longitudinal US scan of left thyroid lobe shows a nodular lesion with eccentric echogenic foci and posterior acoustic shadowing, consistent with macrocalcifications.

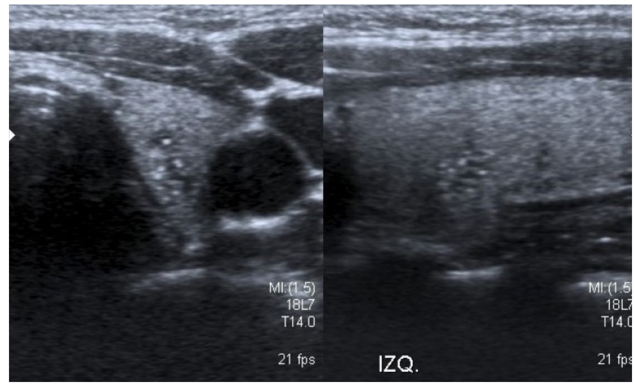

Figure 17. Colloid nodule in a 9-year-old girl. Gray-scale transverse and longitudinal US scan of left thyroid lobe shows a cystic nodule with echogenic foci caused by reverberation, and which may mimic microcalcifications.

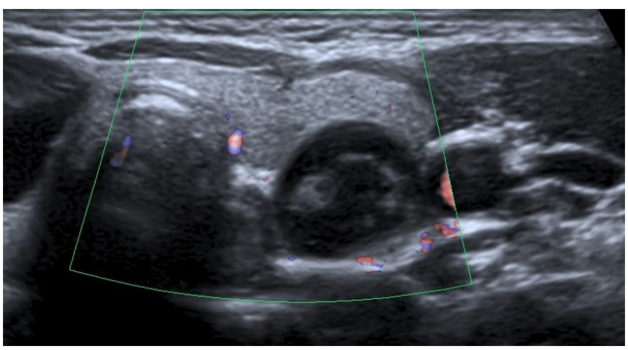

Figure 18. Transverse US scan of the thyroid gland shows a cystic nodular lesion in the caudal region of the left lobe without vascularity on color Doppler examination.

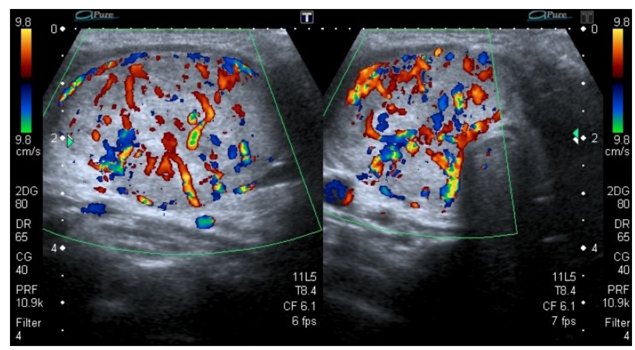

Figure 19. Longitudinal and transverse US scan of the thyroid shows a large solid nodular lesion in the right lobe, with increased chaotic central and peripheral vascularity on color Doppler examination, with a random distribution of nonbranching central vessels.

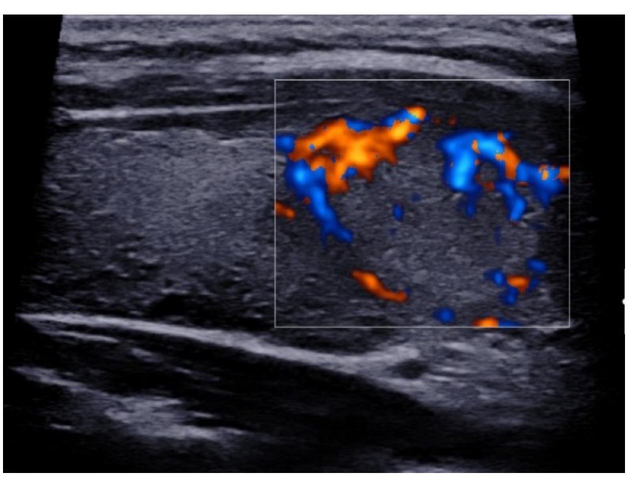

Figure 20. Longitudinal US scan of the right thyroid lobe shows an Isoechoic lesion in the lower pole with peripheral vascularity on color Doppler examination.

Stiffness

Share wave elastography (SWE) is a new ultrasound tool that quantitatively measures tissue hardness or stiffness and reduces the subjectivity of the clinical diagnosis of nodule elasticity. SWE is effective for increasing the sensitivity of ultrasound for the detection of thyroid neoplasms. Some authors consider that increased elasticity of a nodule relative to the adjacent thyroid parenchyma is associated with a higher risk of malignancy. Hazem et al. established a mean value of 33.46 ± 5.02 kPa for benign nodules and of 49.71 ± 11.16 kPa for malignant nodules.[11,25] The guidelines and recommendations of SWE published by Ferraioli et al. in 2021 suggest that benign nodules show a mean elasticity of 15.[3-28] kPa and that the optimal cut-off between benign and malignant nodules is 34.5-37.5 kPa[26] (Figs. 21 and 22).

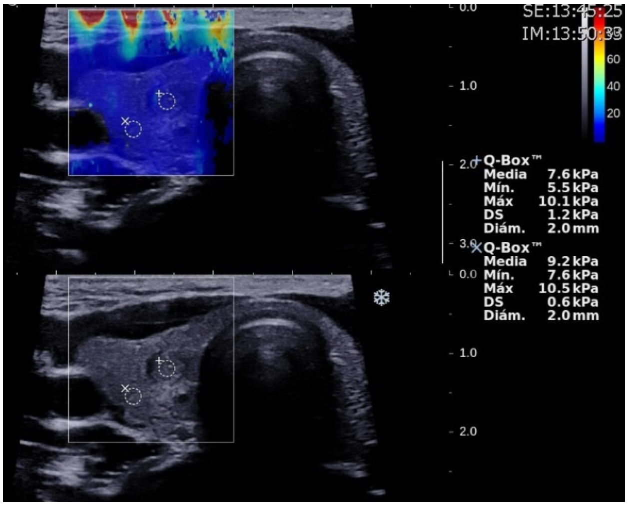

Figure 21. Follicular adenoma in a 15-year-old patient. Elastographic assessment of a nodular lesion in the right thyroid lobe. The region of interest (ROI) was placed inside the nodule and a second ROI was placed in normal thyroid parenchyma. The nodule shows a mean value of stiffness of 7.6 kPa, even lower than that of normal parenchyma, consistent with benign findings.

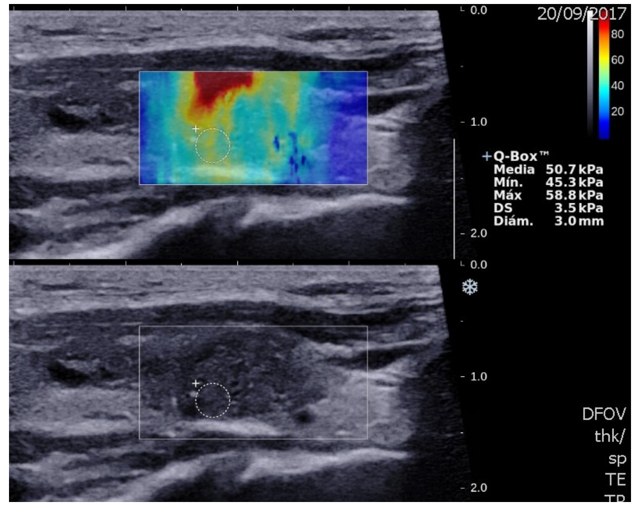

Figure 22. Multinodular goiter in a 14-year-old patient. SWE of dominant nodular lesion in the left thyroid lobe. The nodule shows a high mean value of stiffness, of 50.7 kPa, above the suggested cutoff between benign and malignant nodules.

Lymph nodes

Cervical lymph nodes should be evaluated whenever a thyroid nodule is detected because PTC has a high rate of lymph node metastasis[1]; moreover, metastases are more common in the pediatric population than in adults[14,27,28.]

A lymph node is defined as abnormal or lymphadenopathy (Fig. 23) when it has a heterogeneous echotexture, internal calcifications, rounded shape and absence of echogenic hilum.[2,29] Increased size and vascularity may also raise suspicion for malignancy[2]. According to various authors, the presence of abnormal cervical lymph nodes significantly increases the risk of malignancy of thyroid nodules.[1-3,14,16,20,23,27,30]

The size of the nodule has less relevance in the pediatric population compared with adults because in children thyroid volume changes with age and, in addition, nodule size does not predict malignancy.[1,2,14,17,19,21,23,27,31,32]

None of these features individually constitutes a risk of malignancy, but they should be evaluated as a whole in the clinical context of the patient by the treating medical team.

The American Thyroid Association (ATA) risk stratification guidelines proposed in 2015 by Haugen et al.[29] define the risk for malignancy of thyroid nodules on the basis of sonographic findings (Table 2). This system is also being currently used in pediatrics in the absence of a specific scoring system for this population, as we have previously mentioned.

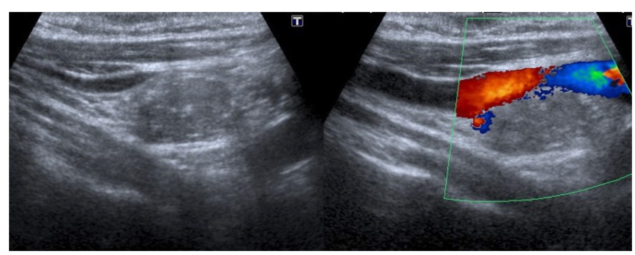

Figure 23. (A) Gray-scale and (B) color Doppler longitudinal US scan of right lateral cervical lymph nodes show a rounded, enlarged, heterogeneous lymph node with internal calcifications and absence of echogenic hilum anteriorly displacing the ipsilateral carotid artery, consistent with lymphadenopathy.

Even if the criteria for malignancy risk reported by the ATA are hypoechoic echotexture, irregular margins, increased central vascularity, presence of microcalcifications and abnormal cervical lymph nodes[1], variations of these criteria exist in the published literature. For this reason and due to the lack of consensus and to the high rate of malignancy of thyroid nodules in the pediatric population, it may be difficult to decide not to perform FNA and reduce the number of unnecessary aspirations in the pediatric setting, and nodules with intermediate features pose an added challenge.

Table 2: Sonographic features and stratification of the risk of malignancy according to the American Thyroid Association (ATA)

Sonographic pattern	Sonographic features	Estimated risk of malignancy
High suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins (infiltrative, microlobulated), microcalcifications, taller than wide shape, rim calcifications with extrusive soft tissue component, evidence of extrathyroidal extension	>70-90%
Intermediate suspicion	Solid hypoechoic nodule with smooth margins without microcalcifications, extrathyroidal extension or taller than wide shape	10-20%
Low suspicion	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, without microcalcifications, irregular margin, extrathyroidal extension or taller than wide shape	5-10%
Very low suspicion	Spongiform or partially cystic nodules without any of the sonographic features described in low, intermediate or high-suspicion patterns	<3%
Benign	Purely cystic nodules (no solid component)	<1%

Adapted from Haugen et al., 201629

Table 3: Sonographic features checklist

1. Composition
2. Margins
3. Echogenicity
4. Calcifications
5. Vascularity
6. Elastography
7. Lymph nodes

Conclusion

Ultrasound is an excellent noninvasive tool for obtaining images in the pediatric population, since it is an affordable and usually available method. It is rapid, inexpensive, it does not use radiation and does not require anesthesia. This method continues to be the modality of choice for evaluation and risk stratification of thyroid nodules, as it allows an assessment of the different features that, as a whole, may provide guidance in differentiating benign from malignant lesions.

As mentioned above, the likelihood of malignancy is estimated on the basis of a combination of sonographic findings. For this reason, at the time of performing a routine ultrasound scan, we suggest using a checklist (Table 3) of the key points that should be assessed for an easy recognition of these features.
Nevertheless, we suggest performing biopsy whenever deemed necessary in the medical judgment of the treating team.

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Conflicts of interest

The authors declare no conflict of interests.

Ethical responsibilities

Protection of human subjects and animals. The authors declare that no experiments were performed on humans or animals for this investigation.
Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the Ethics Committee approval for the analysis and publication of routine clinical data. Patient informed consent was not required because this was a retrospective observational study.

Use of artificial intelligence for text generation. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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