

ORIGINAL ARTICLE

Neuro/Head and Neck Radiology

Sonographic appearances of intrathyroid thymus: emphasis on details

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ABSTRACT

Purpose: To thoroughly describe ultrasonographic findings of intrathyroid thymus including character-istics that have not been previously emphasised.

Material and Methods: Forty-six children aged 21 days-14 years (mean 5.8 years) underwent cervical ultrasonography. Diagnosis of intrathyroid thymus was based on comparison with visible mediastinal thymus and follow-up in all patients, MRI in 2 and needle biopsy in 1 child.

Results: Fifty-two lesions <0.9 cm were identified, 29 (55.8%) left-sided; fifty-one (98.1%) at the lower 2/3 of the respective lobe on sagittal images. No lesion was situated anteriorly on transverse scans. Forty-three (82.7%) lesions exhibited angulated borders at either axial and/or transverse images producing a geographic shape while 9 (17.3%) were round/ ovoid at all images. Thirty-six (73%) lesions reached the thyroid's capsule and 14 were peripheral, within 1-3 mm (mean 2.1 mm) from it. Eighteen (34.6%) lesions exhibited extrathyroid extension and 13 (25%) connecting tissue with mediastinal thymus. Echopattern was identical to the same patient's thymus: hypo-or iso-echoic to the thyroid, containing bright scattered spots in all lesions. Forty-nine (94.2%) lesions exhibited a spared thin hypoechoic rim. Colour Doppler over 31 lesions showed no/ sparce vascularity.

Conclusions: The starry-sky pattern with sparing of a thin peripheral rim, identical to the individual's mediastinal thymus, was seen in 94.2% of intrathyroid thymus. Prevalent characteristics also included no/ sparce vascularity, geographic elongated shape, angulated borders, as well as occasional extrathyroidal extension and connecting thymic tissue between the thyroidal and mediastinal thymus. These appearances, when seen in small posterior/caudal lesions, prompted conservative follow-up instead of invasive management.



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Key words

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1. Introduction

Intrathyroid lesions in children are uncommon before puberty and are considered to occur in less than 1.5% of scrutinised children [1, 2]. Palpable thyroid nodules in children should be thoroughly investigated due to the higher risk of malignancy compared to adults [3, 4]. With the advent of high-resolution Ultrasonography (US), incidental intrathyroid abnormalities have been encountered in 17% of children scanned for cervical lymphadenopathy [5]. Intrathyroid ectopic thymus accounted for 17% of these incidentalomas, exhibiting a prevalence of 3.1-3.9% [5, 6]. Other investigators consider intrathyroidal thymus a less common occurrence and have found a prevalence ranging from 0.4% to 1.1%, inversely associated with age [7-9].

Cervical thymic tissue, either intrathyroidal or neighbouring the thyroid, has been described in small case series or case reports and has been considered an incidental finding at autopsy or at operation which may be mistaken for a thyroid nodule or a neck mass requiring biopsy or surgery [7-23].

The US hallmark of intrathyroid thymic tissue is a fusiform hypoechoic lesion with linear or punctate internal echoes, the so-called "starry sky appearance" [7-9, 21-24]. These lesions have been shown to remain stable or involute with growth [6, 9, 11] and do not require treatment. It is important to be aware of the entity and its particular characteristics in order to suggest appropriate further management. The objective of this study is to thoroughly describe the sonographic findings of intrathyroid thymus in a large number of lesions, to discuss the US appearances with regard to thymic embryogenesis and histology and to underscore those characteristics that, to our knowledge, have not been previously emphasised.

2. Material and Methods

The current study was approved by the local Institutional Review Board and the need for informed consent was waived. During a period of eight years, between June 2009 and June 2017, a total of 3256 children underwent neck US. Clinical data, sonographic findings, US reports and follow-up were available through the hospital's PACS system. A total of 46 children, 27 males and 19 females, aged 21 days-14 years (mean age 5.8 years) were found with the diagnosis of intrathyroid thymus with or without perithyroid thymus. The diagnosis was based on comparison with the visible mediastinal thymus in 46 children, fine needle aspiration biopsy (FNAB) in one patient, correlative magnetic resonance imaging (MRI) in two patients, and US and/or clinical follow-up in 46 children. Follow-up lasted between two months and five years (mean 23.8 months).

Indications for imaging included suspected lymphadenopathy in 16 children, acute parotitis in one, evaluation of a thyroid nodule seen elsewhere in eight, question for obesity-related thyroid disease in three, a positive family history of thyroid disease in 12, follow-up of Hashimoto's thyroiditis in one child, raised TSH in two, and evaluation for thyroglossal duct cyst in three children. All patients underwent US on an iU22 Philips scanner (Philips Medical Systems, Best, the Netherlands) with a 17-5 MHz linear transducer. Images of Colour Doppler applied over the thyroid and the lesion were available in 31 children, utilising low scale settings (+ 2.8 cm/sec).

All available grey-scale and colour images at diagnosis and on follow-up were reviewed on computer screens in DICOM forms by two readers in consensus. Patients with intrathyroid thymus were recorded as having single or multiple, unilateral or bilateral lesions. Thymic rests were recorded as left or right depending on the involved side, and depending on the position of the lesion on axial scans were characterised as anterior (superficial), at the middle third of the respective lobe or as posterior (deep). Lesions were upper, middle or lower depending on the location of the lesion on sagittal images. The size of each lesion was measured on sagittal scans and the maximal longitudinal and anteroposterior diameters of the intrathyroid component of the lesions were recorded.

The following characteristics were assessed: the shape of lesion on axial and sagittal scans, the presence of angulated borders, the position of the lesion in relation to the periphery of each lobe and its distance to the capsule, the presence of extrathyroid extension of the lesion, the presence of tissue connection between the lesion and cervical thymus

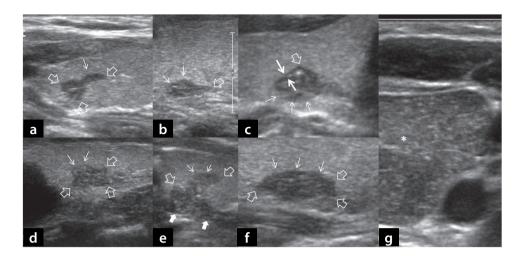


Fig. 1. Geographic shapes. Six different examples **(a-f)** of hypoechoic intrathyroid lesions with thin speckles and geographic shapes. Multiple angulations (open arrows) cause bizarre shapes like a map with rounded (thin arrows) and angulated parts. Note the club-like shape of the lesion in **(b)**, the extrathyroidal extension (white arrows) of the lesion in **(e)**, the fusiform shape of the lesion with three small angulations in **(f)**. The mediastinal thymus (*) of one of the patients is indicatively shown in **(g)**, exhibiting an identical "starry-sky" echopattern as the intrathyroid lesion in **(e)**. Multiple speckles spare the lesion's periphery in **(c)**, producing a thin hypoechoic rim (between thick long arrows).



Fig. 2. Geometric shapes. Two different examples of intrathyroid thymus with a triangular (left) and a square (right) shape due to angulations (crosses). Also note the incomplete spared hypoechoic rim at the periphery of the lesions (between arrows).

and/or the mediastinal thymus and finally the presence of cervical thymic tissue, neighbouring to the thyroid without connection to the intrathyroid thymus. Evaluated internal characteristics also included echogenicity compared to the thyroid, the presence and thickness of a complete or incomplete hypoechoic rim and the presence of linear or punctate internal echoes (speckles). Distribution of speckles was directly compared in each patient with the echopattern of the individual mediastinal thymus, the so-called "starry sky" pattern, and was assessed as: a) uniform, covering the entire area of the lesion, and b) non-uniform. The presence and number of colour dots inside the lesions on colour Doppler were also looked for and recorded.

3. Results

Fifty-two intra-thyroidal thymus lesions were identified in 46 children resulting in a prevalence of 1.6% in our studied population. In one patient two separate thymic lesions were identified at the right side and in five children two thymic rests, one in each thyroid lobe, were recorded. In total, 23 right-sided and 29 left-sided lesions were noted.

Regarding location, with respect to the axial scans, 42 lesions (80.8%) were located posteriorly, 10 (19.2%) lesions were located exclusively at the middle third of the respective lobe and none was anterior. With respect to the long axis, one lesion (1.9%) was located at the upper third of the lobe, 42 (80.8%) at the middle third and nine (17.3%) at the

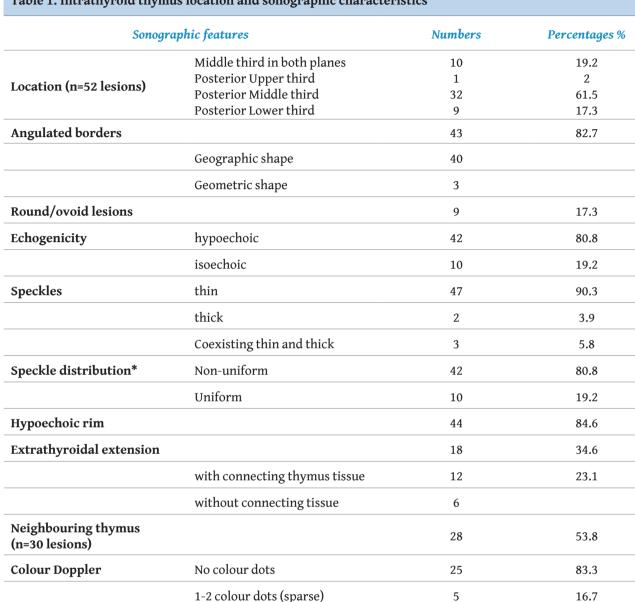


Table 1. Intrathyroid thymus location and sonographic characteristics

*Speckle distribution was always identical to the same patient's mediastinal thymus

lower third of the thyroidal lobe (**Table 1**). In total, 51 lesions (98.1%) were located at the two lower thirds of the respective lobe of the thyroid. Contact with the thyroid's periphery at either axial and/or sagittal scans occurred in 36 lesions (69.2%) while the remaining 16 (30.8%) were peripheral, within 1-3 mm (mean 2.1 mm) from the thyroid's contour.

The lesion's longitudinal diameter ranged from 0.22 cm to 0.9 cm (mean 0.6 cm) and the antero-posterior diameter ranged from 0.15 to 0.46 cm (mean 0.3 cm). At follow up, a decrease of the lesion's size by 3 mm in the antero-posteri-

or diameter was noted in one case, while the remaining lesions were stable in size and shape.

With regard to the shape of the intrathyroid lesions evaluated on longitudinal and axial scans, angulated borders were noted in 43 lesions (82.7%), giving them either a geometric shape, for example a triangle or a polygon, or a geographic shape, with rounded and angulated parts, reminiscent of a map (**Figs. 1, 2**). The remaining nine lesions (17.3%) exhibited a round/ovoid shape at all images. Regarding the echogenicity of the lesion's matrix when compared to the echogenicity of the thyroid, 42 were hypoechoic (80.8%)

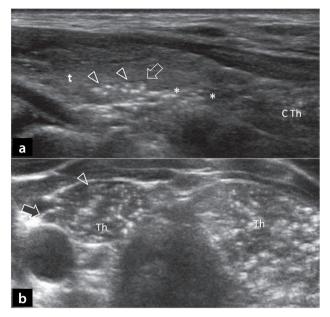


Fig. 3. Typical intrathyroid thymus. (a) longitudinal scan of the left lobe of the thyroid shows a geographic lesion with an angulation (open arrow) abutting the thyroid's periphery. The lesion's matrix is isoechoic to the thyroid (t), is surrounded by a pencil-thin hypoechoic rim (arrowheads) and contains scattered thick speckles. Note the band of thymic tissue (*) towards the neighbouring cervical thymus (C Th). (b) Transverse scan through the mediastinal thymus (Th) of the same patient. The distribution and pattern of speckles within the thyroidal and the mediastinal thymus are comparable. Also note the thin hypoechoic rim at the anterior-right aspect of the mediastinal thymus (open arrowhead) and the angulated lateral contour (black arrow) which were also encountered in the intrathyroid thymus.

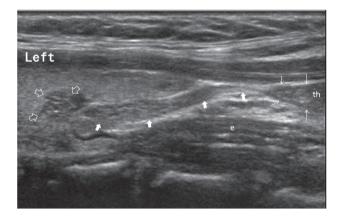


Fig. 4. Longitudinal scan through the left lobe of the thyroid in a 10-year old girl. There is a hypoechoic lesion (open arrows) which contains numerous thin speckles and lines and is connected with a long band of tissue (white arrows) with the adjacent cervical thyroid (thin arrows, th). Note the oesophagus **(e)** visualised separately. The intrathyroid lesion, band of tissue and cervical thymus have the same echo-pattern, consistent with the "starry-sky" appearance.

while 10 were isoechoic (19.2%) (Figs. 1-5). The intrathyroid thymic tissue invariably contained bright spots or lines, the speckles. Speckles were scattered through the entire lesion randomly and uniformly in 10 lesions (19.2%) and non-uniformly in 42 lesions (80.8%) (Figs. 1-5). Speckles were thin in 47 lesions (90.3%), thick in two (3.9%) whereas thick and thin co-existed in three lesions (5.8%). The speckles were identical to the internal spots of the mediastinal or cervical thymus of the same patient in all cases (Figs. 1, 3-5). A peripheral hypoechoic rim (Figs. 1-3) was present in at least one of the available images in 44 lesions (84.6%), complete in 21 and incomplete in 23 cases. Colour Doppler performed in 30 lesions didn't recognise internal colour spots in any image in 25 lesions and sparse (one small or two) colour spots in five lesions (Fig. 5).

Extrathyroid extension beyond the borders of the thy-

roid occurred in 18 lesions (34.6%) (**Figs. 1, 3, 4**). A visible tongue of thymic tissue connecting the intrathyroid thymus with the proximal cervical thymus (**Fig. 4**) was observed in 12 thymic rests (23.1%). Cervical thymus neighbouring the respective thyroid lobe without connecting thymic tissue occurred in 28 lesions (53.8%).

4. Discussion

4.1. General Considerations

Intrathyroid thymic tissue has traditionally been considered a rare cause of a solitary lesion mimicking a nodule in children [7, 11, 13, 18]. Since intrathyroid thymus is not a pathologic nodule and is considered a pitfall, this diagnosis is not mentioned in the US differential diagnosis of solitary thyroid nodules in children in some review articles [25-27]. There are multiple case reports illustrating the difficulty in



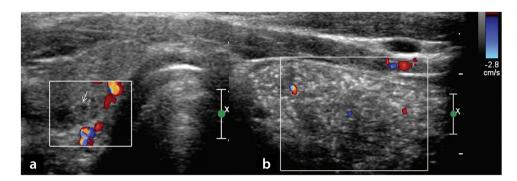


Fig. 5. Colour Doppler evaluation of intrathyroid thymus **(a)** and mediastinal thymus **(b)**. Almost no vascularity is seen in the intrathyroidal lesion with one small dot centrally (thin arrow). Coexisting thin and thick speckles are noted within the intratyhyroid lesion and the corresponding thymus. Note the posterior location abutting the thyroid's surface.

management of children with such lesions requiring surgery or needle biopsy [10, 13-18, 28].

4.2. Prevalence

True prevalence is difficult to estimate because such lesions are almost invariably asymptomatic; in a large screening survey, prevalence ranged between 0.2% and 1.7% in different age groups among the general population and was inversely associated with age [9]. The prevalence of intrathyroid thymus is around 5% in autopsy studies of foetuses [29]. In our series, the mean age and prevalence were 5.8 years and 1.6%, respectively and less compared to other series reporting a prevalence of 3.1%-4.2% [5, 6, 30]. These differences are probably associated with different causes for referral among institutions and different age groups. Children with intrathyroid thymus can be as young as a few days old, as occurred in two neonates in our series [5, 7-9]. Most intrathyroid lesions occurred in children older than two years, therefore intrathyroid thymic rests can be seen at any age and are more likely to be sonographically detected in preschool and school-aged children.

4.3. Location related to embryology

Embryologically, primordial thymic tissue starts from the angle of the mandible, coursing downwards and through the lateral neck, to the suprasternal area and to the superior-anterior mediastinum; this caudal and medial migration, resulting in fusion, occurs during the 6th to 8th week of gestation [14, 31, 32]. Thymic tissue is usually orthotopic or mediastinal, i.e. normally located in the anterior mediastinum [33]. Cervical thymus, i.e. thymic tissue in the neck area, can be either aberrant or ectopic. Aberrant thymus is located along the pre-mentioned course and ectopic thymus is located anywhere in other locations including the pharynx, trachea, posterior neck, posterior mediastinum, oesophagus [12]. Thymic heterotopia and the terms "aberrant" and "ectopic" thymus have interchangeably been used to describe thymic tissue in locations other than the anterior mediastinum [10]. Embryogenesis of thyroid, thymus and parathyroids is connected, because they share a common origin, from the 3rd and 4th branchial pouches [12, 31]. Thymic rests in the thyroid are considered ectopic or aberrant, as the result of arrested descent of thymus during the 9th week of foetal life, sequestrated thymic tissue along the path of descent and failure of this tissue to involute [10, 14]. The low-lying and posterior position of intrathyroid thymus in our series is consistent with the embryological relationship between the thymus and the thyroid and supports the concept that these are congenital lesions at the course of descent of thymic primordium [7, 10].

4.4. Angulated borders, a discrete feature

Angulated borders at intrathyroid thumus result in a geometric (triangular or polygonal) shape or a geographic shape with coexisting rounded and angulated borders. This observation has not been, to our knowledge, previously emphasised. Most authors report a nodular, ovoid or fusiform shape [6, 7, 11, 21, 23]. The phrase "unusual or irregular shape" and the word "polygonal" are mentioned in a single study each [5, 9]. We noted this characteristic in 82.7% of lesions in our study and also observed it in US and histologic images in the literature [5, 14, 18, 21, 23]. Angulations are a common feature of orthotopic and aberrant thymus and are quite prominent in the cephalic aspect of thymus visible at the suprasternal area and at the lateral aspects of mediastinal thymus [27]. We feel that angulation should be meticulously looked for, is a useful sign, and reflects the softness of thymic tissue that does not compress, infiltrate or displace structures but usually shapes itself around pre-existing harder structures. Terminology of "geometric or geographic" instead of "irregular" describes more accurately the diversity encountered in the shape of intrathyroid thymus. These various shapes probably reflect the above mentioned softness or the uneven involution of thymic rests and potentially point towards the course of descent of the thymus during embryogenesis.

4.5. Extrathyroidal extension in intrathyroid thymus

Similarly, embryological incomplete descent can explain extrathyroidal extension and a connecting tongue of tissue between intrathyroidal and cervical or mediastinal thymus, which occurred in 34.6% and 25% of lesions, respectively. Connecting tissue was best appreciated on longitudinal images, should be actively looked for during scanning and has been shown by other authors including the histologically proven case of Avula et al [5, 7]. Extrathyroidal extension towards the mediastinal or cervical thymus should not be synonymous with malignancy and when the characteristic echopattern of thymus compared to the mediastinal thymus of the same patient is also identified, the diagnosis of thymic tissue against an exophytic nodule could be favoured.

4.6. Echopattern and relation with histology

The echopattern of orthotopic, ectopic and aberrant cervical thymus can be correlated with histology, accordingly: the parenchyma consists of a moderately echogenic stroma corresponding to the epithelial component of medulla, surrounded by peripheral hypoechoic areas corresponding to aggregated lymphocytes in the cortex, while internal echogenic dots and lines correspond to connective tissue septa and vessels inside the septa [17, 31, 33]. US differentiation between cortex and medulla is more difficult in vivo than in frozen specimens [33]. The unique pattern of randomly distributed speckles has also been attributed to the presence of large keratinised Hassal's corpuscles [23, 24], or fat against lymphoid tissue [33, 34]. Hassal's corpuscles are characteristic structures of the thymus and are found exclusively in the medulla [33]. In our series, a hypoechoic line or rim, usually pencil-thin, either complete or incomplete, was seen in 94.2% of lesions, and to our knowledge has not been previously described in intrathyroid thymus. We have observed this rim in thymi at the anterior mediastinum and in multiple images of orthotopic and aberrant thymi in the literature [15-17, 21, 23, 33]. We believe it may represent a thin section of hypoechoic thymic cortex, less likely the thymic capsule which appears echogenic at mediastinal thymi (Figs. 2, 3, 5) and should be differentiated from the thick halo encountered in malignant nodules. Echogenicity of lesion's stroma in our series and in the literature was mostly hypoechoic compared to the thyroid. Isoechoic-to-thyroid stroma, seen in 19.23% of studied lesions, has rarely been previously mentioned [23] and probably reflects prominence of the epithelial component of the medulla, either alone or in combination with fatty involution which occurs with advancing age [33-34]. The "starry-sky" pattern has been described as the hallmark of thymic tissue [5-7, 9-15, 21, 23, 24, 30, 31, 33]. In our series, internal bright spots were distributed either uniformly or unevenly and were thick, thin or mixed, but always identical to the individual patient's mediastinal thymus. We found this comparison extremely useful and we feel that speckles inside a solitary thyroid nodule should always be compared to the echo-pattern of the mediastinal thymus in order not to be misinterpreted as calcifications [16], because calcifications are considered a sign of malignancy [35, 36]. Internal speckles should not be mistaken for colloid substance, which is accompanied by the comet-tail appearance and therefore has a different US appearance, or for microcrystals seen in adenomas [5, 19].

4.7. Colour Doppler appearances

Sparce or no vascularity in intrathyroid thymi, as seen in all lesions with available Doppler images in our series, have been previously reported [11, 21, 23]. This is in contrast to the numerous vascular dots within echogenic lines described in aberrant cervical thymus [32] and is probably due to the larger size of aberrant thymus compared to the 1-cm diameter of intrathyroid thymus. Doppler waveforms in ectopic thymus display a non-specific low systolic peak velocity and a high resistive index, consistent with benignity [17]. This contrasts with findings in parathyroid adenomas and hyperplasias, which are hypervascular on colour Doppler and exhibit prominent diastolic flow [37]. Papillary carcinomas, which may present as hypoechoic lesions with tiny echogenic microcalcifications, are associated with hypervascularity with disorganised central vessels, which may help distinguish these lesions from the avascular intrathyroid thymus [26].

4.8. Size

All lesions in our patients were small, less than 1 cm. This was in favour of benignity. According to guidelines for the management of a solitary thyroidal nodule in children, nodules less than 1 cm should not undergo biopsy unless they carry a high risk for malignancy based on US characteristics [2, 18, 35, 36]. During follow-up in our patients, all lesions remained stable with the exception of one which slightly regressed. This is in accordance with other investigators who showed similar diameters of up to 11 mm and no change or some involution with time [5, 7, 8, 15, 23]. However, other series have described intrathyroid thymus lesions larger than 1 cm, with a mean maximal diameter of up to 1.5 cm [7, 21]. We hypothesise that this discrepancy could be due to measurement of the extrathyroidal component of geographic lesions. There have been reports of two females, aged 12 and 16 years old, with a slight increase in lesion size resulting in surgery [14, 15]. Hyperplasia of orthotopic and heterotopic thymus may occur following upper respiratory tract infection, vaccination, trauma, or other forms of stress as a rebound phaenomenon [33, 34, 38]. Therefore a history of recent stress should be considered when deciding surgery or biopsy in such lesions.

4.9. Differential diagnosis

Differential diagnosis includes other causes of hypoechoic thyroid nodules with internal echogenic structures, mainly medullary or papillary carcinomas and parathyroid adenomas [11, 18, 23, 37]. Moreover, malignant tumours related to the thymus inside the thyroid have been described in adults but are rare in children [11, 13, 14, 39, 40]. These tumours include ectopic hamartomatous and ectopic cervical thymomas, spindle epithelial tumours with thymus-like differentiation (SETTLE) and carcinoma showing thymus-like differentiation (CASTLE) [39-42]. US characteristics, including ovoid or round shape, hypoechogenicity, a hypoechoic rim, and internal bright spots can occur in other histological types of benign and malignant thyroid lesions; however malignancies tend to be large (>1 cm), inhomogeneous masses with a round shape [2, 42]. We feel that none of these lesions share US characteristics like angulated borders causing a geometric or geographic shape, "starry sky" appearance identical to mediastinal thymus, associated with exophytic extension and band of thymic tissue connecting to cervical thymus, all seen in intrathyroid thymus. The characteristic echo-pattern of thymic tissue is considered unique enough to make a correct diagnosis of aberrant

cervical thymus especially in conjunction with reduced or absent vascularity on colour Doppler [17, 23]. With high-frequency equipment and newer US techniques, future studies could compare US characteristics of various histologic types of intrathyroid lesions and parathyroid adenomas with the pre-described characteristics of intrathyroid thymus, and investigate the specificity of these findings in the paediatric thyroid.

4.10. Management

The main limitation of the current study is its retrospective nature and lack of histologic confirmation. Our routine scanning of the mediastinal thymus during neck US in conjunction with the typical sonographic findings of intrathyroid thymus aided in management with follow-up instead of operation or needle biopsy. Children with intrathyroid lesions that have characteristic US appearances do not require further evaluation or follow-up and could alternatively be monitored with US only [43]. Potential sonographic follow-up could be performed in six months and then annually. A different protocol should be applied for children with risk factors, especially those related to radiation or with a familiar predisposition and when laboratory tests are abnormal [2, 34]. In cases of needle biopsy, cytology studies may prove more useful in establishing the diagnosis if they are combined with flow cytometric findings [15, 29]; therefore this possibility should be discussed with the clinicians in cases of suspected intrathyroid thymus. MRI is not routinely advocated for evaluation of thyroid nodules since it is an expensive study requiring sedation in young children and with an unknown specificity of findings. Signal intensity of intrathyroidal thymus is identical to the signal intensity of the mediastinal thymus in all sequences, thus supporting the diagnosis [10].

5. Conclusions

Intrathyroid thymus is a possible finding in children, especially around pre-school and school-age. Small lesions, less than 1 cm in diameter in our series, with an echo-texture comparable to the visible mediastinal thymus of the same patient and no internal vascularity on colour Doppler, located peripherally at the middle or lower portion of the respective thyroid lobe, was consistent with embryological maldescent of an ectopic thymus. Angulated borders resulting in a geometric or geographic shape have not been previously emphasised and should be meticulously looked for. Numerous speckles sparing the lesion's periphery may re-



sult in a thin hypoechoic rim, also not previously described, which should be differentiated from the halo in malignancy. Identification of extrathyroid extension in lesions with the above characteristics and possible connections between them and the thymus are additional details that should be looked for. Further studies are needed to investigate the specificity of these findings in the paediatric thyroid.

Conflict of interest

The authors declared no conflicts of interest.

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