

Diagnosis and management of Intrathyroid Ectopic Thymus

Diagnóstico y manejo del Timo Ectópico Intratiroideo

Gazek N.^a, Dujovne N.^a, Ayarzábal V.^b, Teplisky D.^c, Herzovich V.^a, Felipe L.^d

^aServicio de Endocrinología. Hospital de Pediatría Profesor Dr. Juan P. Garrahan. Buenos Aires, Argentina

^bServicio de Cirugía. Hospital de Pediatría Profesor Dr. Juan P. Garrahan. Buenos Aires, Argentina

^cServicio de Intervencionismo. Hospital de Pediatría Profesor Dr. Juan P. Garrahan. Buenos Aires, Argentina

^dServicio de Diagnóstico por Imágenes. Hospital de Pediatría Profesor Dr. Juan P. Garrahan. Buenos Aires, Argentina

Received: October 16, 2020; Approved: December 21, 2020

What do we know about the subject matter of this study?

The intrathyroidal ectopic thymus is a rare, benign condition caused by aberrant thymic migration during embryogenesis. It is asymptomatic and in most cases is diagnosed incidentally as a thyroid nodule.

What does this study contribute to what is already known?

It reports the importance of pediatricians and imaging specialists recognizing this entity, in order to differentiate it from other intrathyroidal lesions and avoid invasive diagnostic studies and/or unnecessary surgeries in these patients.

Abstract

Intrathyroidal ectopic thymus (IET) is a rare benign condition caused by the aberrant thymic migration during embryogenesis. It is usually incidentally diagnosed as a thyroid nodule. **Objective:** To report the intrathyroidal location of ectopic thymic tissue and to describe the ultrasound findings in children. **Patients and Method:** Retrospective descriptive review of the medical charts and thyroid ultrasound studies of children with nodular images in the thyroid gland, in a third level national pediatric hospital, from January 2010 to August 2017. Solid hypoechogenic intrathyroid lesions with multiple linear tracts or hyperechogenic points that did not change their characteristics during follow-up were considered intrathyroidal thymos. The ultrasound follow-up was performed every 4-6 months. The ultrasound characteristics of the lesions (location, laterality, size and shape), the indication of the ultrasound scan and the follow-up time were analyzed. **Results:** Of 147 patients with thyroid nodules, we identified 12 children with lesions suggestive of an IET (8.1%). The mean age at diagnosis was 3.9 years (range 0-8). It was an incidental finding in all cases. Imaging findings were unilateral in eight patients and bilateral in four patients. All lesions were located in the mid and/or posterior portion of the gland. We adopted a watch-and-wait approach with ultrasound follow-up (mean 2.2 years; range 0.83-4) in all patients except in a 7-year-old boy who presented uncertain fin-

Keywords:

Intrathyroid Thymus;
Ectopic;
Thyroid Nodule;
Ultrasound;
Thyroid

Correspondence:
Natalia Gazek
natalia.gzk@gmail.com

How to cite this article: Andes pediater. 2021;92(3):406-410. DOI: 10.32641/andespediatr.v92i3.3439

dings and underwent surgery, confirming IET in the pathological study. **Conclusions:** Thymic inclusions in the thyroid gland are a rare but increasingly frequent finding, possibly related to the increased use of ultrasound studies. Pediatricians and radiologists should be aware of this entity to differentiate it from other thyroid lesions, avoiding unnecessary studies and/or treatments in these patients.

Introduction

In childhood, the thymus is the primary lymphoid organ and is responsible for the formation of mature T-lymphocytes. The thyroid primordium develops as an epithelial thickening in the pharyngeal floor after the second week of gestation. It moves caudally to the fourth pharyngeal pouch, acquiring its definitive location by the seventh week of gestation. Simultaneously, the thymus and parathyroid glands originate from the third and fourth pair of pharyngeal pouches. In the seventh week of gestation both thymopharyngeal ducts migrate caudally and between the eighth to the ninth week, they fuse in the midline reaching their definitive location in the anterior mediastinum. Due to the proximity of the thyroid diverticulum to the gill pouches, the descending parathyroid and thyroid gland and the thymus are closely related, explaining the ectopic location of one within the other¹.

Intrathyroidal ectopic thymus (IET) is a rare benign condition caused by aberrant thymic migration during embryogenesis. Its detection has increased due to the increasing use of ultrasonography. It is asymptomatic and in most cases is diagnosed incidentally as a thyroid nodule². Although it is defined in the literature by characteristic ultrasound findings^{3,4}, it sometimes leads to unnecessary diagnostic studies due to suspicion of malignant nodular pathology. Intrathyroidal thymic tissue remnants can be explained by the close relationship that exists during embryonic development between the thyroid gland and the thymus.

The objective of this report is to describe the intrathyroidal location of ectopic thymic tissue and the ultrasound findings in children to alert physicians to the benign nature of this entity, avoiding invasive diagnostic studies and/or unnecessary surgeries.

Patients and Method

Retrospective review of clinical data and thyroid ultrasound scans performed in patients under 18 years of age who attended the endocrinology service due to diagnosis of thyroid nodule from January 2010 to August 2017 in a third-level pediatric center in Buenos Aires, Argentina.

On admission, anamnesis with a complete physical examination of the cervical region and characteristics of the thyroid gland was performed in each case.

The ultrasonography was performed by the pediatric imaging specialist using a 7.5 MHz linear transducer probe.

Solid hypoechoic intrathyroidal lesions with multiple linear or punctiform hyperechoic tracts that did not change their characteristics during follow-up were considered to be intrathyroidal thymus. Ultrasound follow-up was performed every 4 - 6 months.

The ultrasound characteristics of the lesions (location, lateralization, size, and shape), the indication for ultrasound, and the follow-up time were described.

The study was approved by the Institutional Ethics Committee and full protection of patient data was guaranteed.

Results

147 patients presented with thyroid nodules, either as a single nodule, multinodular goiter, cysts, nodule with adenopathy, or cervical mass. 12 (8 males) had lesions suggestive of intrathyroidal thymus (8.1%) (Table 1). The mean age at diagnosis of the patients was 3.9 years with a range of 0 to 8 years.

All cases were incidental findings and in one of them, the diagnosis was prenatal. Regarding ultrasound findings, the lesions were unilateral in eight patients and bilateral in four patients. All lesions were located in the middle and/or posterior third of the thyroid gland. The range of the largest diameter of the lesions was variable between 3-25 mm (mean 6.4 mm). In terms of shape, seven were rounded and five were fusiform. All but three had defined margins. 11 patients presented solid, hypoechoic lesions in the ultrasound with linear or punctiform images in their hyperechoic interior and without significant vascularization (figure 1).

A 7-year-old patient (case 1) presented a dubious image in the left thyroid lobe with hypoechoic and undefined margins, therefore surgical resection was decided, after 1 year of ultrasound follow-up (figure 2). The anatomopathological report confirmed IET. In the remaining 11 patients, a watchful waiting approach

was taken, with a mean ultrasound follow-up of 2.2 years (range 10 months to 3 years).

Ultrasound examinations showed that the lesions remained stable except in two patients who presented

with bilateral lesions that presented unilateral reduction after 5 and 4 months of follow-up (cases 4 and 9, respectively).

Discussion

In our population, the prevalence of IET was 8.1%. Previous studies report different percentages of prevalence such as 2.17% (15/690)⁵, 3.9% (7/108)⁴, 0.99% (375/37816)⁶, and 0.4% (12/3195)⁷ in which ultrasonography was performed for different reasons. Bang et al.⁵ included patients referred due to cervical masses, goiter, or torticollis. Fukushima⁶ included the study of 37816 children exposed to the nuclear plant accident. This is the only work reported on the prevalence in the general population.

All lesions were incidental findings located in the middle and/or posterior third of the thyroid gland similar to previous reports^{5,7,8}. The mean age at diagnosis was 3.9 years while in previous reports it varied between 13 months⁵ and 7.5 years⁸ although the ranges were from 0 - 18 years. They presented as bilateral and unilateral lesions with no predominance of lateralization. The range of the largest diameter of the lesions was variable between 3-25 mm, coinciding with previous reports^{3,5}.

Case	Sex	Age (years)	Indication for ultrasonography
1	Male	7	Thyroid follow-up
2	Male	5	Thyroid follow-up. Juvenile xantho-granulomatosis
3	Female	3	Thyroid follow-up
4	Male	2	Cervical lymphadenopathy
5	Male	3	CT scan finding in a patient with neuroblastoma
6	Male	5	Thyroid follow-up. Hypothyroidism
7	Male	RN	Prenatal diagnosis of colloid cysts
8	Female	4	Cervical lymphadenopathy. Epileptic encephalopathy
9	Male	2	Thyroid follow-up
10	Female	2	Thyroid follow-up. Celiac disease
11	Female	8	Thyroid follow-up
12	Male	6	Thyroid follow-up

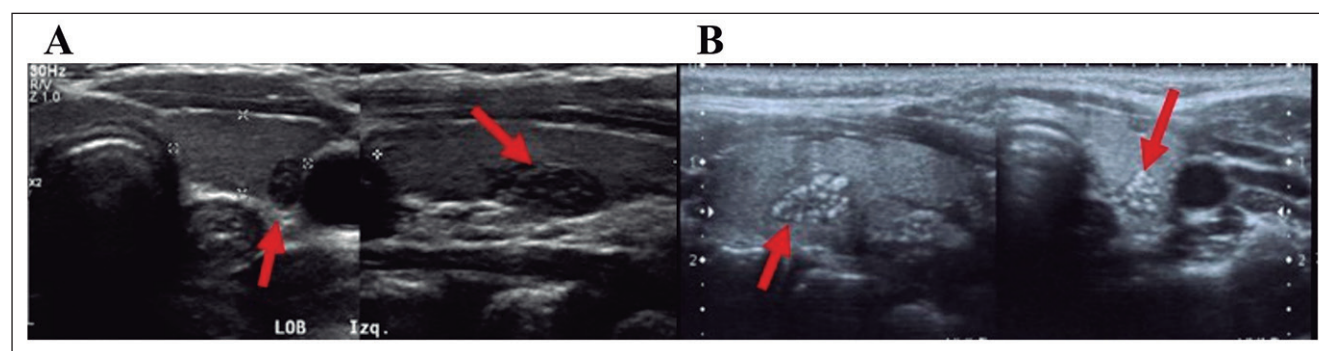


Figure 1. Images of intrathyroid thymuses. 1A: Thyroid gland with a homogeneous echotexture and a solid, heterogeneous, predominantly hypoechoic nodule measuring 2.8 x 9 mm located in the middle third of the left lobe without significant vascularization. 1B: Thyroid gland with a homogeneous echotexture and a solid, heterogeneous, internally hypoechoic nodule measuring 6 x 10 mm with well-defined margins located in the middle third of the left lobe without significant vascularization.



Figure 2. Image of case 1. Thyroid gland with a homogeneous echotexture and a hypoechoic round-shaped nodule with ill-defined margins measuring 4 x 6 mm in the middle and posterior third of the thyroid lobe.

In the follow-up, two patients presented unilateral reduction of the initially bilateral lesions at diagnosis. In the follow-up of 9 children with intrathyroidal thymus, Segni et al. reported the size reduction and echogenicity of these lesions in two adolescent patients (13 and 17 years old), concordant with the reduction of the normal thymus observed at that age⁴. Yildiz et al. described size reduction in 1 of the 9 patients followed up⁸, while Bang et al reported stability of the lesions in 3 patients and size reduction in 1 of those who had ultrasound follow-up. In the study by Fukushima et al, the authors reported that the incidence of IET was inversely correlated with age⁶. However, there is one case of IET reported in a 29-year-old woman⁹.

In our cohort, case 1 was the first patient evaluated who presented with a lesion in the posterior region of the left lobe with suspicious ultrasound characteristics (hypoechoic solid with poorly defined margins) inaccessible to fine-needle aspiration (FNA), so surgery was decided, and the presence of intrathyroidal thymic tissue was confirmed by anatomopathological study. The final diagnosis of IET was striking since the ultrasound did not present the characteristic nodule with defined margins and hyperechoic linear tracts within. This is possibly due to the limitation of the ultrasound technician to define the margins of the nodule, not providing tools for diagnostic certainty.

On the other hand, due to the inaccessibility to FNA and the persistence of these findings suspicious of malignancy after 1 year, a more aggressive therapeutic approach was taken. It should be noted that this was the first patient diagnosed with IET, which generated a greater alert in the treating team about the existence of this entity.

Although the incidence of thyroid nodules is lower in the pediatric age compared with adults, whether detected by physical examination (1.5% vs. 3-6%) or ultrasonography (18% vs. 50%), when faced with a solitary solid nodule the risk of malignancy is higher in children than in adults (22-26% vs. 5-10%)¹⁰. Therefore, misdiagnosing a thyroid nodule with microcalcifications as an IET can lead to unfortunate results. To avoid this, it is necessary to recognize the IET in the ultrasound in order to differentiate it from malignant pathology and avoid unnecessary FNA or even hemithyroidectomies. It is important to emphasize how useful it is for the ultrasound technician to compare the thyroid nodule with the patient's own thymic tissue.

The differential diagnosis of this entity includes as the most frequent findings Hashimoto's thyroiditis with nodule, thyroid adenoma, and thyroid carcinoma. It is possible to identify typical characteristics of each entity, such as the presence of microcalcifications in thyroid carcinoma and the thyroid nodule within a gland of heterogeneous echogenicity in thyroiditis, un-

like IET which is surrounded by healthy thyroid parenchyma and does not present calcifications. Other less frequent entities to consider in the differential diagnosis of IET are ectopic parathyroid adenoma, leukemia, and lymphoma. Rare cases of thymomas¹¹, thymic carcinoma, and lymphomas in ectopic thymic tissue have also been reported¹². More rarely, in children and adolescents, there are malignant intrathyroidal tumors (called spindle epithelial tumors with thymus-like differentiation) considered to originate from ectopic thymic tissue or remnants of the gill pouches¹³.

Although there is no universal standard for the management of IET, we consider that annual ultrasonography should be performed on patients until remission of the lesions. The typical lesion is located in the middle and/or lower third of the thyroid gland; it is hypoechoic, with hyperechogenic line and dots echoes inside, fusiform in shape and well defined, but with slightly irregular margins and without significant vascularization. It is important to emphasize in the follow-up, that when a thyroid nodule increases in size (exceeding 0.8-1 cm) or changes its ultrasound characteristics, it is necessary to perform an FNA.

The limitations of our study include its retrospective design and the fact that histopathologic diagnosis was confirmed in only one of the 12 patients.

Conclusions

Due to the increased use of ultrasonography, the detection of lesions compatible with IET has increased in recent years, so with this small cohort of pediatric patients followed in a tertiary hospital, we intend to report the importance of pediatricians and imaging specialists to recognize this entity, in order to differentiate it from other intrathyroidal lesions avoiding invasive diagnostic studies and/or unnecessary surgeries in these patients.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

References

1. Kabaalioglu A, Oztek MA, Kesimal U, et al. Inthathyroidal ectopic thymus in children: a sonographic survey. *Med Ultrason*. 2017;19(2):179-84.
2. Avula S, Daneman A, Navarro et al. Incidental thyroid abnormalities identified on neck US for non-thyroid disorders. *Pediatr Radiol*. 2010;40:1774-80.
3. Kim HG, Kim MJ, Lee MJ. Sonographic appearance of intrathyroid ectopic thymus in children. *J Clin Ultrasound* 2012;40:266-71.
4. Segni M, di Nardo R, Pucarelli I, et al. Ectopic inthathyroid thymus in children: a long term follow-up study. *Horm Res Paediatr*. 2011;75:258-63.
5. Bang M, Shin J, Lee W, et al. Intrathyroidal ectopic thymus in children. A benign lesion. *Medicine* 2018;97:14.
6. Fukushima T, Suzuki H, Ohira T et al. Prevalence of ectopic intrathyroidal thymus in Japan: The Fukushima Health Management Survey. *Thyroid* 2015;25:534-7.
7. Kim H, Kim M and Lee M. Sonographic appearance of intrathyroid ectopic thymus in children. *Journal of Clinical Ultrasound* 2012;40:266-71.
8. Yildiz A, Ceyhan K, Siklar Z et al. intrathyroidal ectopic thymus in children. Retrospective analysis of grayscale and Doppler sonographic features. *J Ultrasound Med*. 2015;34:1651-6.
9. Kim A, Kang SH, Bae YK. Ectopic intrathyroidal thymus accompanied by intrathyroidal parathyroid as a cause of a solitary thyroid nodule in adult. *Int J Clin Exp Pathol*. 2014;7:6375-8.
10. Niedziela M. Pathogenesis, diagnosis, and management of thyroid nodules in children *Endocr relat Cancer* 2006;13:427-53.
11. Dhall G, Ginsburg HB, Bodestein L, et al. Thymoma in children: Report of two cases and review of literature. *J Pediatr Hematol Oncol*. 2004;26:681-5.
12. Büyükyavuz I, Otcu S, Karnak I, et al. Ectopic thymus tissue as a rare and confusing entity. *Eur J Pediatr Surg*. 2002;12:327-9.
13. Folpe AL, Lloyd RV, Bacchi CE, et al. Spindle epithelial tumors with thymus-like differentiation: a morphologic, immuno histochemical and molecular genetic study of 11 cases. *Am JSurg Pathol*. 2009;33:1179-86.