Intrathyroidal ectopic thymus: an important entity in the differential diagnosis of thyroid nodules

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ABSTRACT

Background. Intrathyroidal ectopic thymus (IET), a benign lesion due to aberrant thymic migration during embryogenesis, is often discovered incidentally. We aimed to present the ultrasound (US) features, diagnostic methods, and follow-up of IET in children and adolescents.

Methods. We searched our database of patients with a nodular thyroid lesion detected by US, between January 2007 and December 2019. In 30/255 (11.7%), IET was diagnosed.

Results. The study included 30 patients (20 males/10 females), mean age 5 years (0.1-12.2, median 5.6) with 34 lesions diagnosed by US as ‘incidentalomas.’ None of the patients had palpable nodules. On US, IET appeared as a hypoechoic lesion, with multiple punctuate internal echoes. 29/34 of lesions had well-defined margins. The most common location of IET was in the middle part (27/34) of the left lobe (19/34). The mean longest diameter at diagnosis was 6.4 mm (2.5–21, median 4.5). Sonographic follow-up was available in 25 patients with 27 lesions. The mean time of observation was 2.7 years (0.3-7.5, median 2.1). While 13/27 cases showed decreased size or regression during follow-up, the other 13 increased in size, and there was no change in size in one. Pubertal progression was associated with both increment and decrease in size of IET. Fine needle aspiration (FNA) was performed in 5 patients and surgery in one.

Conclusions. IET should be considered in the differential diagnosis of pediatric thyroid nodules as a cause of FNA and/or surgery. Regular US monitoring can be used safely in the follow-up of this lesion. We present one of the largest series in the literature with long-term follow-up and description of patients’ pubertal status. IET prevalence was 11.7% among children and adolescents with a nodular thyroid lesion, higher than that stated in the literature.

Key words: children, ectopic thymus, thyroid, ultrasonography, nodule.

The relatively increasing use of ultrasound (US) examination in children and advances in imaging technologies may increase the detection of more thyroid lesions than there used to be. Intrathyroidal ectopic thymus (IET), which is due to aberrant thymic migration during embryogenesis, is one of such lesions. The thymus derives from the third and fourth branchial pouches and descends to the upper mediastinum, reaching its final position. Aberrant thymic migration may result in ectopic thymic rests along the normal pathway of descent, which may persist in the soft tissues of the neck.¹ Because of the close relationship between the two organs’ descents, thymic tissue can get sequestered within the thyroid, the most common site for ectopic cervical thymus.²

While unnecessary investigations may cause anxiety for patients and families with additional costs for the health care system, thyroid lesions found in children need to be thoroughly...
examined. Although thyroid nodules are less frequent in children than in adults, a higher malignancy rate is highlighted in this group.\textsuperscript{3} In most cases, the diagnosis of IET can be made safely with US. The most significant characteristic of this lesion is its echogenicity, which is similar to the normal thymus.\textsuperscript{4} However, IET may also be mistaken for a thyroid nodule, especially a malignant one, due to similar sonographic characteristics. This similarity may lead to fine needle aspiration (FNA) and/or unnecessary surgeries in children.\textsuperscript{5}

Although IET is thought to be a rare entity discovered incidentally, its prevalence is not well known. Most of the reports describe individual cases or small series. Research presenting follow-up is even more scarce.\textsuperscript{6,7} Herein, we report a series of 30 children and adolescents with IET detected by US—and present follow-up results.

Material and Methods

We searched our database of patients under 18 years old with a nodular thyroid lesion detected by US, between January 2007 and December 2019. In 30/255 (11.7\%) IET was diagnosed. We retrospectively studied the clinical and US findings of these patients. The analysis included the reason for referral, age at IET diagnosis, duration of follow-up, pubertal status at diagnosis (i.e. Tanner stages 1 to 5) and at last follow-up, levels of thyroid stimulating hormone (TSH), free T4 and thyroid peroxidase antibody (TPOAb) as well as localization, longest diameter, and US features of IET, and interventions (FNA and surgery). Serum levels of thyroid hormones and thyroid autoantibodies were determined by commercial kits. The US examinations were performed on several US machines by several well-trained radiologists under the supervision of a faculty member. Patients underwent US examinations at 3- to 12-month periods for follow-up. FNA specimens were obtained under sonographic guidance by an experienced radiologist and evaluated by qualified cytopathologists. IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA) was used for statistical analysis. Continuous variables are expressed as mean (range, median).

This retrospective study did not require written informed consent.

The Institutional Review Board approved the study (Karadeniz Technical University, Faculty of Medicine, 28/01/2021, 2020/386).

Results

Out of the 255 children evaluated for a thyroid nodule between 2007 and 2019, IET was incidentally found in 30 (%11.7) (20 males/10 females). The mean age at the first examination was 5 years (0.1-12.2, median 5.6 years) and only 2 patients were pubertal (Tanner stage 2 and above). The indications that led to the initial US were as follows: cervical lymphadenopathy (n=6), congenital hypothyroidism (n=2), elevated serum TSH concentration (n=4), ‘thyroid nodule’ found by US performed elsewhere (n=17), and follow-up imaging after hemato-oncological cancer treatment (n=1). None of the children had a palpable thyroid nodule or clinical evidence of thyroid malignancy at presentation or during the follow-up period. We observed 34 IETs in 30 patients as four patients had IETs bilaterally. While 28 cases were diagnosed by US, five cases were diagnosed by FNA, and one by surgery. Apart from the five patients with FNA and the one who had undergone surgery, all the other patients were diagnosed at the first US. A total of 19 IETs (55.9\%) were located in the left lobe, and most (79\%, 27/34) in the midportion of the thyroid lobe.

On US examination, IET appeared as a round, oval, or irregular hypoechoic area, with regular linear and punctate bright internal echoes. The lesions generally had a typical echo pattern consistent with the descended thymus. The mean longest diameter of IET was 6.4 mm (2.5-21, median 4.5), and 88\% (30/34) were <1 cm in the longest diameter. 85.3\% (29/34) had well-defined margins.
At diagnosis, serum TSH concentrations were within normal levels in 25 patients, slightly above the reference range in 4 patients, and one patient had a significantly high TSH and a low free T4. Four patients were receiving L-thyroxine therapy for primary hypothyroidism (two congenital, two acquired). TPOab was positive in 1 of the 21 patients in which the analysis was available.

A total of 25 children with 27 lesions were followed up with a mean follow-up time of 2.7 years (0.3–7.5, median 2.1 years). No change in size was observed in one lesion after 4.1 years. 13 (48%) lesions showed an increase in the longest diameter by 0.3-4 mm initially, but then the lesions were stable. A decrease in size or complete regression was observed in 13 (48%) lesions after a mean time of 2.4 years (0.3–7.5, median 1.5 years). At the last follow-up, 7 patients were pubertal, and one was postpubertal. Pubertal progression (compared to the initial examination) was associated with both increment and decrease in size of IET. While 4/8 lesions in patients with pubertal progression showed an increase in size, the other 4/8 lesions decreased in size.

In most cases, a conservative approach was used. FNA was performed in 5/30 patients, and hemithyroidectomy in one. The patients having FNA were older (8.7 vs. 4.3 years) and had lesions with a larger longest diameter (8.2 vs. 6.1 mm) compared to the patients without FNA. In these cases, interventions were performed due to the concern that these lesions might represent a malignancy. The only patient who underwent surgery was the ‘first’ IET case in our series and belonged to the earliest years of the study period when surgeons preferred immediate surgery due to concern for malignancy and accuracy of FNA in children with suspicious nodules. The ‘nodule’ size was 10 mm, and there was suspicion of increased vascularity. Regarding the cases with FNA, two of them did not present the typical echotexture of IET, both were ≥10 mm in size and showed an increase in size on follow-up. Two others also did not have the classical appearance, one of them had increased vascularity, and the other had irregular margins. The last case showed increased vascularity and ill-defined margins. Cytologic analysis revealed benign-appearing lymphocytes in all FNAs. In one patient, hemithyroidectomy was performed after two months of observation, and the histological examination confirmed the presence of IET. Intrathyroidal thymus in a 1-year-old girl is presented in Figure 1.

Discussion

Herein, we reported our experience in the evaluation of IET over twelve years. Of the 30 patients with 34 lesions, 28 cases were diagnosed by US findings, five cases were diagnosed by FNA and one by surgery. There are not many reports on IET. A recent review of the pediatric literature revealed only 59 previously published cases of IET masquerading as thyroid nodules or neoplasia in US.8

As IET had been identified by imaging studies performed for other indications in most cases reported in the literature, it can be defined as an ‘incidentaloma.’ Incidental thyroid findings detected on US examinations in children have been documented by Avula et al.9 In a series of 287 neck US performed for non-thyroid indications, they identified 52 patients with thyroid abnormalities (18%), of whom 9 (17.3%) were diagnosed as IET. Yildiz et al.10 reported

![Fig. 1. Intrathyroidal thymus in a 1-year-old girl.](image-url)
a prevalence of 4.2% in 216 children who had undergone a thyroid or neck US examination only in a one-year period. Kim et al. found a prevalence of 0.4% during a seven-year-period among 3195 children. We found this rate as 11.7% among children and adolescents with a nodular thyroid lesion between 2007 and 2019, higher than the previously published literature. The wide range of reported IET prevalence in the limited number of studies is probably due to the different patient selection methods.

Ultrasound is the recommended diagnostic modality for IET because of its unique appearance characterized by a hypoechoic pattern with multiple regular linear and punctate internal echoes. These bright echogenicities in IET represent fat against lymphoid tissue or connective tissue septae and blood vessels. This echotexture is similar to the normal thymus, which is often visible in the suprasternal area in children by US. Another characteristic feature of IET is its location in the middle or the lower third of the thyroid, which is explained by the embryologic origin of the thymus. The predominance of IET occurrence in the middle part of the thyroid lobe was also observed in our study. Most IETs have well-defined margins, but there is inconsistency regarding the shape of IET in reports. While some authors described these lesions as not simply rounded or ovoid nodules having irregular margins, others noted diverse shapes as round, triangular, polygonal, or fusiform on different planes. Our observations are similar to other authors’. Although most authors did not report vascularity, others reported isovascularity with thyroid parenchyma in some patients.

While IET has typical clinical and sonographic characteristics allowing diagnosis, the US differential diagnosis between IET and malignant nodules may be challenging. Due to the hypoechoic texture of benign thymic tissue with microcalcification-like punctate echogenicities, distinguishing IET from suspicious lesions may be difficult, and it might be mistaken as a high-risk nodule that needs to be referred for FNA. Further, irregular margins can additionally suggest malignancy. It is essential to be aware of the sonographic pattern of IET and interpret the findings cautiously to avoid unnecessary investigations and surgery in children. To avoid unnecessary interventions, clinicians and radiologists should be familiar with the sonographic appearance of normal thymic tissue. Differentiating suspicious thyroid nodules from an IET using US requires good experience. Critical features that may help differentiate IET from thyroid nodules are a characteristic hypoechoic solid lesion with multiple linear or punctate internal echoes-an echotexture similar to the thymus, well defined margins, and mid-to low-lying location. A view of the thymus should be considered when US imaging reveals an intrathyroidal lesion with these features. Thus, if the radiologist or the clinician is well-acquainted with the typical characteristics of IET, further invasive procedures could be avoided. However, when sonography results are inconclusive, further evaluation with other techniques such as elastography or FNA, only if certainly needed, could be considered.

In most previously reported cases, the diagnosis of IET was made after FNA and/or surgery. Apart from thyroid nodules, the differential diagnoses also included hematological malignancies such as lymphoma and lymphocytic leukemia in some cases. In addition, there are exceptionally rare cases of intrathyroidal malignancies associated with thymic tissue, e.g., spindle epithelial tumor with thymus-like differentiation. Although surgery was performed in a substantial proportion of previously reported cases, the recent literature supports a conservative attitude and avoidance of surgery in most IETs. Our approach is in line with this recommendation. In our center, we follow-up children with various thyroid diseases with regular long-term US monitoring. Accordingly, in our series, FNA was performed in 5/30 cases with IET and surgery in only one. We support that US and, in select cases, FNA can be used in the diagnosis and follow-up of thyroid lesions such as IET. FNA should be
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avoided in cases demonstrating stability or regression at the US follow-up.

In one-half of the cases described in the current report, we observed a decrease in size or regression with time, and in one patient, there was no change in size over a time period of 4 years. This finding confirms the substantially benign course of IET, which has also been reported in the limited studies presenting follow-up. It has been suggested that the regression may be reflecting the tendency toward thymic involution occurring with advancing age. On the other hand, we observed an increase in size in the other half of cases. This increment may be linked to the normal growth of the thymus or rebound thymic enlargement during childhood. However, these children are going to be followed up for any other differential diagnosis. Observations described by other authors regarding the natural history of IET have varied. While the size did not correlate with the child’s age at diagnosis, an inverse relationship between the size and age was shown, suggesting that these lesions disappear or regress over time. We suggest that the small increases in lesion diameter can be safely monitored by US, along with the rare occurrence of a tumor arising from thymus.

We showed that pubertal progression was associated with both increment and decrease in size of IET. Since eutopic thymus is expected to disappear following puberty, various Tanner stages of patients (ranging from 1-5) at the last follow-up might explain this finding. We couldn’t recognize another study describing pubertal findings of IET patients in detail with follow-up.

Even though we have reported a relatively large series of IET with long-term follow-up, this study has several limitations. First, it was a retrospective review, and we were unable to review the US images of the lesions. Second, we were unable to use elastography, a newly proposed diagnostic modality in the evaluation of IET. Description of the patients’ pubertal status over the follow-up period and its association with changes in size is the strength of the study.

In conclusion, IET may be more common than previously thought and should be considered in the differential diagnosis of incidental thyroid lesions and nodules in children and adolescents, keeping in mind that the US characteristics of IET can suggest a malignant nodule. Awareness of this entity with long-term follow-up can reduce the need for FNA or unnecessary surgery.

Ethical approval

The Institutional Review Board approved the study (Karadeniz Technical University, Faculty of Medicine, 28/01/2021, 2020/386).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: EAC, SK, IE, HD, GK; data collection: EAC, SK, IE, HD, GK; analysis and interpretation of results: EAC, IE, GK; draft manuscript preparation: EAC. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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