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Diagnostic Features of Thyroid Nodules in Pediatrics

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Objective: To investigate a cohort of pediatric patients with thyroid nodules, defining histotype frequency and differences between subjects with hyperthyroidism and euthyroidism and benign and malignant nodules.

Design: Retrospective cohort.

Setting: Consecutive cases from 9 Italian pediatric endocrinology centers for the last 10 years.

Patients: One hundred twenty pediatric patients with thyroid nodules.

Intervention: Doppler ultrasonography was performed in 71 subjects; scintiscan, in 56; fine-needle aspiration biopsy in 104; and 63 underwent surgery.

Main Outcome Measures: The differences in clinical, laboratory, and ultrasonographic data between patients with hyperthyroidism and euthyroidism and malignant and benign nodules were evaluated.

Results: One hundred fourteen patients had euthyroidism and 6, hyperthyroidism. The latter had more compressive signs ($P=.003$), greater nodule diameter ($P=.02$), intranodular vascularization pattern ($P=.01$), and increased scintiscan uptake ($P<.001$). Fine-needle aspiration biopsy disclosed benign lesions in 77 cases, malignant lesions in 19, and "suspicious" lesions in 8. Histologic examination disclosed 1 Hurthle cell and 5 follicular adenomas in patients with hyperthyroidism, whereas in patients with euthyroidism, 33 hyperplasic nodules, 19 carcinomas (14 papillary, 3 follicular, and 2 medullary), 3 follicular and 1 Hurthle cell adenoma, and 1 teratoma were detected. Nine patients had enhanced scintiscan uptake. Among the patients with euthyroidism, malignancies more frequently had palpable lymph nodes ($P<.001$), compressive signs ($P=.004$), microcalcifications ($P<.001$), intranodular vascularization ($P=.01$), and lymph node alterations ($P<.001$).

Conclusions: The diagnosis of pediatric thyroid nodules should be based on a stepwise evaluation that includes clinical, laboratory, and radiographic modalities. While laboratory assessments establish thyroid function, ultrasonographic imaging identifies clinically unapparent nodules and provides detailed nodule characterization for suspected malignant lesions. Scintiscan in patients with hyperthyroidism and fine-needle aspiration biopsy in patients with euthyroidism represent the next logical step.

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Although thyroid nodules in childhood and adolescence are rare, with an estimated prevalence ranging from 0.05% to 1.8%, they are more often malignant (up to 25% of cases) compared with those observed in adulthood[1-5] and therefore require a careful evaluation and a more aggressive diagnostic approach. Moreover, while the clinical and etiological characterization of thyroid nodular disease has been extensively explored in adulthood, in childhood this is not the case because of the challenge of collecting large cohorts of patients. Although thyroid nodular disease comprises a wide spectrum of disorders in pediatrics, attention has mostly focused on the 2 most frequent malignant lesions, papillary and follicular cancer, whereas only a few studies have concentrated on the prevalence or on the clinical and functional characteristics of other histotypes. Although valuable clinical experiences have been collected over the past few years,[1-5] we believe this issue deserves further investigation.

The objectives of the present study were to (1) evaluate the frequency of the various histotypes in a large cohort of children and adolescents affected by thyroid nodules, (2) describe the characteristics of

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subjects with hyperthyroidism, and (3) analyze the clinical and ultrasonographic differences between benign and malignant nodules. Based on these data and by comparing them with recent literature, we then provide a reasoned diagnostic approach to the clinical management of thyroid nodules in pediatrics.

METHODS

We conducted a retrospective study on 120 patients with thyroid nodules diagnosed in childhood or adolescence, gathering data from 9 Italian pediatric endocrinology centers that provided consecutive cases. Subjects younger than 18 years with thyroid nodules with a diameter of 1 cm or more were included in this study. Exclusion criteria were (1) autoimmune thyroid diseases and/or (2) previous oncohematological disorders or history of irradiation exposure. Autoimmune thyroid disease was ruled out by serum antithyroglobulin and antithyroperoxidase antibody tests and by thyroid ultrasonography at finding of the nodule. All patients included had negative serum antibody test results and thyroid imaging normal for typical autoimmune patterns.

Clinical, laboratory, and radiographic data were collected from medical records. Age, sex, reasons for medical consultation, presence of a palpable nodule or lymph nodes, and symptoms attributable to compression of adjacent structures (discomfort, dysphagia, pain, breathing obstruction, hoarseness) were documented. Serum thyrotropin, free thyroxine, and free triiodothyronine levels were determined by highly specific fluorometric or enzyme-linked immunoassays to classify patients according to thyroid function. Serum calcitonin level (reference values <10 pg/mL [to convert to picomoles per liter, multiply by 0.292]) was obtained in 85 cases. All patients underwent thyroid ultrasonography to evaluate the nodule diameter and echoic pattern. Based on the comparison of nodule echogenicity with the normal surrounding thyroid tissue, the echoic pattern was classified as without echoes (anechoic), decreased (hypoechoic), equally echoic (isoechoic), increased (hyperechoic), or a mix of these patterns (mixed). The presence of lymph node alterations was assessed at the ultrasonographic evaluation based on the presence of 1 or more of the following findings: rounded bulging shape, irregular margins, increased size, absence of echogenic hilum, heterogeneous echoic pattern, cystic areas, presence of calcifications, or diffuse/irregular vascularity throughout the lymph node instead of the normal central hilar vessels at Doppler imaging. Doppler ultrasonography was performed in 71 subjects to evaluate nodule vascularization characteristics (intranodular, intranodular plus peripheral, peripheral). Technetium Tc 99m scintiscan was performed in 56 patients and the results were classified into increased, reduced, or normal isotope uptake at the nodule or nodule not found. Cytologic specimens based on fine-needle aspiration biopsy (FNAB) were obtained in 104 cases and the results were categorized as benign, "suspicious," or malignant lesions. Histologic results were obtained in the 63 subjects who underwent surgery.

The subjects were classified as having malignant lesions by histologic examination; otherwise, they were considered to have benign nodular pathology based on histologic (n=44) or cytologic (n=43) examination. Sixteen subjects had euthyroidism and were considered as having benign nodules based on the clinical parameters, ultrasonographic imaging, and course of the disease, according to previously published suspicion criteria.[1] All had regular-margin nodules with a normal vascularization pattern and without any lymph nodal alterations. They underwent neither surgery nor FNAB but were followed up with clinical evaluations and imaging studies.

Finally, FNAB sensitivity (number of true positives divided by the sum of true positives and false negatives), specificity (number of true negatives divided by the sum of true negatives and false positives), and diagnostic accuracy (sum of true positives and true negatives divided by the number of the sample) were calculated in patients with euthyroidism who underwent both FNAB and surgery (n=55).

The Shapiro-Wilk test was used to check the normality of data distribution. Differences between groups were established by *t* test to compare the mean values of continuous variables. This test was used to assess differences between patients with hyperthyroidism and euthyroidism and between benign and malignant nodules with regard to the patient ages and the maximum nodule diameter. To assess differences between the distributions of the categorical binary variables among the groups, a χ^2 test was used. When the sample size was less than 15 and a large sample approximation could not be achieved, a Fisher exact test was used. Both of these tests were used to assess disproportions in sex, the number of palpable nodules, the presence of compressive symptoms, multinodular disease, the presence of microcalcifications, evidence of lymph node alterations, and echoic, vascularization, and scintiscan patterns. The magnitude of the difference between groups was calculated as an odds ratio (OR), as the cross product of the probability of exposure to a certain factor or characteristic in the 2 groups compared. Calculations were considered statistically significant when the *P* value was less than .05. SPSS software (SPSS Inc, Chicago, Illinois) was used.

RESULTS

The study group data are summarized in **Table 1**. Based on thyroid function, 6 patients had hyperthyroidism and 114, euthyroidism. Thyroid nodular disease was more frequent in girls and was diagnosed at a mean (SD) age of 11.5 (3.2) years (range, 2.5-16.9 years; median, 12.3 years). Nodules were detected by palpation in 100 cases (83.3%). Of these, 58 subjects also had palpable lymph nodes and/or compressive symptoms. The other 20 cases presenting with goiter alone or with palpable lymph nodes were found to have thyroid nodules by ultrasonography.

A comparison between clinical data regarding patients with hyperthyroidism and euthyroidism highlighted a significant difference in the presence of compressive signs (OR, 18.7; *P*=.003), which were more frequent in the subjects with hyperthyroidism. Ultrasonography revealed the mean maximum nodule diameter was greater in subjects with hyperthyroidism than in subjects with euthyroidism (*P*=.02). Patients with hyperthyroidism demonstrated central vascularization more often than did subjects with euthyroidism (OR, 8.8; *P*=.01). Nodule scintiscan uptake was also more likely to be enhanced (OR, 105.9; *P*<.001) in subjects with hyperthyroidism. Fine-needle aspiration biopsy was performed in 104 cases (3 with hyperthyroidism and 101 with euthyroidism), detecting benign, "suspicious," and malignant lesions in 77, 8, and 19 cases, respectively. The 3 hyperthyroid cases all had a "suspicious" lesion. In 7 cases, FNAB retrieved unsatisfactory specimens (6.7%). All of them were repeated to gather more precise information, and at the second evaluation, 2 of them resulted in a benign, 3 in a suspicious, and 2 in a malignant lesion.

Table 1. Clinical, Instrumental, and Cytohistologic Characteristics of the Patients

	No. (%)			
	All Cases	Hyperthyroidism	Euthyroidism	*P* Value
Clinical data				
Sample size	120	6	114	
Female/male	90/30	4/2	86/28	.64
Age, y, mean (SD) [median]	11.5 (3.2) [12.3]	11.6 (1.3) [11.4]	11.4 (3.3) [12.5]	.88
Palpable nodule	100 (83.3)	6 (100.0)	94 (82.5)	.59
Symptoms attributable to compression	29 (24.2)	5 (83.3)	24 (21.1)	.003
Palpable lymph nodes	39 (32.5)	1 (16.7)	38 (33.3)	.66
Ultrasonographic features				
Uninodular (vs multinodular)	85 (35)	6 (0)	79 (35)	.18
Maximum nodule diameter, cm, mean (SD) [median]	2.1 (1.0) [2.11]	3.15 (0.93) [3.32]	2.19 (0.95) [2.04]	.02
Nodule diameter range	1.00-4.50	1.60-4.20	1.00-4.50	
Echoic pattern				.66
Anechoic	10 (8.3)	0	10 (8.8)	>.99
Hypoechoic	41 (34.2)	1 (16.7)	40 (35.1)	.66
Isoechoic	26 (21.7)	0	26 (22.8)	.34
Hyperechoic	11 (9.1)	2 (33.3)	9 (7.9)	.09
Mixed	32 (26.7)	3 (50.0)	29 (25.4)	.34
Patients with microcalcifications	15 (12.5)	1 (16.7)	14 (12.3)	.56
Central vascularization pattern[a]	25 (35.2)	4 (100)	21 (24.1)	.01
Lymph nodal alterations	16 (13.3)	0	16 (14.0)	>.99
Scintiscan uptake[b]				
Decreased	42 (75.0)	0	42 (84.0)	.09
Normal	4 (7.1)	0	4 (8.0)	>.99
Increased	9 (16.1)	6 (100)	3 (6.0)	<.001
Nodule not found	1 (1.8)	0	1 (2.0)	>.99
Fine-needle aspiration biopsy	104	3	101	
Benign	77 (74.0)	0	77 (76.2)	
Suspicious	8 (7.7)	3 (100)	5 (4.9)	
Malignant	19 (18.3)	0	19 (18.9)	
Histology (No. available)	65	6	57	

[a] Seventy-one patients underwent Doppler ultrasonography evaluation (4 in the hyperthyroidism group, 87 in the euthyroidism group).
[b] Fifty-six patients underwent scintiscan (6 in the hyperthyroidism group, 50 in the euthyroidism group).

Table 2. Histotypes, Relative Frequency, and Thyroid Function in 63 Pediatric Thyroid Nodules

Histotype	No. (%)	Thyroid Function at Nodule Diagnosis
Goitrous nodule	33 (53.4)	33 Euthyroid
Papillary carcinoma	14 (22.2)	14 Euthyroid
Follicular adenoma	8 (12.7)	5 Hyperthyroid, 3 euthyroid
Follicular carcinoma	3 (4.7)	3 Euthyroid
Hurthle cell adenoma	2 (3.2)	1 Hyperthyroid, 1 euthyroid
Medullary carcinoma	2 (3.2)	2 Euthyroid
Benign teratoma	1 (1.6)	1 Euthyroid

The histologic data of the 63 patients who underwent surgery are reported in **Table 2**. Sixty-one patients underwent total or subtotal thyroidectomy and 2 underwent lobectomy. Five patients (3 with hyperthyroidism and 2 with euthyroidism) did not undergo FNAB prior to surgery. By histologic examination, 19 nodules were considered to be malignant and 44, benign. Among the latter, 33 nodules had hyperplasic thyroidal tissue with degeneration or colloid areas without defined capsules and were considered to be hyperplasic/goitrous nodules, whereas 11 had a differentiated, uniform, orderly architecture with few mitoses and discrete capsules and were classified as benign adenomas. Four patients with confirmed papillary thyroid cancer had no palpable nodules or symptoms and the malignant nodule was found incidentally. In the 6 patients with hyperthyroidism, histologic examination demonstrated 1 Hurthle cell and 5 follicular adenomas, whereas in patients with euthyroidism histologic examination detected 19 malignant tumors (14 papillary, 3 follicular, and 2 medullary cancers) and 38 benign lesions, including 3 follicular and 1 Hurthle cell adenomas, and 1 teratoma. Based on the 55 subjects with euthyroidism who underwent both FNAB and surgery, all 19 subjects with cancer were correctly identified as having malignant lesions by FNAB, and 30 adenomas/hyperplasic lesions were identified as benign. The histologic examination of the 6 suspicious FNAB specimens demonstrated 4 follicular adenomas (2 hyperthyroid, 2 euthyroid), 1 benign teratoma (euthyroid), and 1 Hurthle cell adenoma (hyperthyroid). Based on these results, FNAB had 100% sensitivity, 83.3% specificity, and 89.1% diagnostic accuracy.

All 16 patients who underwent neither surgery nor FNAB, based on clinical and ultrasonographic characteristics highly indicative for benign nodules, were followed up by clinical, laboratory, and ultrasonographic evaluation every 6 to 12 months for a mean (SD) period of 1.9 (1.1) years. No modifications in nodule or lymph node characteristics occurred in this period.

Table 3. Comparison of Clinical and Ultrasonographic Characteristics of Patients With Euthyroidism With Benign and Malignant Nodules

	No. (%)		
	Benign	Malignant	*P* Value
Clinical data			
Sample size	95 (83.3)	19 (16.7)	
Female/male	70/25	16/3	.40
Age at nodule diagnosis, y, mean (SD) [median]	11.4 (3.3) [12.4]	11.3 (3.1) [12.1]	.88
Palpable nodule	79 (83.1)	15 (78.9)	.74
Symptoms attributable to compression	15 (15.8)	9 (47.4)	.004
Palpable lymph nodes	25 (26.3)	13 (68.4)	<.001
Ultrasonographic features			
Uninodular (vs multinodular)	67 (28)	12 (7)	.41
Maximum nodule diameter, cm, mean (SD) [median]	2.23 (0.86) [2.11]	2.10 (0.95) [2.10]	.76
Echoic pattern			
Anechoic	10 (10.5)	0	.21
Hypoechoic	32 (33.7)	8 (42.1)	.60
Isoechoic	21 (22.1)	5 (26.3)	.77
Hyperechoic	8 (8.4)	1 (5.3)	>.99
Mixed	24 (25.3)	5 (26.3)	>.99
Microcalcifications	5 (5.3)	9 (47.4)	<.001
Vascularization pattern, central (vs other)[a]	12 (23.1)	9 (47.4)	.01
Lymph nodal alterations	3 (3.2)	14 (73.7)	<.001
Scintiscan uptake	39	11	
Decreased	32 (82.0)	10 (90.9)	.67
Normal	4 (10.3)	0	.56
Increased	2 (5.2)	1 (9.1)	.53
Nodule not found	1 (2.5)	0	.99

[a] Fifty-two patients in the benign group and 15 in the malignant group underwent Doppler echography.

Plasma calcitonin level was evaluated in 85 patients and was high in 2 (1910 and 115 pg/mL, respectively). Both patients underwent surgery and were diagnosed as having medullary thyroid cancer.

Fifty-six patients underwent scintiscan; hot nodules (increased scintiscan uptake) were significantly more frequent in the hyperthyroidism group ($P<.001$), as found in 6 of 6 patients with hyperthyroidism and 3 of 50 patients with euthyroidism. Of the 3 subjects with euthyroidism with increased uptake, 1 was diagnosed as having multifocal papillary carcinoma. All the other nodules investigated by scintiscan disclosed normal or decreased uptake with respect to the gland and, in particular, 42 of 50 of the patients with euthyroidism had decreased scintiscan uptake. In 1 case, the nodule was not found.

Table 3 compares the clinical, laboratory, and ultrasonographic characteristics of patients with euthyroidism. Among these, the statistical comparison between benign and malignant lesions showed a difference for both clinical features and ultrasonographic parameters. Patients with malignant nodules more often disclosed palpable lymph nodes (68.4% of patients vs 26.3% with benign nodules; OR, 6.1; $P<.001$) and compressive signs (47.4% of patients vs 15.8% with benign nodules; OR, 4.8; $P=.004$), whereas ultrasonography revealed that, when compared with benign nodules, malignant nodules were more likely characterized by microcalcifications (47.4% of cases; OR, 16.2; $P<.001$), lymph node alterations (73.7%; OR, 85.8; $P<.001$), and intranodular central vascularization pattern (47.4%; OR, 5.0; $P=.01$).

COMMENT

Thyroid cancer must be suspected when a thyroid nodule is found in children and adolescents because it has been estimated that up to 20% to 25% of nodules in pediatric patients are malignant, compared with 5% in adults.[1-8] In a recent review by Niedziela et al,[1] the incidence was estimated to range from 9.2%[9] to 50%,[6] with a mean of 26.4%. Moreover, most reports in pediatrics focused on papillary and follicular carcinomas and much less is known about other histotypes. Therefore, because thyroid nodule management guidelines are based on the experience prevalently gained in adults,[7,10,11] the characteristics in childhood need to be addressed with specific diagnostics.

In this study, we presented a large cohort of children and adolescents with thyroid nodules characterized clinically, functionally, and ultrasonographically to provide further insight into this issue to propose a reasoned diagnostic approach. In our case series, 19 patients (16%) had malignant tumors. Cancer frequency in pediatric thyroid nodules is confirmed to be high and greater than that seen in nodules in pediatric autoimmune thyroiditis (9.6%).[12] Moreover, papillary carcinoma is confirmed to be the most common malignant histotype and no undifferentiated thyroid cancer was found.

It is well-known that an increasing number of thyroid nodules in adulthood have been incidentally discovered in recent decades because of the widespread use of neck ultrasonography or other imaging methods.[13] In

children, too, the incidental diagnosis of thyroid nodules is not uncommon. In our case series, 20 patients with euthyroidism (16.7%) were referred to a pediatric endocrinologist for the incidental ultrasonographic finding of a thyroid nodule, and of these, 4 (20%) were diagnosed with papillary cancer. Because some authors attribute the same risk of malignancy to accidentally discovered nodules and to clinically evident nodules,[11,14,15] whereas others suggest nonpalpable thyroid nodules present an overall low risk,[13] there is considerable controversy over whether clinically unapparent thyroid lesions should be assessed by FNAB. Cancer rates in patients with incidentally discovered nodules (20%) strikingly match those we detected in patients with palpable nodules (16%). It therefore appears reasonable to assert that palpable and nonpalpable pediatric nodules have a similar risk and a common diagnostic approach should be used. Similarly, it is debated whether isolated and multiple thyroid nodules have the same risk of malignancy. Consistent with other reports,[11,15,16] our results suggest that thyroid cancer can be also present in multinodular thyroid disease, although the majority of malignant nodules present as isolated.

While valuable data are available on pediatric thyroid malignant nodules, much less is known about other histotypes. Despite being histologically benign, some tumoral histotypes might necessitate a diagnostic and surgical management strictly resembling those used in cancer. The large study group we investigated allowed us to provide some interesting data about these less common histotypes that are still poorly characterized in pediatrics. Tumor frequency rises 25% when taking into account follicular adenoma, teratoma, and Hurthle cell adenoma. Among the aforementioned, of particular interest is the subgroup responsible for hyperthyroidism that is always associated with a toxic adenoma. This group, accounting for 5% of our case series, showed a high frequency with respect to previous reports.[8,17] Follicular adenomas in 5 patients and a Hurthle cell adenoma in 1 were responsible for hyperthyroidism. The latter histotype, usually presenting as a cold, nonfunctioning nodule, has only been exceptionally associated with hyperthyroidism.[18] Patients with hyperthyroidism apparently demonstrate frequent compressive signs, a predominantly central vascularization pattern, a larger nodule diameter, and a hot scintiscan uptake pattern. Besides a laboratory assay, scintiscan was the most important tool for the correct workup of toxic nodules, as they always showed a hot scintiscan uptake. On the other hand, FNAB had lower value, as it provided no additional information in the diagnostic characterization.

However, the vast majority of thyroid nodules occur in a euthyroid condition, as cancer commonly does. Therefore, the main objective of the diagnostic approach is the identification of clinical and ultrasonographic characteristics associated with malignancy. We, thus, compared nodule features in benign and malignant cases. Patients with thyroid cancer were more likely to present with palpable lymph nodes and compressive symptoms. Both ultrasonography and FNAB proved useful in patients with euthyroidism. The first provided an initial characterization of nodules suspected as being malignant, as they most likely have microcalcifications, a central intranodular vascularization pattern, and lymph node alterations, according to previous reports.[1,4,15,19] It is remarkable that, although the vast majority of cancers showed a hypoechoic pattern at the ultrasonographic evaluation, this feature was of poor clinical utility, as it was also frequently encountered in benign lesions. Fine-needle aspiration biopsy had high diagnostic accuracy (88.7%) only a few points lower than that estimated in a previous report (90.4%).[20,21] This difference is possibly due to the variable rate in suspicious lesions, mainly follicular ones that are currently well-known as the major pitfall.[22] Therefore, FNAB allows a selection of patients to undergo surgery. Scintiscan provides no additional information to further characterize euthyroid nodules; 94% of these patients had a reduced or normal tracer uptake. Moreover, in 1 case, scintiscan did not identify the nodular lesion, and 3 patients had an increased tracer uptake at the nodule, with a normal uptake in the gland. These 3 patients had high-normal borderline thyrotropin levels with normal thyroid hormone levels, and 1 of them was diagnosed with papillary carcinoma. Although we can confirm that scintiscan may only be of use in cases of hyperthyroidism,[4,17] we suggest caution, as enhanced uptake at scintiscan imaging does not automatically imply hyperthyroidism and benign histologic results. In these cases, FNAB may be of value because a small fraction of thyroid carcinomas can present with hot/warm scintiscan uptake.[1]

Measuring thyrotropin, free thyroxine, and free triiodothyronine levels at diagnosis is mandatory to assess thyroid function and establish the further workup. Patients with hyperthyroidism are likely to be affected by toxic adenomas, and therefore, scintiscan is indicated. However, the large majority of patients have euthyroidism. In addition to the assessment of thyroid function, other laboratory assays are limited in the diagnostic workup and management of thyroid nodules. We can add only blood calcitonin level at nodule detection because it proved useful in finding medullary carcinoma at an earlier stage,[23] as occurred in both cases in our cohort.

The retrospective design is a limitation of this study. Our cohort does, however, represent one of the largest and most recent case series in pediatrics, where all retrievable data are retrospective because of the rarity of thyroid nodules. Furthermore, because some of the subjects in the cohort were considered to have benign nodules based only on clinical and ultrasonographic characteristics, our study possibly underestimates cancer prevalence. Moreover, data must be interpreted considering that Italy is a country characterized by mild to moderate iodine deficiency depending on the geographical areas, leading to an increased incidence of goiter.[24,25] As a consequence, benign nodule prevalence can be overestimated.

In conclusion, based on data from a large pediatric cohort of patients with thyroid nodules, we suggest a reasoned approach based on a first-step clinical, ultrasonographic, and laboratory evaluation. Palpable lymph nodes should alert clinicians because they are associated with malignant nodules in about 70% of cases. Although ultrasonography cannot reliably discriminate between be-

nign and malignant lesions based on the ultrasonographic pattern, it does provide an index of suspicion that is helpful in selecting patients to be evaluated by FNAB; microcalcifications, lymph node alterations, or increased intranodular vascularization are highly suspected for malignancy. Ultrasonography, moreover, identifies clinically unapparent nodules that might also be malignant. Determination of blood thyrotropin, free thyroxine, and free triiodothyronine levels is aimed at identifying patients with hyperthyroidism, estimated as 5% of all patients. In these cases, scintiscan, usually disclosing an increased uptake, represents the next logical diagnostic step, and benign histologic results (toxic adenoma) are expected, although surgery is commonly needed. Otherwise, in the most likely case of euthyroidism, FNAB is indicated, as it discloses an 89.1% diagnostic accuracy, potentially allowing the selection of patients to undergo surgery.

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