Ultrasonographic Features of Benign Nodules, Follicular Lesions and Malignant Nodules in the Thyroid Diagnosed Mainly by Fine Needle Aspiration Biopsy

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The purpose of this study was to compare the ultrasonographic features of benign nodules, follicular lesions and malignant nodules in the thyroids of patients who underwent fine-needle aspiration biopsy. We retrospectively analyzed the ultrasonographic features of 231 nodules, which were diagnosed as benign, follicular lesion or malignant nodules with respect to solitariness, echogenicity, echostructure, border characteristics, presence or absence of calcifications, internal vascularity and the presence of a halo. The ultrasonographic features of benign nodules, follicular lesions and malignant nodules were compared using the Fisher-Freeman-Halton exact test. Differences were statistically significant if \( p < 0.05 \). With regard to cytopathology, there were 186 benign nodules, 10 follicular lesions and 35 malignant nodules. The distribution of frequencies of the ultrasonographic features including hypoechogenicity \([46/186 (24.7%), 4/10 (40%), 29/35 (82.9%)\]\), solid echostructure \([63/186 (33.9%), 7/10 (70%), 34/35 (97.2%)\]\), irregular margin \([29/186 (15.6%), 3/10 (30%), 27/35 (77.1%)\]\), microcalcification \([16/186 (8.6%), 2/10 (20%), 15/35 (42.9%)\]\) and absence of a halo \([55/186 (29.5%), 5/10 (50%), 33/35 (94.2%)\]\) between benign nodules, follicular lesions and malignant nodules, respectively, was statistically significant (Fisher-Freeman-Halton, \( p < 0.05 \)). The frequencies of solitariness \([35/186 (18.8%), 2/10 (20%), 7/35 (20%)\]\) and internal vascularity \([101/186 (54.3%), 7/10 (70%), 21/35 (60%)\]\) between benign nodules, follicular lesions and malignant nodules, respectively, were not statistically significant \( (p > 0.05) \). Ultrasound features including hypoechogenicity, solid echostructure, irregular margin, presence of microcalcification and absence of a halo might be effective in the differentiation of malignant nodules and follicular lesions from benign nodules.

KEY WORDS — benign diseases, follicular lesion, malignant diseases, thyroid nodules, ultrasonography
Introduction

With regard to the evaluation of thyroid diseases, ultrasound (US) has become a standard imaging tool; it is noninvasive and inexpensive. Nevertheless, the majority of malignant thyroid nodules have equivocal findings on US [1]. In fact, the lack of definitive US criteria for malignant thyroid nodules presents a real diagnostic problem for radiologists. Follicular lesions present a second diagnostic dilemma. Even cytopathologists cannot distinguish reliably between follicular adenomas and follicular carcinomas. As a result of this, a definite diagnosis is only reached after surgical excision and histopathologic examination [2,3].

The purpose of this study was to compare the ultrasonographic features of benign nodules (colloidal-hyperplastic-adenomatous), follicular lesions (follicular adenoma, follicular carcinoma), and malignant nodules in patients, who underwent fine needle aspiration biopsy (FNAB).

Patients and Methods

The patient group consisted of 231 patients, who were referred to our radiology department for FNAB from March 2006 to January 2008. In each patient, only one nodule (the largest) was biopsied. The mean size of the biopsied nodules was 16.4±9.2 mm (range, 4.5–70 mm). The mean size of the benign nodules, follicular lesions and malignant nodules were 17±8.5 mm, 23.7±20.6 mm and 10.9±4.8 mm, respectively.

The mean age of the patients with benign nodules, follicular lesions and malignant nodules were 46.5±12.1, 49.8±13.7 and 42.3±11.6 years, respectively. The benign nodules group included 33 males and 153 females, the follicular lesion group included 4 males and 6 females and the malignant nodule group included 3 males and 32 females.

US exams were performed by three radiologists (A.O., B.C. and H.M.) in a standardized fashion, including color Doppler examination. The equipment used was an Acuson Antares system (Siemens Medical Solutions, Erlangen, Germany) with a high frequency small part probe (5–13 MHz). Each nodule was assessed with respect to nodule size, solitariness, echogenicity, echostructure, border characteristics, presence or absence of calcifications, internal vascularity and presence of a halo. The echogenicity of each lesion was classified as hypoechoic, hyperechoic, or isoechoic in comparison with the background thyroid tissue. The internal architecture was defined as solid, solid with cystic elements, or predominantly cystic. Predominantly cystic lesions were those containing cystic components that constituted more than 50% of the lesion. Margins of lesions were categorized as well defined when clear demarcation with normal thyroid was noted around more than 50% of a nodule and were considered poorly defined when more than 50% of the border of the lesion was not clearly demarcated. The presence of a complete or incomplete hypoechoic halo around each lesion was also documented, and the predominant blood flow pattern was classified as absence of flow, perinodular or intranodular flow. If a nodule showed both intranodular and perinodular blood flow, it was classified as having intranodular blood flow.

Biopsies were performed with a 23-gauge heparinized needle, according to a previously described technique[4,5]. One to three passes were performed for each nodule. The aspirated contents were expelled onto glass slides. The slides were air-dried and stained with May-Grunwald Giemsa stains. Next, an experienced cytopathologist (K.P.) immediately checked the samples for adequacy. Samples were defined as sufficient when six or more clusters of follicular cells with each group containing at least ten follicular cells were present on the slides. The aspiration samples were classified by the cytopathologist as malignant, benign, inadequate or follicular lesion. The ultrasonographic features of benign nodules, follicular lesions and malignant nodules were compared using the Fisher-Freeman-Halton exact test. Differences were statistically significant if $p<0.05$. 


Results

With regard to mean size, the differences between the benign and malignant nodules and between the follicular lesions and malignant nodules were statistically significant \((p<0.05\) analysis of variance [ANOVA], \(p<0.05\) post hoc Tukey’s test). The difference between benign nodules and follicular lesions was not significant. With regard to mean age, the difference between the groups was not significant \((p>0.05,\) ANOVA). With regard to sex distribution, there was no significant difference between the groups \((p>0.1,\) Fisher-Freeman-Halton test).

All FNAB specimens \((n=231)\) had sufficient material to reach a diagnosis. Of the 231 nodules that were biopsied, 44 (19%) were solitary; and in 187 patients there was more than one nodule and only one was biopsied \((n=187, 81%)\). According to the cytopathological analysis, there were 186 benign nodules, 10 follicular lesions and 35 malignant nodules. All patients with malignant nodules underwent surgery; 34 of them had papillary carcinomas (Figs. 1–4) and in one patient the diagnosis was medullary carcinoma (Figs. 5 and 6).

Of the 186 benign nodules, 35 (19%) were solitary and 151 (81%) were non-solitary (Table). Of the 10 follicular lesions, 2 (20%) were solitary and 8 (80%) were non-solitary. Of the 35 malignant nodules, 23 (66%) were solitary and 12 (34%) were non-solitary. The diameter of the nodules varied between 5 and 40 mm (mean: 15.6 mm).

One patient had a thyroid mass \((n=1)\) that was not included in this study.
nodules, 7 (20%) were solitary and 28 (80%) were non-solitary ($p > 0.05$).

Of the 186 benign nodules, 46 (24.7%) were hypoechoic, 140 (75.3%) were nonhypoechoic (133 isoechoic, 7 hyperechoic). Of the 10 follicular lesions, 4 (40%) were hypoechoic and, 6 (60%) were nonhypoechoic (5 isoechoic, 1 hyperechoic). Of the 35 malignant nodules, 29 (82.9%) were hypoechoic, and 6 (17.1%) were isoechoic. With regard to the frequency of hypoechogenicity, there was a statistically significant difference between the groups ($p < 0.0001$).

Of the 186 benign nodules, 63 (33.9%) were solid, 110 (59.1%) were predominantly solid and 13 (7%) were predominantly cystic. Of the 10 follicular lesions, 7 (70%) were solid and 3 (30%) were predominantly solid. Of the 35 malignant nodules, 34 (97.2%) were solid, and 1 (2.8%) was predominantly solid. With regard to the frequency of solid echostructure, there was a statistically significant difference between the groups ($p < 0.0001$).

Of the 186 benign nodules, 29 (15.6%) had irregular margins and 157 (84.4%) had smooth margins. Of the 10 follicular lesions, 3 (30%) had irregular margins and 7 (70%) had smooth margins. Of the 35 malignant nodules, 27 (77.1%) had irregular margins, and 8 (22.9%) had smooth margins. With regard to the frequency of irregular margin, there was a statistically significant difference between the groups ($p < 0.00001$).

In 160 (86%) of the 186 benign nodules, no calcification was present. In 10 (5.4%) benign nodules, amorphous calcification and in 16 (8.6%) benign nodules microcalcification was detected. In 8 (80%) of the 10 follicular lesions, no microcalcification was present. In two (20%) nodules, microcalcification was detected. In 16 (45.7%) malignant nodules, no microcalcification was present. In four (11.4%) malignant nodules, there were amorphous calcifications. Microcalcifications were detected in 15 (42.9%) malignant nodules. With regard to the presence of microcalcification, there was a statistically significant difference between the groups ($p < 0.0001$).

In 37 (19.9%) of the 186 benign nodules, no vascularity was detected on color Doppler sonography. Perinodular and intranodular flow were detected in 48 (25.8%) and in 101 (54.3%) of benign nodules, respectively. In three (30%) of the 10 follicular lesions, the vascularity was perinodular; in the other seven (70%) follicular lesions, the vascularity was intranodular. In eight (22.9%) of the 35 malignant nodules, no vascular flow was present. Perinodular and intranodular flow was detected in six (17.1%) and 21 (60%) of the malignant nodules, respectively. With regard to the presence of intranodular vascularity, the difference between the groups was not statistically significant ($p > 0.05$).

In 55 (29.5%) of the 186 benign nodules, no halo was present. In the remaining 131 (70.5%)
benign nodules, a halo was present. In 5 (50%) of the 10 follicular lesions, no halo was present. Five (50%) follicular lesions had a halo. In 33 (94.2%) malignant nodules, no halo was present. Only two (5.8%) malignant nodules had a halo. With regard to the absence of a halo, the difference between the groups was statistically significant ($p < 0.0001$).

The frequency of ultrasonographic features—solitariness, echogenicity, echostructure, border characteristics, calcification, vascularity and halo—in benign, follicular and malignant nodules is presented in the Table.

### Discussion

In this study, the frequency of sonographic features including hypoechoogenicity, solid echostructure, irregular margin, microcalcification and absence of a halo, was higher in patients with malignant nodules than in patients with benign nodules and follicular lesions. Furthermore, the same sonographic features were encountered more frequently in patients with follicular lesions compared with those with benign nodules. Regarding the spectrum—benign nodules, follicular lesions,
malignant nodules—there was a trend of an increase in frequencies of the above-mentioned ultrasonographic features. On the other hand, with regard to lesion number (solitary vs. multiple) and vascularity, the differences between the groups were not significant.

To the best of our knowledge, this is the first study of its kind to evaluate the ultrasonographic features of “follicular lesions” as a separate cytopathological category. The histologic follow-up of cases diagnosed as follicular lesions of neoplasm includes hyperplastic/adenomatoid, follicular adenoma and follicular carcinoma [2,3]; surgical excision is recommended for definitive diagnosis on histopathologic examination. It is well-known that follicular lesions cannot be differentiated through cytopathological analysis; to reach a definite diagnosis on the nature of follicular lesions, surgical excision and histopathological analysis are needed.

With regard to the high frequencies of sonographic features including hypoechogenicity, solidity, irregular margin, presence of microcalcification and absence of a halo in malignant nodules, our results are consistent with the current literature [1,6–12].

The usefulness of intranodular blood flow on color Doppler examination [7], in differentiating thyroid nodules is still controversial. Intrinsic, or intranodular flow is more common than perinodular flow and is found in 67–84% of malignant nodules [6,7,13,14]. Nodules with extensive intranodular flow with or without perinodular flow are more likely to be malignant, however, 15% of benign nodules may also demonstrate this pattern [7]. In our study, intranodular flow pattern on color Doppler sonography was seen in 60% of malignant and 54.3% of benign nodules; the difference was not significant.

The risk of malignancy of a nodule in a multinodular thyroid is similar to that of a solitary thyroid nodule. In Papini et al’s series, 9.2% of solitary thyroid nodules and 6.3% of nodules in multinodular thyroids were malignant [6]. In our series, regarding the solitariness, there was no significant difference between the groups.

According to our results, the frequencies of sonographic features including, hypoechogenicity, solid echostructure, irregular margin, presence of microcalcification and absence of a halo in follicular lesions were higher than those encountered in benign nodules and lower than those encountered in malignant nodules. In fact, the available literature shows that some of the lesions that are diagnosed as follicular lesions with FNAB and cytopathologic examination are follicular adenomas (benign) and some are follicular carcinomas (malignant) according to histopathological examination following surgical excision. Therefore, in our opinion, a thyroid nodule showing one of the above-mentioned five sonographic features, has to be investigated further with FNAB. It is crucial to differentiate malignant and follicular lesions from benign nodules with regard to further diagnostic and therapeutic work-up of the former categories.

Our study has some limitations, the most major and obvious of which is the patient selection bias. All patients included in this study were referred to our department for FNAB. Furthermore, surgical and histopathological confirmation was available only for a limited number of patients, and it should be remembered that FNAB cannot differentiate between follicular benign and malignant lesions. Therefore, we considered follicular lesions as separate entities while correlating US findings with cytopathology. These limitations are due to the retrospective nature of this study.

In conclusion, US features including hypoechogenicity, solid echostructure, irregular margin, presence of microcalcification and the absence of a halo might be effective in the differentiation of malignant nodules and follicular lesions from benign nodules. Nevertheless, with regard to the limitations of our study, further prospective studies are needed.

References

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