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Original Article

Differences in the sonographic features of papillary thyroid microcarcinoma and nonmicrocarcinoma: a study of 279 patients

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Abstract: Objectives: The aim of the present study was to compare the Papillary Thyroid Microcarcinoma (PTMC) with nonPTMC, retrospectively, regarding the sonographic, clinical and laboratory features, to improve the diagnostic value of ultrasonography. Methods: We retrospectively analyzed the sonographic, clinical and laboratory features of patients who underwent thyroid ultrasound imaging from June 2010 to September 2014. Thyroid cancers were diagnosed by the Pathology Department, Renmin Hospital of Wuhan University. Results: A total of 279 patients were included. Within the 279 patients, 406 thyroid nodules were defined by ultrasound examination including 172 PTMC and 234 nonPTMC. No significant differences were found regarding the age, gender and serum TSH level between the PTMC and nonPTMC groups. Compared with the nonPTMC group, regarding the sonographic features, the margins of the PTMC nodules smoother, and fewer cystic changes, less central vascular flow and cervical lymph nodes enlargement were detected in the PTMC cases ($P<0.01$). Conclusions: Ultrasound was an important manner to diagnose the PTMC and to reduce unnecessary treatment or biopsy. PTMC showed specific differences regarding the ultrasonic features from the nonPTMC.

Keywords: Papillary thyroid microcarcinoma, ultrasound, clinical and laboratory features

Introduction

The incidence of papillary thyroid carcinoma (PTC) is increasing in several epidemiological studies worldwide [1]. In accordance with a retrospective (1973-2006) survey of the incidence rate of PTC, the increased PTC incidence is mainly due to microcarcinoma in patients older than 45 years [2]. Papillary thyroid microcarcinoma (PTMC) is defined as PTC that is less than or equal to 10 mm in its greatest dimension [3, 4]. Recent studies have suggested that the overall increase in the incidence of PTC is partially fueled by the 441% increase in the incidence of PTMC reported between 1983 and 2010 [4, 5]. However, in PTMC, the rates of incorrect and missed diagnoses are high due to the atypical clinical manifestations and more aggressive behavior with regional and distant metastases [6, 7]. Ultrasound (US) examination has been the best method of diagnosing PTC with the advantage of being a noninvasive procedure and providing immediate information compared with fine-needle aspiration (FNA) [8]. However, whether PTMC and papillary thyroid nonmicrocarcinoma (nonPTMC) exhibit the same ultrasonic performances is controversial [9, 10]. The aim of the present study was to retrospectively compare PTMC with nonPTMC regarding their sonographic, clinical and laboratory features to improve the diagnostic value of ultrasonography.

Materials and methods

Patients

We retrospectively analyzed the sonographic, clinical and laboratory features of patients who underwent thyroid ultrasound imaging from June 2010 to September 2014. Clinical variables included age and gender. Laboratorial variable was TSH levels. All of the patients underwent preoperative ultrasonography from

Table 1. Characteristics of patients included in the study

Characteristic	nonPTMC n=234	PTMC n=172	P
Age			
<20	4	1	0.450
20-45	40	37	Reference
>45	190	134	0.286
Sex			
Male	58	47	Reference
Female	176	125	0.564
TSH level			
Normal	214	159	Reference
Hypothyroidism	8	3	0.480
Hyperthyroidism	12	10	0.795

6 days to 4 weeks, and a final diagnosis was confirmed and pathological examination after surgery. Exclusion criteria included patients with abnormal neck anatomy and incomplete information for statistical analysis. The study was conducted according the Declaration of Helsinki and with approval from the Ethics Committee of Renmin Hospital of Wuhan University (Wuhan, China).

US examinations

GE Healthcare color Doppler US (Model: Vivid E9, Norway) and a superficial probe (Model: 4C-D, 7.5-10 MHz) were used for standard US. A retrospective review of the sonographic images was performed by two radiologists, independently, and both of whom had experiences in thyroid sonographic imaging for more than 6 years. The sonographic image review was conducted before the operation and pathologic examination. Each of the two radiologists made a final diagnosis for each of the nodules as being malignant or benign based on their US characterizations. And the final decision was reached by consensus. If any inconsistency was found, a third radiologist was consulted to arrive at a consensus.

The nodule localization, number, size (cm), ratio of length/width (A/T), the presence of cystic change, echogenicity, margin (well, ill-defined or spiculated), type of calcification and vascularization pattern (type I: absence of blood flow; type II: peripheral vascular flow; type III: central vascular flow) were evaluated using standard US. The internal structure was termed as primarily cystic if the solid component was less than 50%. The echogenicity of the solid component was classified into two categories: hypoechogenicity and equal/hyperechogenicity. Calcification within the nodule was classified into three categories: type I: absence of calcification; type II: coarse or rim calcifications; and type III: microcalcifications. Microcalcification was defined as hyperechoic spots less than 2 mm. The A/T ratio was assessed as the ratio of the anteroposterior (A) to transverse (T) dimensions (A/T<1 or A/T≥1). The cervical lymph nodes was defined as enlargement if irregular shape presented, A/T>1, and the leather/medulla ratio disorder was observed.

Pathologic diagnosis

All pathologic diagnoses were conducted by experienced pathologist in the pathologic diagnosis of thyroid cancer followed the previously established criteria [3]. Lesions were classified as malignant and benign groups based on the pathologic diagnosis. The malignant group was subcategorized as with PTMC and nonPTMC further, based on the pathologic analysis.

Statistical analysis

All statistical analyses were performed using the SPSS 17.0 statistical software. The measurement data were expressed as the mean ± standard deviation, and their differences were evaluated by independent sample t-test. The enumeration data were analyzed using χ^2 test or Fisher's exact test for categorical variables and the non-parametric test (Mann-Whitney) for the quantitative variables of the groups. *P* values less than 0.05 were considered to indicate a statistically significant difference. Odds ratios (ORs) and 95% CIs were calculated.

Results

Clinical findings

A total of 279 patients were included. Within the 279 patients, with 406 thyroid nodules were defined by ultrasound examination included including 172 PTMC and 234 nonPTMC. Of the 279 patients 188 were women and 91 were men, with a mean age of 48.46 years (range: 14-77 years). The cancers were diagnosed 1 day to 1 month after the clinical, serum TSH

Table 2. Comparison of sonographic characteristics between PTMC and nonPTMC

Characteristic	nonPTMC n=234	PTMC n=172	P
No of nodules			
1	82	69	Reference
≥2	76	52	0.394
Margins			
Smooth	127	124	Reference
ill defined or Spiculated	107	48	P<0.001
Vascular flow			
I	40	99	Reference
II	67	50	P<0.001
III	127	23	P<0.001
A/T			
<1	32	22	Reference
≥1	202	150	0.795
Internal Structure			
Cystic (Solid ≤50%)	36	9	Reference
Solid (Solid >50%)	198	163	0.001
Echo of solid component			
Hypoechoic	152	106	Reference
Equal/hyperechoic	26	17	0.848
Calcifications			
No	55	32	Reference
Microcalcifications	131	117	0.093
Coarse or Rim	48	23	0.565
Cervical lymph nodes			
Normal	113	142	Reference
Enlargement	121	30	P<0.001

level, and ultrasound examinations. No significant differences were found regarding thein age, gender and serum TSH level between the PTMC and nonPTMC groups (**Table 1**).

Sonographic findings

Several ultrasonographic images were significantly associated with PTMC compared with nonPTMC (**Table 2**; **Figure 1**). Compared with the nonPTMC group, regarding the sonographic features, the margins of the PTMC nodules revealed more smoother margins than did nonPTMC, and as well as fewer cystic changes, and less central vascular flow and cervical lymph nodes enlargement were detected in the PTMC cases (P<0.01). Ill-defined/speculated margins and II/III vascular flow accounted for 27.9% (48/172) and 42.4% (73/172) of all the PTMC cases, respectively. In contrast, in nonPTMC group, ill-defined/spiculated margins and II/III vascular flow accounted for 45.7% (107/234) and 82.9% (194/234) of all the cases, respectively. 51.7% (121/234) of the nonPTMC cases were detected with enlargement of cervical lymph nodes, while in the PTMC group only 22.7% (30/132) of the cases with cervical lymph nodes. 6.8% (9/132) of the PTMC cases were observed with cystic changes; however, the rate of cystic change in the nonPTMC cases occupied 15.4% (36/234), and the difference was statistically significant (P=0.001).

Discussion

Due to the widespreaded use of imaging procedures, such as US, many small thyroid nodules can be observed and analyzed with massively increased clarity and resolution. What's more, ultrasound-guided FNA of nonpalpable thyroid nodules and more accurate histopathological search and extensive histologic sampling of the resected thyroids contribute to the increase [11]. The occurrence of PTMC is dramatically increased globally nowadays. Therefore, it was important to characterize the clinicopathological features of PTMC which contribute to cancer progression, as well as compare the US characteristics of PTMC and nonPTC.

No significant differences were found regarding the serum TSH level between the PTMC and nonPTMC groups. In the present study, advanced age (>45 years), female gender and a normal TSH level still dominated in all two of the groups. A previous study [12] showed that the average age of patients who had PTMC was younger than the average age of patients with nonPTMC (50.6 vs. 54.6 years), but they did not perform a longitudinal analysis. Another study [13] found that no significant association between the TSH level and tumor progression, as verified during the nonsurgical observation trial for PTMC; TSH was not a good predictor of PTMC growth, finding that was consistent with our results.

Specific differences regarding the US features were observed in between the PTMC and nonPTMC cases. Ill-defined/spiculated margins and cystic changes were found more in nonPTMC than in PTMC cases; however, because the thyroid tumor grew slowly and with low degree

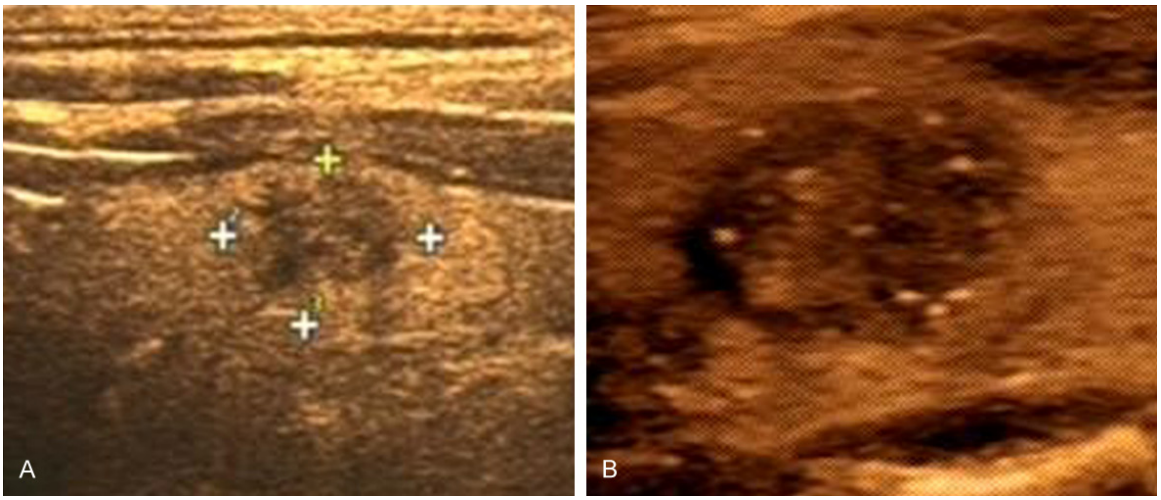

Figure 1. Transverse sonographic image of thyroid nodules. A. PTMC in 45-year-old man shows irregular, A/T>1, hypoechoic nodule with spiculated margin, heterogeneous echotexture of solid portion. This nodule was classified as PTMC. B. nonPTMC in 46-year-old woman shows A/T>1, hypoechoic nodule with spiculated margin, heterogeneous echotexture of solid portion and sporadic microcalcification. This nodule was classified as nonPTMC.

of malignancy, ill-defined/spiculated margins were considered as an unmarked showing. As the tumors grow faster, liquefaction necrosis and cystic changes occur [14]. Neovascularization provides nutrients for the growth of malignant tumors. In our study, the blood flow of the PTMC nodules was primarily grade I (51.7%, 89/172), whereas the blood flow in the nonPTMC nodules was mainly grade III (54.2%, 127/234). This kind of difference may attribute to the no or less neovascularization of PTMC; therefore, the low blood signals were difficult to observe. The presence of lymph node metastasis in patients with PTMC ranged from 5% to 44.2% when the patient was subjected to therapeutic or necessary dissection [15, 16]. A previous study reported that tumor size was a predictive factor of cervical lymph node metastases in PTC patients [17], which could be confirmed by the results of our study: cervical lymph nodes enlargement accounted for 51.7% (121/234) in nonPTMC, which is significantly more than the 17.4% (30/172) observed in PTMC.

Because the study was conducted retrospectively, selection bias is unavoidable. In conclusion, the US was important to diagnose PTMC and to reduce the unnecessary treatment or biopsy of ???. The PTMC cases showed specific differences in their ultrasonic features from the nonPTMC ones but the diagnosis of benign nodules accompanied with occasional microcancer has limitations. For cases that are difficult to diagnose, FNA or ultrasound-guided biopsy may still be necessary.

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Original idea by SSR and WQ. WQ and LX designed and conducted the survey and gathered the data. LJJ, WJ and SF performed statistical analysis, figures, which was reviewed and approved by SSR and CC. All authors read and approved the final manuscript.

Disclosure of conflict of interest

None.

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