Annals of Diagnostic Pathology 19 (2015) 175–179

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Cytologic-Pathologic Correlation

Cytomorphologic features and ultrasonographic characteristics of thyroid nodules with Hurthle cells

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ARTICLE INFO

Keywords:
Thyroid nodule
Hurthle cell
Ultrasonography
Cytomorphology

ABSTRACT

This study was designed to evaluate the ultrasonographic and histopathologic features of nodules composed predominantly of Hurthle cells detected during cytological examination. Fifty-seven patients with thyroid nodules composed predominantly of Hurthle cells on fine needle aspiration cytology were retrospectively analyzed. Patients were evaluated by thyroid ultrasonography (US), and biopsy samples taken by US-guided fine needle aspiration cytology were assessed histopathologically. There were 57 patients and 57 nodules with Hurthle cells in cytological examination; 49 (86%) were classified as Bethesda 1, and 8 (14%) were classified as Bethesda 3. Histopathologically, 45 (78.9%) nodules were benign and 12 (21.1%) were malignant. Nuclear groove, transgressing blood vessel, and absence of colloid were observed with a higher frequency in malignant nodules compared to benign nodules ($P < .05$). There were no specific morphological features (nodule echogenity, presence of microcalsification, presence of cystic areas, absence of halo, margin irregularity, and increased blood flow) predicting malignancy in the US evaluation of nodules including Hurthle cells. Nuclear groove, transgressing blood vessel, and absence of colloid on cytomorphological evaluation are indicative of malignancy in nodules containing Hurthle cells.

1. Introduction

Hurthle cells are characterized cytologically as large polygonal cells with abundant eosinophilic, granular cytoplasm and a large hyperchromatic nucleus with a prominent nucleolus [1]. Hurthle cells are present in a variety of nonneoplastic conditions involving the thyroid and are not specific for any disease process [2,3]. Thyroid nodules containing Hurthle cells are present in patients with a wide range of pathologic entities, including Hashimoto thyroiditis (HT), Hurthle cell adenomas (HCAs), Hurthle cell carcinomas (HCC), oncocytic variant of papillary carcinoma, and medullary carcinoma [4,5].

Many morphologic studies have attempted to identify cytomorphologic features that distinguish benign Hurthle cell lesions (BHCLs) from Hurthle cell neoplasms (HCNs). Among the features that distinguish BHCL from HCN are nonmacrofollicular architecture, absence of colloid, absence of chronic inflammation, presence of transgressing blood vessels (TBVs), predominantly Hurthle cells, small cell dysplasia, large cell dysplasia, nuclear crowding, and marked dyshesion [2,3,6–8]. This study was designed to assess the ultrasonographic, cytologic results and histopathologic features of thyroid nodules containing Hurthle cells in patients who underwent surgery for various reasons.

2. Materials and methods

2.1. Study protocol

This study was a retrospective evaluation of 57 patients found by fine needle aspiration cytology to have thyroid nodules consisting predominantly of Hurthle cells and who underwent surgery between June 2009 and June 2010. Medical history was obtained, and all patients underwent thyroid examinations. Concentrations of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), and the thyroid autoantibodies thyroid peroxidase antibody (anti-TPO) and anti-thyroglobulin antibody (anti-TgAb) were measured. Thyroid ultrasonography (US) was performed by an experienced specialist using the same US machine. Fine needle aspiration biopsy (FNAB) was performed by an experienced specialist in thyroid nodules and evaluated by a cytopathologist. Patients were reevaluated by US and Doppler US and discussed by a multidisciplinary team consisting of endocrinologists, general surgeons, and pathologists; this evaluation guided surgeons in determining the surgical approach in patients who required surgery.

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http://dx.doi.org/10.1016/j.anndiagpath.2015.03.002
1092-9134/

Indications for surgery in patients with nodules containing Hurthle cells included large nodule diameter, compression symptoms, and increased nodule diameter over time. Nodules showing evidence of HCN were removed surgically because of a high suspicion of malignancy. Fifty-seven patients underwent total thyroidectomy in our hospital, with all operations performed by the same surgical team. The resected nodules were evaluated histopathologically by the same cytopathologist who evaluated the FNAB specimens.

The study protocol was approved by the local ethical committee (Ankara Ataturk Research and Education Hospital Local Ethical Committee Decision: Date: 01.06.2009; Decision Number: 10.06.2009).

2.2. Exclusion criteria

Patients younger than 18 years and those with a previous history of thyroid surgery or percutaneous invasive procedure for thyroid nodule or radiotherapy of the head and neck region were excluded from the study. Also excluded were patients with cardiac or pulmonary disease that could complicate surgery; those with pure cystic nodules, hemorrhagic nodules, multinodular coalescent nodules of undetermined sizes, anaplastic carcinoma, and Riedel thyroiditis; and patients with extensive cervical metastasis that may need radical neck dissection. Patients who refused surgery were also excluded.

2.3. Laboratory examination

Serum TSH, fT3, fT4, anti-TPOAb, and anti-TgAb concentrations were measured by chemiluminescence methods using commercial kits (Chemiluminescent Microparticle Immunoassay, CIMA®) with an Abbott Architech machine. Reference ranges for TSH, fT3, fT4, Tg, anti-TPOAb and anti-TgAb were 0.35 to 4.94 IU/mL, <10 IU/mL, 1.57 to 4.71 pg/mL, 0.61 to 1.12 ng/dL, 0 to 55 ng/mL, and <30 IU/mL, respectively.

2.4. Ultrasonography

Esaote color Doppler US (MAG Technology Co, Ltd. Model: 796FDII Yung-ho City, Taipei; Taiwan) and a superficial probe (Model No: LA523 13-4, 5.5-12.5 MHz) were used for standard US. Standard US was utilized to evaluate nodule localization, diameter (mm), volume, halo, echogenicity, marginal regularity, and type of calcification and vascularization pattern (stage 1, absence of blood flow; stage 2, peripheral vascularization; stage 3, intranodular vascularization; stage 4, marked intranodular vascularization).

2.5. US guided FNAB

FNAB was performed under US guidance using a General Electric Logiq pro 200 (Model number: 2270968; GE Healthcare Korea, Seongnam-SI, Gyeon GGI-DO, Korea) and a 5.5 to 7.5 MHz probe.

2.6. Cytological and histopathological examination

Materials obtained by US guided FNAB were air dried, stained with May-Grünwald-Giemsa stain and classified according to the Bethesda system [9] (Table 1). The 14 cytomorphologic features used to distinguish BHCL from HCN were cellularity, background colloid, macrophage count, lymphocyte count, TBV, capillaries, nuclear crowding, Hurthle cells, cellular dyshesion, nuclear enlargement, small cell dysplasia, large cell dysplasia, macronucleoli, and binuclear Hurthle cells. Transgressing blood vessels were defined as capillaries passing through clusters of Hurthle cells [10].

The US-determined location of the nodule or nodules in the thyroid tissue was shown to the surgeon using a simple drawing. The surgical team marked the nodule or nodules with a surgical suture before sending the specimen for histopathological examination, so that the suspicious area could be examined with particular interest. Thyroidectomy specimens were examined macroscopically by the cytopathologist, photographs were taken and all the specimens were scored using standard methods, thus enabling previous US and cytology data to be compared with the histopathologic findings, as determined using the 2004 WHO classification [11].

Table 1
The Bethesda system for reporting thyroid cytopathology: recommended diagnostic categories

I. Nondiagnostic or unsatisfactory
Cyst fluid only
Virtually acellular specimen
Other (obscuring blood, clotting artifact, etc.)
II. Benign
Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodul,etc.
Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
Consistent with granulomatous (subacute) thyroiditis
Other
III. Atypia of undetermined significance or follicular lesion of undetermined significance
IV. Follicular neoplasm or suspicious for a follicular neoplasm
Specify if Hurthle cell (oncocytic) type
V. Suspicious for malignancy
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
Other
VI. Malignant
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma
Carcinoma with mixed features (specify)
Metastatic carcinoma
Non-Hodgkin lymphoma
Other

2.7. Statistical analysis

All statistical analyses were performed with SPSS 18.0 (SPSS Inc., Il., USA) statistical soft-ware. Qualitative data were reported as frequencies and compared using χ^2 tests; quantitative data were reported as mean ± SD and compared using unpaired Student *t* test or Mann–Whitney *U* tests. $P \leq .05$ was defined as statistically significant.

3. Results

Fifty-seven nodules in 57 patients were retrospectively evaluated. Mean age was 46.12 ± 11.69 years (range, 19-73 years). Of the 57 patients, 52 (91.2%) were female and 5 (8.8%) were male. All patients were euthyroid at the time of investigation, with a mean serum concentration of TSH of 1.51 ± 1.01 μIU/mL. Twenty-four patients (42.1%) were positive for anti-TPOAb and/or anti-TgAb.

According to the Bethesda classification of cytology, 49 (86%) of the 57 nodules were Bethesda 2 and 8 (14%) were Bethesda 4. These two subgroups were similar in age, sex distribution, thyroid function test results, nodule volume, sonographic features and nodule vascularization pattern. Of the 57 nodules, 12 (21.1%) were diagnosed on final histopathology as malignant and 45 (78.9%) as benign. These two subgroups were also similar in age, sex distribution and thyroid function test results, as well as in nodule volume, gray-scale US features, and vascularization pattern.

Evaluation of cytological features showed that cellularity, the presence of Hurthle cells, and large cell dysplasia were significantly more frequent in the Bethesda 4 than in the Bethesda 2 group ($P < .05$; Table 2). Moreover, nuclear groove, TBV, and absence of colloid were significantly more frequent in malignant than in benign nodules ($P < .05$; Table 3) (Figs. 1, 2, 3). Histopathological examination of the 12