

HUERTHLE CELL NEOPLASMS OF THE THYROID: PREDICTING MALIGNANT POTENTIAL

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Objective. Assessment of malignancy criteria in Hürthle cell neoplasm.

Methods. This study intends to review retrospectively the patients who were operated for Hürthle cell neoplasia at Gazi University, Department of General Surgery between January 1986 and October 1999. Pathological specimens from 63 patients (20 males and 43 females) were evaluated, 48 of which revealed Hürthle cell adenoma (HCA) and 15 revealed Hürthle cell carcinoma (HCC). The mean age of the patients with HCA was 40.7 ± 1.59 yr, while that in patients with HCC was 51.3 ± 1.83 yr. Mann-Whitney U-test and chi-square tests were used for statistical analysis.

Results. Fifty-two of the 63 patients had fine needle aspiration (FNA) biopsy prior to operation. Among them 49 were reported to have suspected Hürthle cell neoplasia (HCN) and three had suspected HCC. The sensitivity of FNA for HCN was 20 %, specificity was 100 %, positive predictive value was 100 % and negative predictive value was 76 %. For all patients, peroperative frozen section (FS) biopsy was examined. Fifty-nine of the FS specimens revealed HCN and four revealed HCC. The sensitivity, specificity, positive predictive value and negative predictive value of FS biopsy were 27 %, 79 %, 28.5 % and 77.5 %, respectively.

Conclusion. Statistically significant correlations were found between the malignancy and size of the tumor ($P < 0.05$) by chi-square test, and also a between the malignancy and age of the patient ($P < 0.05$) by Mann-Whitney U-test. In cases where FS and FNA biopsies cannot adequately define the benign or malignant nature of the tumor, the age of the patient and the diameter of the tumor must be taken into consideration for the appropriate surgical strategy. Particularly for 50 year-old and elderly, the incidence of malignancy is statistically significant irrespective of patient's sex.

Key words: Hürthle cell – Fine needle aspiration – Frozen section

Hürthle cell adenoma (HCA) and Hürthle cell carcinoma (HCC) constitute 3-10 % of epithelial tumors of the thyroid gland (BONDESON et al. 1981; CHEN et al. 1998). The presence of Hürthle cell neoplasia in follicular and papillary cancers of the thyroid gland is 15-20 % and 2-8 %, respectively (CHEN et al. 1998). In a former study performed by our department, the frequency of HCC was 1.6 % (TANERI et al. 1998).

The exact differentiation between benign and malignant Hürthle cell neoplasia can only be made by the presence or absence of capsule or vascular invasion (AZADIAN et al. 1995; CHEN et al. 1998). Hürthle cell neoplasms are aggressive tumors and

tend to have an increased metastatic potential and low survival rates compared to other differentiated thyroid tumors. Therefore, Hürthle cell carcinomas are treated by total thyroidectomy, while lobectomy is preferred for adenomas.

To determine the most accurate surgical strategy, the tumor must be exactly diagnosed as benign or malignant either preoperatively or intraoperatively. Fine needle aspiration and frozen section biopsies cannot always interpret the exact diagnosis (ARGANINI et al. 1986; CHEN 1998; GOSAIN et al. 1984). Therefore, the aim of this study is to investigate other factors in determining the malignancy.

Table 1: The correlation between malignancy and tumor size

	<i>Number of patients according to tumor size</i>			Total
	< 1 cm	1-4 cm	> 4 cm	
Adenoma	6	38	4	48
Carcinoma	0	12	3	15
Total	6	50	7	63

Subjects and Methods

The pathological findings in patients, who underwent thyroid operations at Gazi University Department of General Surgery between January 1986 and October 1999 were evaluated retrospectively. Capsulated thyroid lesions, which have at least 50 % Huerthle cells, are defined as Huerthle cell neoplasia (HCN) (CHEN et al. 1998; GUNDRY et al. 1983). For exact diagnosis of Huerthle cell carcinoma, the presence of vascular and/or capsular invasion was examined. Sixty-three patients were found to have HCN and included in the study. Age and sex of the patients were recorded as well as the size and multicentricity of the tumor. Chi-square test was used for evaluating the correlation between the malignancy and size of the tumor, while Mann Whitney U-test was used for evaluating the correlation between the malignancy and age of the patient.

Results

Patient demographics. Of the 63 patients, 48 permanent pathological sections revealed adenoma and 15 carcinoma with a malignancy frequency of 23.8 %. Forty-three of the patients were females and 20 were males. The average age was 49.8 ± 1.74 for females and 43.7 ± 1.81 for males. Patients with Huerthle cell adenoma (HCA) had an average age of 40.7 ± 1.59 and patients with carcinoma (HCC) 51.3 ± 1.83 . No history of radiotherapy to head and neck was reported. The correlation between the malignancy and age was statistically significant ($P < 0.05$).

Diagnostic studies. Forty two of the patients underwent FNA preoperatively and 49 revealed HCN (37 of these had HCA and 12 had HCC in the permanent sections), three had suspected malignancy (all of which had HCC in permanent sections). For

HCN, the sensitivity of FNA was 20 %, specificity 100 %, positive predictive value (PPV) 100 % and negative predictive value (NPV) 76 %.

The results of the frozen section biopsies revealed HCN in 59 patients (48 HCA, 11 HCC in permanent sections) and HCC in four patients. Preoperative FNA results of the three patients who had HCC according to the FS biopsies also had suspected malignancy. The sensitivity, specificity, PPV and NPV of FS were 27 %, 79 %, 28.5 % and 77.5 %, respectively.

The correlation between malignancy and size of the tumor is shown in Table 1 and the average ages with regard to the size of the HCN are shown in Tab. 2.

Surgical strategy. Of the 48 patients with HCA, 40 (83 %) underwent lobectomy/isthmectomy, 7 (17 %) underwent total thyroidectomy. Two of the seven total thyroidectomized patients had temporary hypocalcaemia. Fifteen patients with HCC underwent total thyroidectomy. None of these patients had local invasion in permanent sections.

Discussion

Huerthle cells are wide-polygonal, eosinophilic cells, which have a hyperchromatic nucleus and a granulated cytoplasm rich in mitochondria. These cells can also be seen in Hashimoto thyroiditis, nodular goiter and well-differentiated thyroid cancers (AZADIAN et al. 1995; CARCANGIU et al. 1991; CHEN et al. 1998; GUNDRY et al. 1983).

There has been a consensus that total or near-total thyroidectomy for HCC and lobectomy plus isthmectomy for HCA are the appropriate surgical procedures for HCNs (CHEN et al. 1998; GUNDRY 1983). In our study, no evidence of carcinoma in short term follow-up has been observed clinically or according to thyroglobulin levels. But this observation needs a longer follow-up period.

Several studies proved the reliability of FNA for the diagnosis of HCN (ARGANINI et al. 1986; AZADIAN et al. 1995; GOSAIN et al. 1984). In our study, the specificity, sensitivity, PPV and NPV of FNA are 100 %, 20 %, 100 % and 76 %, respectively. However, for most of the patients, the diagnosis of neoplasia could not be documented by using FNA. Three patients were considered to have malignancy according to FNA and the presence of nuclear atypia was accepted to be the main factor.

Table 2: Average age with regard to tumor diameter of HCN.

Tumor diameter	Number of patients with adenomas	Number of patients with malignancy	Average age (adenoma)	Average age (malignancy)
< 1 cm	6	0	41.5±1.25	—
1-4 cm	37	12	40.1±2.21	52.4±1.92
> 4 cm	4	3	40.7±1.59	50.3±1.76

Peroperative FS biopsy is the most common procedure performed in order to differentiate malignancy. But some studies suggested that FS biopsy has been inadequate for accurate diagnosis (AZADIAN et al. 1995; ERSOY et al. 1999, GOSAIN et al. 1984). For this reason, investigation of some other factors for assessing malignancy has gained popularity. It has been reported by some authors that, age, sex, radiation therapy to head and neck in childhood or adolescence cause a high risk for malignancy (ARGANINI et al. 1986; BONDESON et al. 1981; CARCANGIU et al. 1991). Although some of the reports indicated that there was no significant relationship between age and malignancy (AZADIAN et al. 1995, CHEN et al. 1998; GOSAIN et al. 1984), we have found it statistically significant. Some authors claim that the greater diameter of the tumor, the more risk of malignancy. In a study by THOMPSON et al, tumors greater than 2 cm had a high risk of malignancy (GUNDY et al. 1983). Our results were also in accordance with this suggestion. Azadian et al claim that diameter greater than 2.3 cm for adenomas and 4,3 cm for carcinomas had an increased risk for malignancy (AZADIAN et al. 1995). CARCANGIU et al. (1991) have shown that, in a group of 153 patients, none of the tumors less than 1 cm was malignant and none of the tumors greater than 10 cm was benign. In our study, there was no malignancy among the tumors less than 1 cm diameter, 24 % was malignant between 1-4 cm and 42.85 % among the ones greater than 4 cm diameter. This proved a statistically significant difference between the diameter of the tumor and malignancy ($P<0.05$).

In cases where FS and FNA biopsies cannot adequately define the benign or malignant behaviour of the tumor, age of the patient and the diameter of the tumor must be taken into consideration for accurate surgical strategy. Particularly for 50 year-old and eld-

erly, incidence of malignancy is statistically significant without considering sex of the patient.

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BOOK REVIEW

THYROID CANCER A COMPREHENSIVE GUIDE TO CLINICAL MANAGEMENT

EDITED BY LEONARD WARTOFSKY (WASHINGTON, DC)

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"It sometimes seems that thyroid carcinoma is a neglected orphan among human cancers, which is at the root of some important issues. Thyroid carcinomas comprise a diverse group of malignancies ranging from indolent microscopic papillary carcinomas that pose no threat to survival to anaplastic carcinomas that are the most vicious carcinomas afflicting humans. Yet, because of its low incidence, there have been no prospective randomized clinical trials of the treatment of thyroid carcinoma." This is a fragment of the "Foreword" written by outstanding thyroid surgeon Ernest L. Mazzaferri.

This comprehensive book brings an instructive review of present knowledge on the pathology, etiology, epidemiology, diagnostic methods and the methods of surgical, radioiodine and chemotherapeutic treatment of various forms of thyroid cancer. Written by outstanding experts and professionally edited by Leonard Wartofsky, it may be considered of substantial utility to all physicians dealing with thyroid diseases.

A total of 52 comprehensive chapters is divided into 9 sections dealing with the diagnostics and management of thyroid nodule (Part I), general considerations on the thyroid cancer (Part II), clinical aspects, pathology, treatment, follow-up, prognosis and special aspects in children of papillary carcinoma (Part III), the same aspects of follicular (Part IV) and anaplastic carcinoma (Part V) and lympho-

ma (part VI). Next sections are devoted to medullary carcinoma (Part VII), unusual thyroid cancers (Part VIII) and future directions (Part IX). A number of up to date references and instructive tables, figures and photos are attached to each chapter. In addition to basal theoretical knowledge on each problem discussed in individual chapters, there is a number of practical and handy instructions such as a detailed description of fine needle aspiration technique, detailed descriptions of external irradiation techniques and doses, sonography, various imaging procedures and strategies of follow-up the patients after the surgical and radiation treatment. However, some actual questions on the extent of thyroidectomy such as lobectomy versus subtotal or near-total thyroidectomy would perhaps deserve more detailed discussion.

Of special value may be considered the chapters on molecular pathology of thyroid cancer including significant recent achievements of molecular genetic analysis of inheritance pattern in families with medullary carcinoma.

Finally, again few words of Ernest L. Mazzaferri: *"I believe the knowledge contained in Thyroid Cancer will give the practicing clinicians the necessary information to provide patients the latest and best diagnostic and therapeutic techniques."*

Pavel Langer