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# Hürthle Cell Tumor of the Thyroid: Analysis of 188 Cases

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**Abstract. We reviewed 188 cases of Hürthle cell tumor of the thyroid (HCT) between 1982 and 1996. There were 160 women and 28 men with a mean age of 51.8 years. Thirty-one of the patients had cancer, and the others had adenoma. Age, size of the primary tumor, and preoperative thyroglobulin level were not significantly different in the cancer and adenoma patients. The gender ratio, however, was significantly different ($p < 0.05$). Recurrent HCT was observed in three patients with adenoma. Two patients had subcutaneous recurrence (suspected implantation), and the other patient had recurrence in the residual thyroid gland. All patients with recurrence of adenoma underwent partial lobectomy at the initial operation. Three cancer patients had recurrent disease. Locoregional recurrence was observed in one patient and distant metastases in two patients (lung in one, lung and bone in one). One of the patients with distant metastasis died from the disease, and the other is alive with the disease. Tumor implantation was observed in patients with adenoma, so intraoperative handling of the tumor requires care. It also means that this tumor, even though benign, is aggressive in terms of proliferative activity. All patients with Hürthle cell tumor should be treated by total lobectomy at least. The outcome of the cancer patients was not as poor as in previous reports.**

The clinical behavior of various types of thyroid tumor has been much studied during the past several decades; and the histologic features, surgical management, and prognostic factors of follicular and papillary tumors in particular have been clarified to a considerable degree. By contrast, there has been controversy concerning management of Hürthle cell tumors of the thyroid. Hürthle cell tumor is not a common disease, making it impossible to obtain sufficient clinical data at a single institution. Some authors have reported that all Hürthle cell tumors are aggressive and should be treated as malignant tumors [1, 2]. Others believe that an accurate differential diagnosis can be made between cancer and adenoma on the basis of pathology studies [3–5]. We have employed a rather conservative surgical approach to treating Hürthle cell tumors. In this study we reviewed pathology specimens and retrospectively analyzed the clinical outcomes of patients with Hürthle cell tumor. The aims of this study were to clarify the clinical manifestation of this tumor and to ascertain if the surgical procedure affected the clinical outcome.

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## Patients and Methods

The material used for this study was obtained from the pathology files of Ito Hospital. Between 1982 and 1996 a total of 208 patients underwent surgery and were postoperatively diagnosed as having Hürthle cell tumor. All histologic material for this study was reviewed by one pathologist (KK). The pathologic diagnosis was changed in 46 patients. Altogether, 20 patients were diagnosed as having adenomatous goiter and 21 as having ordinary follicular tumor (not oxyphilic); in 5 patients the diagnosis changed from adenoma to cancer (one patient) or from cancer to adenoma (four patients). Hürthle cell nodules associated with an adenomatous goiter without a definite capsule and follicular tumors containing fewer than 75% Hürthle cells were excluded. Cancer was diagnosed only when capsular or vascular invasion was observed. One patient with an initial diagnosis of adenoma showed definite capsular invasion, and four patients were initially diagnosed as having cancer because of cellular atypism only without definite capsular or vascular invasion.

A total of 188 patients with Hürthle cell tumors were the subjects of this study. There were 157 adenomas and 31 cancers in 160 women and 34 men, with a mean age of 51.8 years (range 19–82 years). Follow-up periods ranged from 2 to 15 years (mean 8 years). The patients' charts were reviewed with reference to age, gender, preoperative thyroglobulin level, tumor size, extent of operation, and clinical outcome including recurrence.

The frequency of distant metastasis and local recurrence in patients with cancer was analyzed from the standpoint of the extent of thyroidectomy and AMES prognostic criteria. AMES prognostic criteria have been described by Cady and Rossi [6] (Table 1).

## Results

### *Patient Characteristics*

The patients with adenoma consisted of 135 women and 22 men (F/M 6.1:1.0), with a mean age of 51.6 years (range 21–82 years). The cancer patients comprised 20 females and 11 males (F/M 1.8:1.0) with a mean age of 52.4 years (range 19–76 years). Age

**Table 1.** AMES scoring system.

| |
|---|
| Low risk |
| All women < 51 years and all men < 41 of age without distant metastasis |
| All older patients with tumors < 5 cm and no extrathyroidal extension of tumor (if papillary) and no major capsular invasion (if follicular) |
| High risk |
| All patients with distant metastasis |
| All women ≥ 51 years of age and all men ≥ 41 years with tumors ≥ 5 cm or extrathyroidal extension of tumor (if papillary) and major capsular invasion (if follicular) |

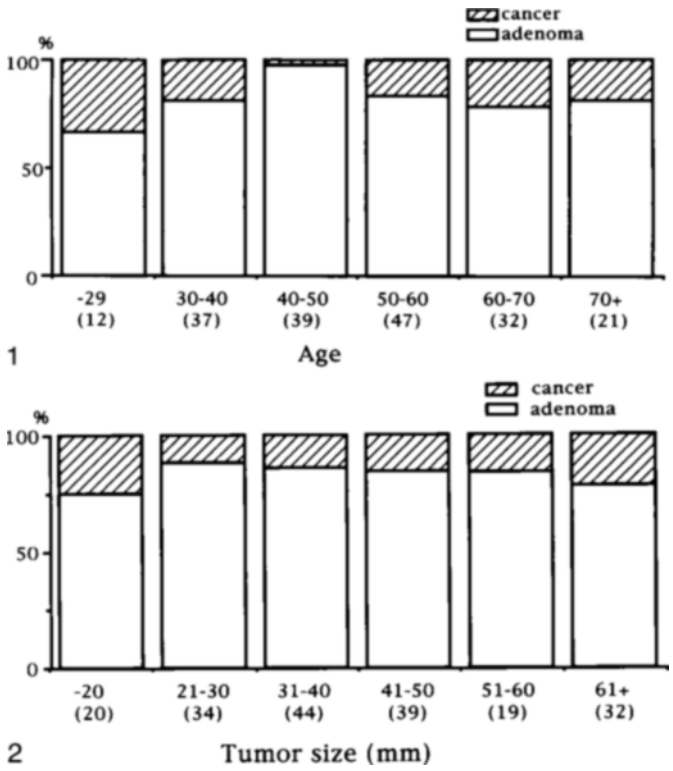


**Fig. 1.** Age distribution of the patients. No significant tendencies were observed. Figures in parentheses are numbers of patients.

**Fig. 2.** Tumor size distribution. There were no significant differences between adenoma and cancer. Figures in parentheses are numbers of patients.

distribution is shown in Figure 1. Age was not significantly different in adenoma and cancer patients, but the gender ratio was significantly different ($p < 0.05$). Hürthle cell tumor occurred more often in women, but the malignancy ratio was significantly higher in men. There were no significant differences in the distribution of primary tumor size (Fig. 2). Serum thyroglobulin was measured preoperatively in 135 patients, and the 9 patients found to have anti-thyroglobulin antibody were excluded (104 with adenoma, 22 with cancer). The mean thyroglobulin levels of patients with adenoma or cancer were 573 and 1782 ng/dl, respectively. More patients with cancer had a higher level of thyroglobulin than those with adenoma, but there were no significant differences.

A total of 145 patients were examined by fine-needle aspiration biopsy cytology (FNABC) before surgery. The results of FNABC are summarized in Table 2. Only 52 patients (35.9%) were diagnosed as having Hürthle cell tumor by FNABC before surgery, but 133 patients (91.7%) were diagnosed as having follicular thyroid tumor, including Hürthle cell tumor. Altogether, 26 of the cancer patients were examined by FNABC. Six patients (23.1%) were diagnosed as having Hürthle cell tumor, but only one patient was suspected of having cancer based on the FNABC results. Among those with adenoma, 119 patients underwent FNABC, and 46 patients (38.9%) were diagnosed as having Hürthle cell tumor. Three patients with adenoma were diagnosed as suspected of having cancer based on FNABC results.

**Table 2.** Preoperative diagnosis by fine-needle aspiration biopsy cytology.

| Diagnosis (pathologic and FNABC) | No. |
|---|---|
| Adenoma ($n = 157$) | |
| HCT | 46 (29.3%) |
| FT | 64 (40.8%) |
| Others | 9 (5.7%) |
| ND | 38 (24.2%) |
| Cancer ($n = 31$) | |
| HCT | 6 (19.4%) |
| FT | 17 (54.8%) |
| Others | 3 (9.7%) |
| ND | 5 (16.1%) |

FNABC: fine-needle aspiration biopsy cytology; HCT: Hürthle cell tumor; FT: follicular tumor; ND: not done.

### *Surgical Procedures*

The extent of thyroidectomy ranged from partial lobectomy to total thyroidectomy. Among the adenoma patients, partial lobectomy was performed in 112 patients (71.4%), total lobectomy in 39 (24.8%), and near-total or total thyroidectomy in 3 (3.8%). Among the cancer patients, partial lobectomy were performed in 10 (32.3%), total lobectomy in 12 (38.7%), and near-total or total thyroidectomy in 9 (29.0%). Because some of the patients diagnosed as having cancer postoperatively subsequently underwent completion total thyroidectomy, more of these patients underwent total thyroidectomy than did those with adenoma.

### *Surgical Outcome*

Although the term "recurrence" may not be suitable for adenoma, recurrent Hürthle cell tumor in the neck was observed in three adenoma patients (1.9%). Two of them had "recurrences" in subcutaneous tissue, and the other patient had a "recurrence" in the residual thyroid gland. Histologic examination of the lesions of these three patients revealed the same pathologic features as in the lesions resected at the time of the initial surgery. All of the patients had undergone partial lobectomy at the time of the initial surgery.

Three of the patients with cancer experienced recurrence. Locoregional recurrence was observed in one patient and distant metastasis in the other two (lung and bone in one, lung in one). The patient with both lung and bone metastasis was treated by radioiodine therapy, but there was no accumulation in the lesions; he died of the disease 46 months after the initial surgery. The patient with lung metastasis had a solitary pulmonary lesion with

**Table 3.** Surgical outcome and extent of thyroidectomy in patients with cancer.

| Surgery | No. of patients | Local recurrence | Distant metastasis | Dead of the disease |
|---|---|---|---|---|
| Partial lobectomy | 10 | 1 | 0 | 0 |
| Total lobectomy | 12 | 1 | 1 | 0 |
| Near-total or total thyroidectomy | 9 | 0 | 1 | 1 |

**Table 4.** Surgical outcome and AMES criteria in patients with cancer.

| AMES | No. | Local recurrence | Distant metastasis | Dead of the disease |
|---|---|---|---|---|
| Low risk | 21 | 1 | 1 | 0 |
| High risk | 10 | 1 | 1 | 1 |

a negative radioiodine scan. Because no recurrent lesions were detected by computed tomography or ultrasound examination, tumor resection was performed by thoracotomy. Although her serum thyroglobulin level is detectable, she currently has no obvious recurrent disease in the neck or lung.

The frequency of distant metastasis and local recurrence according to the extent of thyroidectomy is shown in Table 3. There were no significant differences among the surgical procedures.

Ten patients were in the AMES high risk group, and 21 patients were in the AMES low risk group. Although the only patient who died of the disease was in the AMES high risk group, the frequency of distant metastasis and local recurrence in the high risk and low risk groups was not significantly different (Table 4).

## Discussion

Although a great deal has been reported about the pathologic diagnosis and surgical management of Hürthle cell tumor, controversy still exists [1–5]. It is attributable to the fact that Hürthle cell tumor is a rather uncommon tumor, and there is little experience with the disease at any single institution. Hürthle cell tumor is sometimes grouped with follicular tumors. It is generally regarded as behaving aggressively, and the differential diagnosis between adenoma and cancer is difficult, the same as for ordinary follicular thyroid tumors. We do not have an impression of Hürthle cell cancer being aggressive in our general clinical practice, which led us to undertake this study. Partial lobectomy was often employed to treat Hürthle cell tumor at our institution in the past. Recently, however, total lobectomy is being performed as initial surgery for all Hürthle cell tumors; and if the pathologic diagnosis is cancer, completion total thyroidectomy is usually performed. Based on the outcome, our conservative surgical strategy is thought to be satisfactory.

Thompson et al. [1, 2] advocated total thyroidectomy for all Hürthle cell tumors because recurrence occurred in 3 of their 26 patients with histologically benign adenoma, and recurrence can be lethal. However, several studies have shown that Hürthle cell tumor is not particularly aggressive, and conventional pathology can distinguish adenoma from cancer. Bondeson et al. [3] and Gosain and Clark [4] advocated total lobectomy for Hürthle cell tumor and recommended completion total thyroidectomy only if the postoperative pathologic diagnosis is cancer. In our study, two patients pathologically diagnosed as having adenoma had recurrence in subcutaneous tissue, but it was attributed to tumor implantation during initial surgery. Subcutaneous implantation of thyroid tumor is rather uncommon and demonstrates the aggressiveness of this tumor. Implantation was observed in patients who had undergone partial lobectomy, and it could have been prevented by careful intraoperative handling of the tumor. In general, partial lobectomy or subtotal thyroidectomy is often performed for adenomatous goiter to preserve the parathyroid glands. Hürthle cells are often observed in hyperplastic nodular lesions, and the differential diagnosis by FNABC between adenomatous goiter and Hürthle cell tumor is sometimes difficult. Thus partial lobectomy or subtotal thyroidectomy may be performed for patients with Hürthle cell tumor.

Several groups have reported the clinical features of cancer and adenoma and the differences between them. Carcangiu et al. [7] reported that patients with cancer had the larger primary tumor in size, and Chen et al. [8] reported that the size of primary tumor had predictive value as a criterion for malignancy, although others [9, 10] and we could not confirm it. In the present study, Hürthle cell tumor occurred more often in women than men, but the cancer ratio was higher in men. Preoperative diagnosis of cancer is not easy, as for ordinary follicular tumors. Although several studies have shown that the Hürthle cell tumor can be reliably diagnosed by FNABC, the differential diagnosis between adenoma and cancer cannot be made by FNABC [11, 12]. Some have reported that intraoperative frozen section analysis is a useful diagnostic tool for the delineation between adenoma and cancer [13], whereas others have reported that it is not reliable [14]. In the present study we performed FNABC in 145 patients: only 55 were diagnosed as having Hürthle cell tumor (38%), 81 had follicular thyroid tumor, and 9 had nonneoplastic thyroid lesions. This is thought to be an unsatisfactory outcome of the diagnostic ability of FNABC for Hürthle cell tumor. We have not performed intraoperative frozen-section evaluations and cannot comment on its value. There are no definitive parameters differentiating adenoma from cancer at the present time, and operative management should be based on the final definitive histologic diagnosis.

Several papers [15, 16] have reported that follicular cancer and Hürthle cell cancer have almost the same outcome. The AMES criteria comprised one of the early prognostic scoring systems and was reported to be able to distinguish between high risk and low risk groups, even among those with Hürthle cell cancer. Although the follow-up period was not long enough, only a one of our patients died of Hürthle cell cancer, and that patient was categorized as being at high risk based on the AMES score. Because most of our patients with Hürthle cell cancer had a rather good outcome regardless of AMES score, we could not show the superiority of total thyroidectomy in the improvement of the surgical outcome of Hürthle cell cancer. Total thyroidectomy facilitates the use of radioiodine and the use of thyroglobulin as markers for recurrence, however, Hürthle cell cancer does not accumulate radioiodine, and total thyroidectomy put the recurrent laryngeal nerve and parathyroid glands at risk to some extent. Thus total thyroidectomy for all Hürthle cell tumors at initial surgery is unnecessary. Hemithyroidectomy for all Hürthle cell tumors at initial surgery is the treatment of choice; and when the postoperative pathologic diagnosis is Hürthle cell cancer, completion total thyroidectomy should be considered only if the patient is at high risk.

**Résumé**

On a revu les dossiers de 108 cas de tumeur de cellules de Hürthle de la thyroïde (HCT) observées entre 1982 et 1996. II y avait 160 femmes et 28 hommes avec un âge moyen de 51.8 ans. Trente et un patients avaient un cancer alors que les autres avaient un adénome. L'âge, la taille de la tumeur primitive et le taux de thyroglobuline préopératoire ne différaient pas de facon significative entre les patients ayant un cancer ou un adénome. Le sexe ratio, cependant, différait de façon significative ($p < 0.05$). On a observé une récidive de tumeur de cellules de Hürthle chez trois patients ayant un adénome. Deux patients avaient une récidive sous-cutanée, probablement par implantation, alors que le troisième avait une récidive au niveau du moignon thyroïdien. Tous les patients ayant une récidive d'adénome ont eu une lobectomie partielle au moment de l'intervention initiale. Trois patients ont eu une récidive. On a observé une récidive locorégionale chez un patient et des métastases à distance chez deux patients (poumon n = 1, os, n = 1). Un seul ayant des métastases à distance est décédé. L'implantation tumorale a été observée chez les patients ayant un adénome et ainsi, la manipulation de la tumeur en peropératoire semble être un facteur important. II va de soi, également, que la tumeur, même si elle est bénigne, est agressive en termes d'activité prolifération. Tous les patients ayant une HCT doivent être traités, au moins, par lobectomie totale. L'évolution des patients ayant un cancer n'était pas aussi péjorative que rapporté antérieurement.

**Resumen**

Se revisan entre 1982 y 1996, 188 casos de tumores de tiroides con células de Hürthle (HCT). 160 eran mujeres y 28 hombres con edad media de 51.8 años. Se registraron 31 casos de cánceres, siendo los restantes adenomas. La edad, el tamaño del tumor primario y los niveles preoperatorios de tiroglobulina no mostraron diferencias significativas entre los cánceres y los adenomas. Sin embargo, la incidencia por lo que al sexo se refiere fue muy significativa ($p < 0.05$). Recidiva del HCT se constató en 3 pacientes con adenomas. Dos presentaron recidivas subcutáneas (sospechosas de implantación celular) y otro enfermo desarrolló la recidiva en tejido glandular residual del tiroides. En todos los pacientes con recidiva adenomatosa se habia efectuado, como operación inicial, una lobectomia. Tres enfermos con cáncer recidivaron; recidiva loco-regional se observó en uno y metástasis a distancia en dos (una pulmonar y otra ósea); uno de los pacientes con metástasis a distancia falleció; el otro vive con su enfermedad. Implantación tumoral se constató en pacientes con adenoma por lo que la manipulación intraoperatoria de estos tumores requiere sumo cuidado. Este hecho demuestra que los HCT aunque sean benignos son agresivos por lo que a su actividad proliferativa se refiere. En todos los pacientes con HCT debe realizarse al menos una lobectomia total. Los resultados en pacientes con cáncer no fueron tan malos como los referatados en trabajos previos.

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