

Hurthle Cell Carcinoma: Expanded View

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Abstract

Background: The definition, rarity, and natural history of Hurthle Cell Cancer (HCC) is not well understood, which makes the diagnosis and management of this cancer a controversial issue.

Purpose: The objective of this study is to report a series of patients with HCC and to discuss the clinical behavior along with the prognostic indicators of this disease in an attempt to make more accurate suggestions for treatment.

Methods: We conducted a retrospective study reporting on all patients with HCC observed at Jordan University Hospital (JUH) and King Abdullah University Hospital (KAUH), during the period from January 2001 to December 2008. Data were collected, analyzed and compared with different results published in the literature.

Results: There were 56 Patients with Hurthle Cell Tumor (HCT), diagnosed on fine needle aspiration, of those; 16 were diagnosed as hurthle cell carcinoma by histopathology. All patients with HCC were treated by total thyroidectomy; and patients with Hurthle Cell Adenoma (HCA) were treated with less than total thyroidectomy. Postoperatively, all patients with HCC were treated with radioactive iodine except for 3 patients. Follow-up period for all patients with HCC ranged from 6 to 84 months. No recurrence or distant metastasis were documented during the study period.

Conclusion: We could not find higher incidence of local recurrence, distant metastasis or mortality rates compared to literature. HCC seems to have favorable outcome in our part of the world when treated with total thyroidectomy.

Keywords: Hurthle cell, thyroid cancer, radioactive iodine.

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Introduction

The thyroid gland is the largest of the endocrine glands and by far the most common site of all primary endocrine cancers.

However, thyroid cancer is relatively rare, accounting for only 1% of all cancers.¹ Kent and colleagues reported that the incidence of differentiated thyroid cancer increased by 146%

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over the 12-year study period, for an overall increase of 13% per year.²

Hürthle cell carcinoma was first described by Ewing in 1928,³ it accounts for less than 5% of all differentiated thyroid malignancies. These tumors are heterogeneous neoplasms that display a wide range of biological behavior.

True Hürthle cells (Synonym: oxyphil cell, Askanazy cell) are large oxyphilic, eosinophilic cells found in the thyroid gland. They are metabolically altered follicular cells which accumulate large numbers of mitochondria and hyperchromatic nucleus. The first description of these cells by Askanazy was reported to be in 1898.⁴

These cells are observed in some non-neoplastic conditions of the thyroid gland; particularly Hashimoto's thyroiditis, nodular and toxic goiter. Hurthle cells have also been described as occurring in salivary gland, esophagus, pharynx, trachea, kidney, pituitary, larynx, and liver.⁵

The aim of this study is justified by the increment need for reevaluation of treatment options of Hurthle cell carcinoma of the thyroid, for more documentation in the literature about encountered cases, and the success of management, looking for diminishing controversy and improving outcomes of surgical treatment.

Materials and Methods

A total of 56 cases of Hürthle cell tumors (HCT) were diagnosed at King Abdullah University Hospital (KAUH), and Jordan university hospital (JUH), during a 7-year period (2001 through 2008). Of the 56 cases of HCT, 16 (28%) were diagnosed as Hürthle cell carcinoma (HCC). Medical records of all patients with HCC were reviewed. Data about age, gender, diagnostic modalities, histologic findings, type of surgery, adjuvant therapy (radioactive iodine), recurrence and current status of the patients were collected.

Preoperative assessment of the disease was accomplished using evaluation of free thyroxin T4 and thyroid stimulating hormone levels, in addition to autoantibodies. All patients had fine needle aspiration biopsy (FNAB) at their initial presentation to the clinic, as the first line of management. The policy of both institutions was to operate on every patient with Hurthle cell tumor of the thyroid; however, the selection of the type of surgery was based primarily on clinical and histological findings.

Histological diagnosis was performed by two pathologists. Classification into adenoma and carcinoma was based exclusively on the presence of either capsular invasion figure (1), or vascular invasion figure (2).

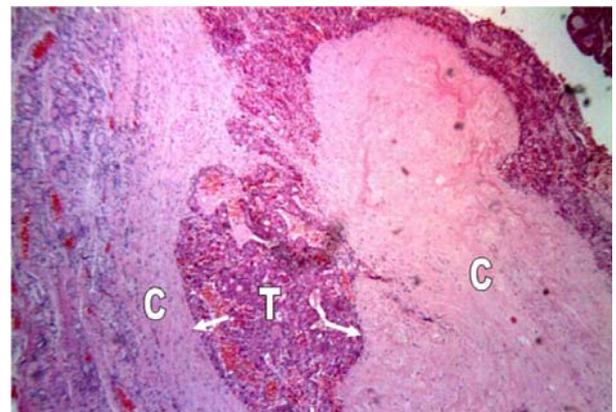


Figure (1): Invasion of the capsule (C) by HCC (T).



Figure2. Invasion of blood vessel (B.V.) by HCC (T).

Radioactive iodine ablation in this series was conducted to all patients except for 3; the cause behind that could not be found in the files. The Follow-up period for all patients ranged from 6 months to 84 months, with a mean follow-up period of 42 months.

Results

All cases of hurthle cell tumor diagnosed at both institutions from Jan 2001 to Dec 2008 were included in the study. A total of 56 cases of HCT was initially diagnosed on fine needle aspiration, among them 40 cases (71%) were diagnosed as hurthle cell adenoma, and 16 cases (29%) were diagnosed as hurthle cell carcinoma on final histopathological examination, (table 1). For the 56 patients, the mean age at diagnosis was 42 years. Forty-seven percent of patients with HCT were older than 45 years, with female- to-male ratio 2:1, for patients with HCC the mean age at diagnosis was 48 years, 56% of patients at the time of diagnoses were above the age of 45 years, and with 2:1 female-to-male ratio.

Among the 56 patients with HCT, 45 patients (80%) had unilateral disease or tumor size less than 4 cm. The initial surgery done for them was

extended hemithyroidectomy, among this group 10 patients proved to have hurthle cell carcinoma by histopathology and proceeded to total thyroidectomy. The remaining 11 patients (20%) underwent initial total thyroidectomy, 7 patients because of large tumor size (more than 4 cm), 5 of them proved to have HCC, and 4 patients because of the presence of thyroid nodule on the contra lateral side, one of them had HCC.

No regional lymph-nodes involvement or distant metastases were noticed at the time of surgery.

Malignant nodules were variable in size, they ranged from 1 to 5 cm, with the mean size of the malignant nodules being 2.5cm. 11 patients had tumor size less than 4 cm and 5 patients had tumor size more than 4 cm.

Total or near total thyroidectomy was performed for all patients with HCC; patients with HCA were treated with extended hemi-thyroidectomy, or total thyroidectomy. Table (2).

Follow-up period ranged from 6-84 months, during this time there was no disease-related mortality, and no evidence of local recurrence or any distant metastasis documented.

Table (1): Clinical, pathological and surgical Data of HCT patients.

| | No. | % of total |
|------------------------------------|-----|------------|
| Age | | |
| ≤45 y | 30 | 53% |
| >45 y | 26 | 47% |
| Sex | | |
| Female | 37 | 66% |
| Male | 19 | 34% |
| Pathology: | | |
| Hurthle cell Adenoma | 40 | 71% |
| Hurthle Cell carcinoma | 16 | 29% |
| History of thyroid disease | | |
| Multinodular goiter | 4 | 7% |
| Cystic thyroid lesion | 1 | 2% |
| Surgical intervention | | |
| Total thyroidectomy | 21 | 37% |
| Less than total thyroidectomy | 35 | 63% |
| Radioactive iodine ablation | | |
| Yes | 13 | 23% |
| No | 43 | 77% |
| Recurrence | | |
| | Nil | 0% |

Table (2): Clinical, pathological and surgical data of HCC patients.

| | No. of patients | Percentage |
|------------------------------------|------------------------|-------------------|
| Age | | |
| Above 45 years | 9 Patients | %56 |
| Below 45 years | 7 Patients | 44% |
| Gender | | |
| Female | 10 patients | 63% |
| Male | 6 patients | 37% |
| Type of surgery | | |
| Initial total thyroidectomy | 6 patients | 37% |
| Completion thyroidectomy | 10 patients | 63% |
| Size of malignant nodule | | |
| More 4cm | 5 patients | 31% |
| Less than 4cm | 11 patients | 69% |
| Distant metastasis | 0 patients | |
| Radioactive iodine ablation | | |
| Yes | 13 patients | 81% |
| No | 3 patients | 19% |
| Recurrence | 0 patients | |
| Discussion | | |

Although still controversial; surgical treatment of HCT has been discussed thoroughly in literature. Many have chosen to totally remove thyroid in case of HCC and only half the gland in case of HCA.

Several authors support the role of total thyroidectomy in the treatment of HCC because different reports in literature have documented the presence of contra lateral foci of carcinoma in 40–70% of cases of HCC,^{6, 7} and 15 to 35% incidence of multiple foci of HCC at the same lobe.⁸

Paunovic et al. managed all carcinoma patients with total thyroidectomy with a low complication rate.⁵ Consequently, they stated that total thyroidectomy is the treatment of choice for HCC, and reserve hemithyroidectomy for adenomas. Bondeson et al. and Gosain and Clark all have adopted the same treatment because they believe that tumor behavior is predicted by histologic characteristics.^{9, 10}

Azadian et al. in one of the large series of HCC recommended total thyroidectomy together with lymph node sampling for all cases of HCC and

near total thyroidectomy for HCA.¹¹ Sanders and Silverman found that Follicular thyroid carcinoma (FTC) and Hürthle cell carcinoma with minimal capsular invasion behaved benignly. with no significant difference in a 20-year survival rate between patients with HCC versus FTC. Their recommendation was to go for total thyroidectomy as the surgical option for HCC and FTC which show vascular or major capsular invasion.¹²

Certain studies have shown that 2.5% of benign-appearing Hürthle cell lesions have later metastasized.^{13,14} Therefore, some surgeons have chosen to do more aggressive approach performing total thyroidectomy initially in dealing with patients who have HCT on fine needle aspiration biopsy. Thompson et al. advocate total thyroidectomy for all cases of HCT because of the concern of the unpredictable behavior of even histologically benign neoplasia¹³. This is in contrary to Tollefsen et al. and Watson et al. who recommend hemithyroidectomy for all patients with HCA.^{15,16}

In elderly patients, HCC are generally more aggressive with less favorable prognosis compared to younger patients, it is therefore recommended to offer total thyroidectomy.¹⁷

All patients in this series were treated initially by extended hemi-thyroidectomy if the FNAB was consistent with HCT, in selected cases; total thyroidectomy was adopted if tumor size was more than 4 cm or if there is a contra lateral thyroid nodule. Completion surgery was performed in cases with histopathologic evidence of malignancy. Evidence of contralateral foci of malignant cells was almost always present in histologic evaluation of thyroid specimens post surgery. In all patients who did not have evidence of capsular or vascular invasion by histopathology, malignant behavior was not reported during the period of follow up.

Radioactive iodine is considered the most useful non-surgical therapy for well-differentiated thyroid carcinoma. It has been postulated for a long time that HCC is less responsive to radioactive iodine therapy than other differentiated thyroid malignancies.¹⁸

According to Sanders and Silverman,¹² the use of radioactive iodine does not produce a better outcome, with 71% 20-year survival rates both with and without radioactive iodine. However they recommend this modality of treatment in spite of questionable efficacy, because of limited other treatment options,¹⁹ and the malignant cells sometimes take it up.¹⁸

Hanief et al. have demonstrated several factors that justify radioactive iodine ablation therapy post thyroidectomy.²⁰ Firstly, the presence of thyroid remnant can obscure I¹³¹ uptake in cervical or lung metastases.^{21, 22} Secondly, distant metastases may be seen only on the post treatment whole body scan after remnant ablation.²³ Finally, remnant ablation may destroy precancerous cells or occult tumors if present.²⁴

The impression regarding this type of tumors has been recently called into question by Besic et al. who found uptake in recurrent disease or in distant metastases in 11 of 16 patients.²⁵

Although radioactive iodine doesn't seem to influence outcome and prognosis as declared by different researches; we adopted this adjuvant therapy in most of our HCC cases.

In thyroid malignancies, it is well known that fine needle aspiration is most sensitive at detecting anaplastic (almost 100%) and papillary (around 90%) carcinomas.²⁶⁻²⁸

Although Hurthle cell lesion can be easily picked up on FNAB, thyroid FNAB is believed to be not adequate to distinguish benign from malignant follicular or Hurthle cell neoplasms,²⁹⁻³² because in both cases the diagnosis of HCC or FTC one has to demonstrate vascular and/or capsular invasion.

McIvor and colleagues in a study over a 12-year duration showed that fine-needle aspiration for Hurthle cell neoplasia had a sensitivity of 83.8% and positive predictive value of 93%, provided that the aspirate is of adequate cellularity. However, they concluded that the differentiation between benign and malignant lesions is not reliable on the basis of FNAB.³³

In other study by Nguyen et al. they have demonstrated that the presence of small tumor cells with ill-defined cytoplasm and prominent nucleoli in the FNAB of a thyroid nodule should alert the observer about the strong possibility of an HCC.³⁴

In our cases, diagnosis of HCC is established postoperatively. Fine needle aspiration biopsy was the guidance for surgical option; however, the decision to progress to total thyroidectomy was dependent on final histopathologic evaluation.

Prognosis in HCC can be predicted by different factors. Many studies have shown that advanced age (>45), male sex, size of primary tumor (>4 cm), degree of invasion and recurrence are poor prognostic indicators.^{17,35,36} In addition, the presence of distant metastasis at the time of diagnosis was considered important risk factors for HCC, according to Kushchayeva et al.³⁷

In our series, 69% of our patients were above the age of 40 years, 5 patients have tumor size more than 4 cm, and 6 patients were males who still have no local recurrence or distant metastasis up to the completion of this study.

Conclusion

The presence of Hürthle cells in FNA indicates the need for surgery. In the presence of certain risk factors such as male sex, age more than 40, and nodule size more than 4 cm, total thyroidectomy is recommended. In patients with no risk factors and HCT on FNAB, total thyroidectomy can be delayed until the final histopathology diagnosis of HCC is available. The role of post-operative radioactive iodine ablation is still controversial although most authors will still use it; we recommend using it in all our patients.

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سرطان خلية هيرثل: نظرة شاملة

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الملخص

تشخيص وعلاج سرطان خلية هيرثل (Hurthle) لا يزال مختلف عليه ولا يوجد عليه إجماع نظراً لندرة المرض.

الهدف: الغاية من هذه الدراسة هي عمل تقرير حول مجموعة من المرضى المصابين بسرطان خلية هيرثل ولناقشة السلوك السريري بالترافق مع المؤشرات الإنذارية لهذا المرض كمحاولة لإيجاد اقتراحات دقيقة لعلاج هذا المرض.

الوسائل: دراسة استرجاعية حول جميع المرضى المصابين بسرطان خلية هيرثل في مستشفى الجامعة الأردنية ومستشفى الملك المؤسس عبد الله الأول الجامعي خلال الفترة من كانون الثاني 2001 ولغاية كانون الأول 2008. جمعت جميع المعلومات وحللت وقورنت بنتائج مختلفة نشرت في الأدب الطبي.

النتائج: (56) مريضاً مصاباً بورم خلية هيرثل شُخص من خلال الخزعة بالإبرة الرفيعة، (16) منهم شُخص بأنه مصاب بسرطان خلية هيرثل (HCC) عن طريق الفحص النسيجي المرضي.

عولج جميع المرضى المصابين بسرطان خلية هيرثل باستئصال كامل للغدة الدرقية، بينما المرضى المصابين بالورم الغدي الحميد لخلية هيرثل (HCC) عولجوا باستئصال جزئي للغدة الدرقية، بعد إجراء العمليات الجراحية لجميع المرضى المصابين بسرطان خلية هيرثل تم إعطاؤهم جرعات اليود المشع باستثناء 3 مرضى. كانت فترة متابعة المرضى المصابين بسرطان خلية هيرثل بعد هذا العلاج تتراوح بين (6-84) شهراً. ولم يلاحظ أي عودة أو انتشار بعيد للمرض خلال فترة هذه الدراسة.

الخلاصة: لم تتمكن من التوصل إلى وجود معدلات عالية لعودة المرض الموضعي، الانتشار البعيدة أو الوفيات مقارنة بما نُشر في الأدب الطبي، مما يدل على ما يبدو أن سرطان خلية هيرثل إذا ما عولج باستئصال كامل للغدة الدرقية تكون النتائج جيدة.

الكلمات الدالة: خلية هيرثل، سرطان الغدة الدرقية، اليود المشع.