Demographic and histological subtypes of Hurthle cell tumours of the thyroid in a South African setting

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Background: Report of Hurthle cells following fine needle aspiration cytology from a thyroid nodule raises possibility of Hurthle cell carcinoma (HCC), which is a distinct entity and accounts for 3–10% of thyroid malignancies.
Aim: To determine if there are demographic and histopathological features which may be used to differentiate HCC from Hurthle cell adenoma (HCA).
Methods: Histopathology records of patients who had thyroidectomy from January 2001 to October 2015 were reviewed. Data retrieved included indications for thyroidectomy, patients' demographics, histology and preoperative FNAC results.
Results: At total of 2641 records were reviewed of which 25.6% (676/2641) were for neoplasms. 15.8% (107/676) of the neoplasms were Hurthle cell neoplasms (HCNs) and 25.2% (27/107) of HCNs were HCCs. 77.2% (71/92) of HCAs and 77.8% (21/27) of HCCs were from female patients. Preoperative FNAC results were available for 54.2% (58/107) and were suspicious of HCN in 12.1% (7/58). Average tumour size for HCCs and HCAs was 4.9 +/- 2.7 cm and 3.5 +/- 2.0 cm, respectively. The difference was statistically significant with a p-value of 0.016. The risk of malignancy increased from 11.1% in HCNs less than 1 cm to 53.8% for tumours which were greater than 4 cm in diameter.
Conclusion: HCNs are more common in females. The likelihood of HCC rises as the size of the HCN increases. Malignancy rate exceeds 50% for HCNs which are greater than 4 cm in diameter.
Key words: Hurthle cell neoplasm, Hurthle cell carcinoma, FNA, tumour size

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Introduction

Hurthle cell neoplasms (HCNs) include Hurthle cell carcinoma (HCC) which accounts for 5–10% of thyroid malignancies.[1] Hurthle cell carcinoma is different from follicular neoplasms morphologically and in clinical behaviour.[2] Subtypes of HCC include classical, papillary and the medullary carcinoma variant.[3]

Hurthle cells may be found in benign conditions such as multinodular goitre (MNG), thyroiditis and Graves' disease.[3-6] Non-neoplastic Hurthle cells have also been reported in other malignant neoplasms of the thyroid gland such as follicular, papillary and medullary carcinoma.[7]

Diagnosis of HCN is only considered if more than 50–75% of fine needle aspiration cytology (FNAC) specimen from the lesion is composed of Hurthle cells.[1] It is however not possible to diagnose HCC following FNAC as confirmation of HCC requires demonstration of evidence of invasion of the capsule, blood vessels or both. The Bethesda System for Reporting Thyroid Cytopathology (Bethesda) is preferred for interpretation of FNAC result and guidance regarding further management.[10] The Bethesda system categorises FNAC result into six categories: non-diagnostic (Bethesda I), benign (Bethesda II), atypia of undetermined significance or follicular lesion of undetermined significance (Bethesda III), follicular neoplasm or suspicious of follicular neoplasm (Bethesda IV), suspicious of malignancy (Bethesda V) and malignant (Bethesda VI). Recommended management of Bethesda III and IV thyroid lesions is either to repeat FNAC or to perform diagnostic lobectomy. At best FNAC from HCN is likely to show an indeterminate result, i.e. Bethesda III or IV lesion.[8-10]

Gender and age of patients, together with size of thyroid nodules have been used to try to predict the risk of malignancy in HCN.[9,11-13] The aim of this study was to determine if there are demographic and histopathological features which may be used to differentiate HCC from Hurthle cell adenoma (HCA).

Materials and methods

Histopathology records of all patients who had thyroidectomy from January 2001 to October 2015 at Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Academic Hospital were reviewed. Data retrieved included demographics and histopathology results. Histopathological data collected included tumour type, size, HCN subtypes and corresponding preoperative FNAC results. Demographic and histopathological data were entered into an Excel spreadsheet and analysed using Statistical Package for Social Sciences version 13.1 of 2015. Data for age and tumour size were presented as mean +/- standard deviation. Fisher's exact test was used to compare categorical data and student's t-test for continuous data. The level of significance was set at p-value less than 0.05. Ethical approval was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (M150944). Furthermore, permission to access records was obtained from the Department of Anatomical Pathology of the National Health Laboratory Services (NHLS) and Research Review Boards of Chris Hani Baragwanath Academic Hospital and Charlotte Maxeke Johannesburg Academic Hospital.

Results

A total of 2641 records were reviewed. 74.4% (1965/2641) of thyroidectomies yielded benign thyroid conditions and were excluded from further analysis.

The remaining 25.6% (676/2641) of thyroidectomies were for neoplasms. The mean age of patients who had thyroidectomy for neoplasms was 47.3 ± 15.9 years and 82.5% (558/676) of them were females. 71.2% (481/676) were malignant of which 62.0% (298/481) were papillary carcinomas and 5.6% (27/481) HCCs (Table 1).

Table 1: Benign and malignant thyroid tumours

Pathological diagnosis	n = 676	
Benign tumours (n = 195)		Percent
Follicular adenoma	115	59.0%
Hurthle cell adenoma	80	41.0%
Malignant tumours (n = 481)		
Papillary carcinoma	298	62.0%
Follicular carcinoma	82	17%
Medullary carcinoma	40	8.3%
Hurthle cell carcinoma	27	5.6%
Anaplastic carcinoma	15	3.1%
Lymphoma	6	1.3%
Metastatic carcinoma	8	1.7%
unspecified carcinoma	3	0.6%
Malignant teratoma of thyroid	1	0.2%
Malignant solitary fibrous tumour	1	0.2%

A total of 107 patients had HCN of which 75.0% (80/107) were HCAs. 86.0% of patients who had HCNs were females. 88.7% (71/80) of HCAs and 77.8% (21/27) of HCCs were in female patients (Table 2).

Table 2: Characteristics of patients who had HCNs (n = 107)

Parameter	Hurthle cell carcinoma	Hurthle cell adenoma	*p*-value
No. of Patients	27	80	
Males	6 (22.2%)	9 (11.3%)	
Females	21 (77.8%)	71 (88.7%)	
M : F ratio	1.0 : 4.5	1.0 : 8.9	0.156
Age groups			
< 45 years	7 (26%)	29 (36.3%)	
45–65 years	13 (48%)	31 (38.8%)	
> 65 years	6 (22%)	19 (24.9%)	
Mean age +/- SD (years)	55.0 +/-15.0	52.3+/-15.6	0.274
Age range	32–84 years	23–95 years	
Mean tumour size (cm) +/-SD	4.9 +/- 2.7	3.5+/- 2.0	0.016
Size range	0.8–10.0 cm	0.2–9.0 cm	
Size groups			
< 1.0 cm	3/26 (11.1%)	0/52 (0%)	
1–4.0 cm	9/26 (33.3%)	34/52 (65.4%	
> 4.0 cm	14/26 (52.8)	18/52 (34.6%)	

Preoperative FNAC results were available for 54.2% (58/107) of the records of patients who had HCNs. In 1.7% (1/58) of the cases malignancy (Bethesda V) was suspected whereas 15.5% (9/58) showed Bethesda IV lesions (Table 3).

Table 3: Comparison of preoperative FNAC results and final histology in HCNs (n = 58)

Category	HCC	HCA	Total
Non-diagnostic	1	5	6
Benign	1	7	8
Bethesda III	1	4	5
Bethesda IV	9	22	31
Suspicious of malignancy	1	0	1
Malignant	0	7	7
Total	**13**	**45**	**58**

HCC = Hurthle cell carcinoma, HCA = Hurthle cell adenoma

The average tumour size for HCCs and HCAs was 4.9 ± 2.7 cm and 3.5 ± 2.0 cm. The difference was statistically significant with a p-value of 0.016. The probability of HCC in HCN increased as the size of the thyroid nodule got bigger and was 53.8% in nodules which were more than 4 cm in diameter.

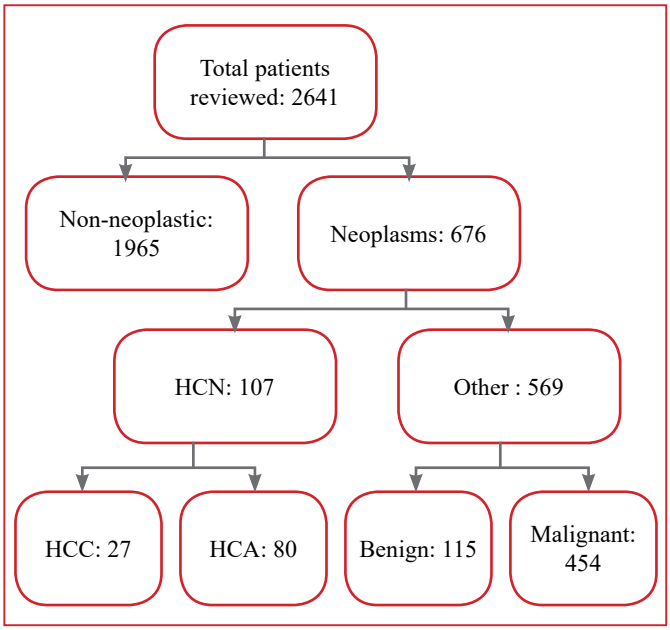

Figure 1. Breakdown of records of thyroidectomies based on underlying pathology

66.7% (18/27) of the HCCs were follicular variant of HCC, whereas 11.1% (3/27) were papillary variant and 22.2% (6/27) were pure HCC. 41.1% (44/107) of patients with HCN underwent total thyroidectomy and 50.5% (54/107) had thyroid lobectomy. In 22.2% (6/27) of the patients, HCC was incidentally found following total thyroidectomy for MNG. Additionally, 18.5% (5/27) who had total thyroidectomy preoperative FNAC showed oxyphilic cell in the background of either MNG or Hashimoto's thyroiditis. 48.1% (13/27) of patients with HCC had thyroid lobectomy as the initial procedure.

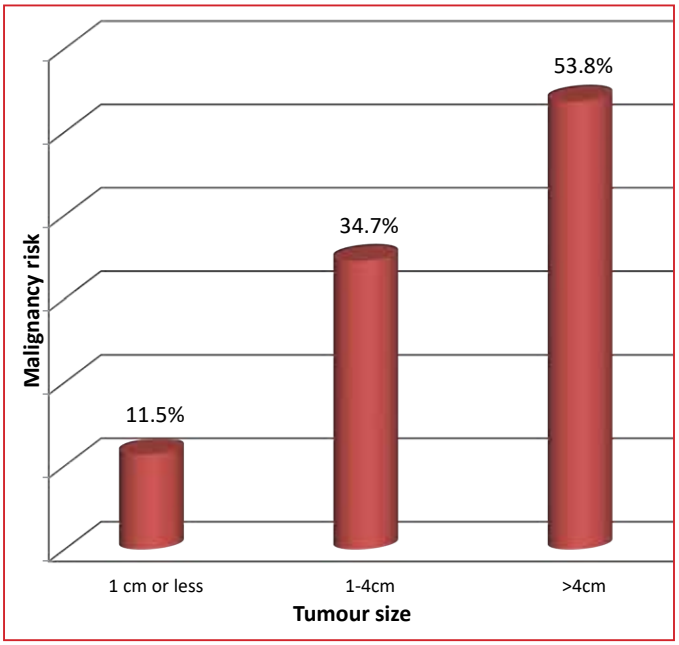

Figure 2. Relationship between HCN size (cm) and risk of malignancy (%)

Capsular invasion was found in all HCCs whereas 59.3% (16/27) had both capsular and vascular invasion. Two patients who had completion thyroidectomy following diagnostic lobectomy which showed HCC were found to have HCA in the contralateral lobe.

Discussion

Over 70% of thyroidectomies in our setting are performed for non-neoplastic conditions. The incidence of HCN ranges from 3–10% of differentiated thyroid tumours. Several studies have shown the prevalence of malignant HCC ranging from 5–35%.[9,11,12,14] In the current study HCC represented 5.6% of all differentiated thyroid cancers. The prevalence of malignancy amongst HCNs was 25.2%, which is similar to what has been reported in literature.[9,11,14]

The diagnosis of Hurthle cell carcinoma is made if capsular and/or vascular invasion is/are demonstrated on histology.[1] Several studies have shown that FNAC is a reliable test to diagnose HCNs. However, the distinction between benign and malignant HCN preoperatively is not possible.[1,15] In this study we confirmed that FNAC cannot diagnose HCC. FNAC was also not useful for the diagnosis of HCA. Differentiating HCC from HCA or any other benign Hurthle cells bearing lesion is critical because appropriate definitive surgery such as total thyroidectomy may be indicated ab initio if HCC is highly likely.[11,13,14,16] Pisanu et al.[14] would recommend consideration of total thyroidectomy for HCNs in which the likelihood of HCC is high.

Several clinical and histopathological features have been investigated to determine if they could be used to predict the likelihood of HCC in patients who have HCNs. These features include patient's age, gender, and tumour size.[11,16,17] The majority of FNAC results when available in the current study were indeterminate, i.e. Bethesda III and IV. The rate of HCC of 29.7% in the indeterminate lesions from the current study is consistent with what is already known.[12,13,18-20]

No demographic parameter was found to be useful in predicting final diagnosis of HCC in the current study. The patient's gender is not useful for predicting malignancy in HCN. Patients who had HCC were older than the ones who had HCA but the difference was however not statistically significant. Carcangiu et al.[19] and Lopez-Penabad et al.[20] found that HCC patients were older than patients who had HCA.

Several authors have reported that the risk of malignancy rises as the size of HCN increases. Straziser et al.[14] reported that malignancy rate in patients with tumour size between 1 and 4 cm and greater than 4 cm were 20% and 40%, respectively. Chen et al.[13] also reported that HCN of the size of 1 cm or less had 17% chance of being malignant. Malignancy risk is 23% for tumours 1 to 4 cm in diameter and 65% for those which are 4 cm or larger.[14]

There is as yet no agreement as to the appropriate management of HCNs because of controversies involving diagnosis and biological behaviour. Some investigators recommended thyroid lobectomy as an initial surgical procedure, followed by completion thyroidectomy upon

histological diagnosis of HCC.[13,26] Others would recommend total thyroidectomy citing unpredictable biological behaviour,[13] propensity for multifocality,[16] and high likelihood of the malignancy.[11,14]

Limitation of the study

The study is an audit based on histopathology reports and therefore relies heavily on histology reports, and no other medical records have been reviewed. Some details were incomplete and information regarding subsequent management for Hurthle cell carcinoma in term of completion thyroidectomy and RAI ablation therapy were not looked into. In addition, the majority of the FNA results were not available for review. It could also not be established whether some of the patients who had diagnostic lobectomy which yielded HCC subsequently had completion thyroidectomy.

Conclusion

HCNs are more common in females and almost half of them are diagnosed following thyroidectomy performed for other thyroid pathologies. The likelihood of HCC rises as the size of HCN increases. Capsular invasion is reported more in HCCs than vascular invasion. Size of Hurthle cell neoplasm is the only parameter which is predictive of malignancy.

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Conflict of interest

All the authors have no conflict of interest to declare.

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