



Hürthle Cell Neoplasms of Thyroid in South-Western Region of Saudi Arabia

Tumeurs A Cellules De Hürthle De La Glande Thyroïde Dans La Region Du Sud-ouest De L'arabie Saoudite

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ABSTRACT

BACKGROUND: Thyroid Hürthle cell neoplasm (THCN) is relatively rare.

OBJECTIVE: To describe the presentation, diagnostic approach and management of THCN in our institution.

METHODS: This was a retrospective chart review of all thyroid Hürthle cell neoplasms diagnosed at Aseer Central Hospital (ACH), Saudi Arabia during the period from October 1998 to April 2007. Data including clinical, cytopathologic, radiologic, histopathologic and surgical treatment were extracted for analysis.

RESULTS: Nine patients were diagnosed as THCN (eight females and one male). Their ages ranged from 24–49 years. Three cases were Hürthle cell carcinomas and six cases were Hürthle cell adenomas. Carcinomas presented as solitary nodules (two cases) and as multinodular goiter (one case). Adenomas presented as solitary nodules (two cases), as multinodular goiter (three cases) and as diffuse swelling (one case). Fine needle aspiration cytology (FNAC) was diagnostic for THCN in two cases of carcinoma that presented as solitary nodules and hence total thyroidectomy was performed. Total thyroidectomy was also done in one case of adenoma.

Hemithyroidectomy was performed in two cases of adenoma in which FNAC showed benign lesion and in one case of carcinoma based on clinical and ultrasonographic impression of benign MNG in the involved lobe and inconclusive FNAC result. Subtotal thyroidectomy was performed in one case of adenoma.

CONCLUSION: Preoperative diagnosis and management of THCN is still a dilemma. Neither clinical nor FNAC findings can exclude carcinoma. Therefore a combination of clinical, radiological, FNAC and histopathological results should be used for a more definitive subtyping and proper management. *WAJM 2010; 29(6): 398–402.*

Keywords: Thyroid, Hürthle cell, Tumours, Carcinoma, Adenoma, Saudi Arabia, Fine needle aspiration cytology, Diagnosis.

RÉSUMÉ

CONTEXTE: Les tumeur thyroïdiens à cellules de Hürthle (THCN) sont relativement rares.

OBJECTIF: Décrire la présentation, l'approche diagnostique et la gestion des THCN dans notre institution.

METHODES: Il s'agissait d'une étude rétrospective de toutes les tumeurs thyroïdiens à cellules de Hürthle diagnostiquée à l'Hôpital Central de Aseer (ACH) d'Arabie saoudite au cours de la période allant d'Octobre 1998 à Avril 2007. Les données cliniques, cytopathologiques, radiologiques, histopathologiques, et le traitement chirurgical ont été extraites pour analyse.

RESULTATS: Neuf patients ont été diagnostiqués comme THCN (huit femmes et un homme). Leur âge variait de 24 à 49 ans. Trois cas de tumeurs à cellules de Hürthle étaient des carcinomes tandis que six cas étaient des adénomes. Les carcinomes se présentaient comme un nodule solitaire dans deux cas ; et un cas de goitre multinodulaire. Les adénomes se présentaient sous forme de nodules solitaires dans deux cas, multinodulaires dans trois cas et une tumefaction diffuse dans un cas.

La cytologie du produit de ponction-aspiration à l'aiguille fine (FNAC) a permis de porter le diagnostic de deux cas de cancer se présentant sous forme de nodules solitaires et, partant, une thyroïdectomie totale a été réalisée. Une thyroïdectomie totale a été également réalisée dans un cas d'adénome. Une hémithyroïdectomie a été réalisée dans deux cas d'adénome dans lesquels la FNAC a montré une lésion bénigne et dans un cas de carcinome fondée sur l'impression clinique et échographique de goitre multinodulaire bénin dans le lobe en cause et des résultats de FNAC non concluants. Une thyroïdectomie subtotale a été réalisée dans un cas d'adénome.

CONCLUSION: Le diagnostic préopératoire et la gestion des THCN est toujours un dilemme. Ni les données cliniques, ni la FNAC ne peuvent exclure un carcinome. Par conséquent, une combinaison des données cliniques, radiologiques, cytologiques et des examens histopathologiques devraient être utilisés pour une sous-typage plus précis et une meilleurs prise en charge. *WAJM 2010; 29(6): 398-402.*

Mots-clés: Thyroïde, Cellules de Hürthle, Tumeurs, Carcinome Adénome, Arabie Saoudite, la Cytologie Aspiration à l'aiguille fine, Diagnostique.

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Abbreviations: FNAC, Fine needle aspiration cytology; MNG, Multinodular goiter; THCA, Thyroid Hürthle cell adenoma; THCC, Thyroid Hürthle cell carcinoma; THCN, Thyroid Hürthle cell neoplasm.

INTRODUCTION

Hürthle cells, which are also known as oncocytes, oxyphilic cells, or Askanazy cells were first described by Langhans in 1907.^{1,2} They are characterized morphologically by abundant granular eosinophilic cytoplasm and round nuclei with prominent nucleoli. The cytoplasmic granularity is due to the abundance of mitochondrial organelles.³ Hürthle cells in fact are considered as a variant of the follicular cells, as demonstrated by the presence of thyroglobulin immunoreactivity and a functional thyrotropin receptor-adenylate cyclase system in many Hürthle cell tumours.⁴ Thyroid Hürthle cell lesions include a wide range of non-neoplastic and neoplastic pathologic entities. The neoplastic group is defined as tumours composed predominantly or entirely of Hürthle (oncocyctic) cells. The non-neoplastic entities include hyperplastic Hürthle cell nodules that can be seen in multinodular goiter (MNG) and Hashimoto thyroiditis.⁵ The neoplastic Hürthle cell thyroid nodules include Hürthle cell adenomas, Hürthle cell (oncocyctic) variant of papillary carcinoma, and Hürthle cell carcinomas. Hürthle cell thyroid neoplasms are relatively rare,⁶ and have an aggressive biological behavior.^{3,7}

Shedding light on these rare neoplasms and increasing awareness of surgeons and residents/registrars in training programs are of clinical relevance. In this study we reviewed all cases of thyroid Hürthle cells neoplasms diagnosed at the Department of Pathology, Aseer Central Hospital, Abha, Saudi Arabia. We analyzed the clinical presentation, diagnostic approach and management of thyroid Hürthle cell neoplasms.

SUBJECTS, MATERIALS, AND METHODS

Aseer region (population of 1,200,000) lies in the southwestern part of Saudi Arabia, extending over an area of more than 80,000 km². The area extends from the high mountains of Aseer with an altitude of about 3000 m above sea level westwards to the Red sea, and southwards to the border of neighboring Yemen. Health services delivery in the Aseer region is provided through a

widespread network of 238 primary health care centers scattered over 14 integrated health sectors and 16 general hospitals and one tertiary care 400-bedded hospital (Aseer Central Hospital).⁸

In this retrospective analysis, all cases attending Aseer Central Hospital over a period of eight and a half years, from October 1998 to April 2007, and were diagnosed on histological *and/or* (FNAC) examinations as Hürthle cell lesions of the thyroid specimens were included in this study. Patients with Hürthle cell lesions encountered in conditions such as Hashimoto's thyroiditis, hyperplastic nodule, or multinodular goiter as well as thyroid Hürthle cell (oncocyctic) variant of papillary carcinoma were excluded from the study.

The FNAC and histopathological reports together with the age, gender, clinical presentations and the management offered for these cases were reviewed and analyzed. The pathology materials were reviewed by at least two pathologists.

Frequency, percent, arithmetic mean, standard deviation and median are used to present data. The following non-

parametric tests of significance were used; Fisher's exact 2 sided P, Mann Whitney test and Kruskal Wallis test. The chosen level of significance was set at $p \leq 0.05$.

RESULTS

The present retrospective study included nine cases of Hürthle cell neoplasms of the thyroid gland (eight females and one male). Their ages ranged from 24 years to 49 years with an average of 37.89 ± 7.71 SD years and a median of 40 years.

Cytopathological Features

Three cases were diagnosed histopathologically as thyroid Hürthle cell carcinoma (THCC), and six cases as thyroid Hürthle cell adenoma (THCA). Figure 1 shows the cytomorphologic features of thyroid Hürthle cell neoplasm, and Figures 2 and 3 show the histologic features of thyroid Hürthle cell carcinoma. The mean age of patients who had THCC (35.67 ± 7.77 years) was not significantly different (Mann-Whitney $p=0.714$) from that of THCA (39.01 ± 8.15 years). All three cases of patients who had THCC were females compared to five (83.3%) cases among THCA, $p=0.67$. All six cases of

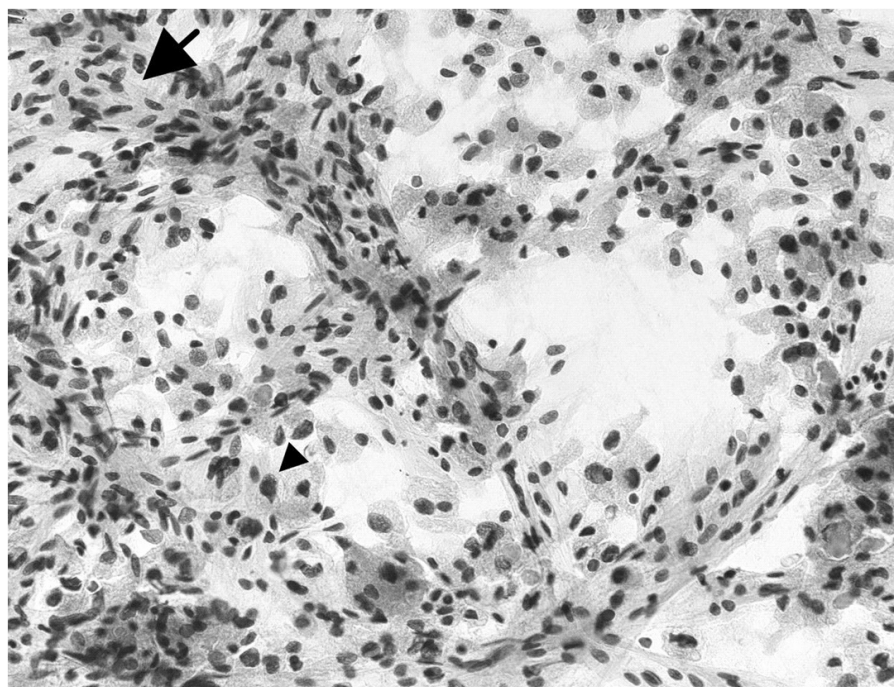


Fig.1: Photomicrograph (original magnification, x 20; PAP stain) shows a highly cellular aspirate composed of three-dimensional group of Hürthle cells adixed with dispersed population of Hürthle cells having abundant cytoplasm and eccentric round nuclei (arrow head). Transgressing blood vessels is a frequent feature in aspirates proven to be Hürthle cell carcinoma (arrow, left upper corner).

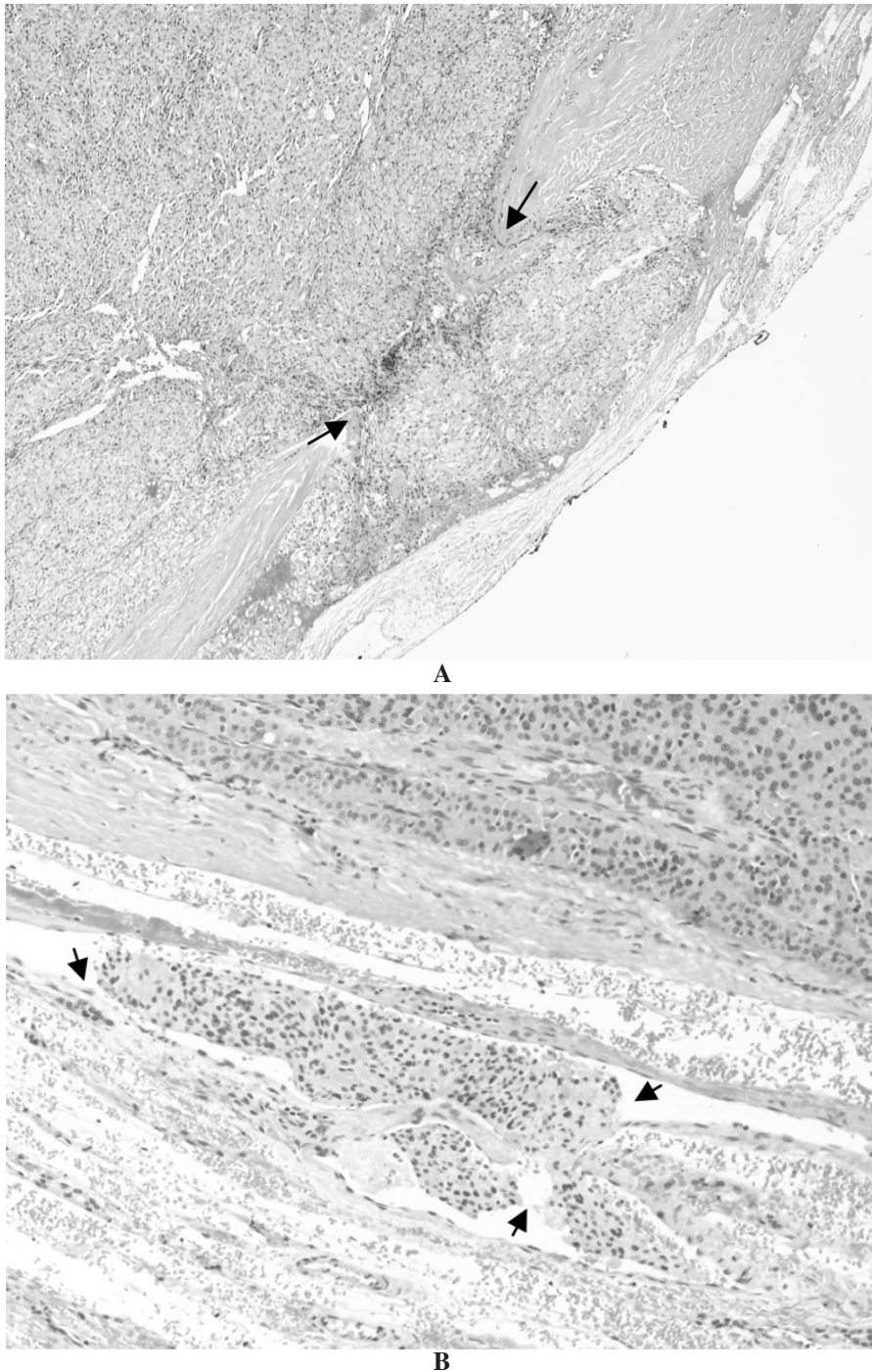


Fig. 2: Photomicrograph (original magnification, x 20; H & E stain) shows (A): capsular invasion and (B) vascular invasion in Hürthle cell carcinoma (arrow within a blood vessel).

THCA were Saudis compared to two (66.7%) cases among THCC. The difference is not statistically significant (Fisher Exact 2 sided $p=0.33$).

Clinical Presentation

Two cases of THCC clinically presented as solitary nodule while one case presented as multinodular goiter

(MNG). On the other hand, in the THCA group, two cases presented as solitary nodule, three as MNG, and one case as diffuse goiter. The differences in clinical presentation were not statistically significant (Fisher Exact 2 sided $p=0.72$).

The average duration of complaints among patients who had THCC (2.56 ± 3.06 years) was not significantly different

(Mann-Whitney $P=0.904$) from that of patients with THCA (3.01 ± 2.06 years). Neither THCC nor THCA patients had complained of respiratory difficulty, or change of voice or dysphagia.

In our series, seven cases had FNAC; two of them were diagnosed as Hürthle cell neoplasm, and one case as Hürthle cell lesion. On the other hand, the remaining 4 cases were reported as colloid nodule (two cases), benign lesion (one case) and inconclusive (one case).

Treatment

Hemi-thyroidectomy was performed in only one case of THCC versus four cases of THCA. On the other hand, two cases of THCC were treated by total thyroidectomy, compared with one case of THCA. In addition, one case of THCA was treated by subtotal thyroidectomy. Although two cases of THCC presented as solitary nodule, FNAC showed Hürthle cell neoplasm, and hence they were treated by total thyroidectomy. Hemi-thyroidectomy was carried out in two cases of THCA whose FNAC showed benign lesions. Furthermore, hemi-thyroidectomy was performed in one case of THCC on the background of clinical and ultrasonographic impression of benign MNG in the involved lobe and inconclusive FNAC result.

DISCUSSION

Thyroid Hürthle cell tumours are considered by the World Health Organisation (WHO) as a subtype of follicular derived neoplasms.⁹ THCC have been reported to have more aggressive biological behavior compared to non-Hürthle cell follicular tumours.¹ However uncertainties remain unresolved as to their incidence, diagnosis, management and prognosis, and institutions' experience in dealing with THCC is limited.^{10,3}

THCC is characterized morphologically by the presence of more than 75% Hürthle cells, with one or more of the following pathologic features: capsular invasion that penetrates the full thickness of the capsule, spread to adjacent tissues, vascular invasion, and local or distant metastases.³ Although some investigators believe that Hürthle cells are a variant of the follicular cells, it has been shown up by many studies that

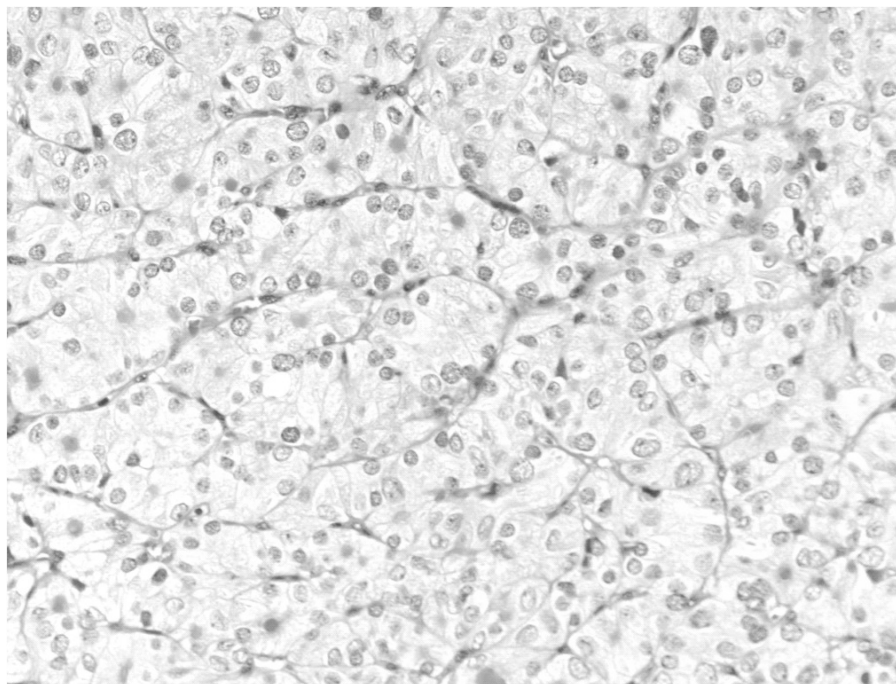


Fig. 3: Photomicrograph (original magnification, x 40; H & E stain) shows Hürthle cell neoplasm composed of large polygonal cells with granular eosinophilic cytoplasm.

Hürthle cell carcinoma is more often multifocal and bilateral and more frequently involves regional nodes than does follicular carcinoma³. It appears to be a more aggressive tumour than papillary or follicular carcinoma of the thyroid gland, with a greater tendency to metastasise to distant sites and a higher mortality rate.³

Role of Fine Needle Aspiration

FNAC is utilized by surgeons or endocrinologists as an initial diagnostic test to categorise the thyroid nodule; and it has been found that FNAC can predict Hürthle cell neoplasm; however it cannot distinguish between THCA and THCC.⁵ It has been proposed in many reports^{11,3} that surgical resection should be applied in cases where FNAC categorises the thyroid nodule as a dominant Hürthle cell neoplasm for final diagnosis. In our series FNAC was diagnostic of Hürthle cell neoplasm in two cases, Hürthle cell lesion in one case, and inconclusive in one case, while it was reported as benign in the remaining cases. This suggests that the diagnostic yield of FNAC is variable depending on many factors including aspiration technique, and the experience of the cytopathologist. All FNAC specimens in our series were taken

without ultrasound guidance. More recent studies demonstrate that aspiration of thyroid nodules guided by ultrasound is not only yielding better material but also is cost-effective compared to palpation-based thyroid aspiration maneuver.¹²

FNACs of HCN tend to be monomorphous, composed almost exclusively of microfollicular Hürthle cells, without histiocytes, or colloid that may be seen in nodular goiters, or the lymphocytes that may be seen in Hashimoto's thyroiditis. It is essential for the cytopathologist to exclude the Hürthle cell (oncocyctic) variant of papillary thyroid carcinoma, which typically reveals the nuclear features such as intranuclear pseudo-inclusion and the nuclear grooves.¹

Histopathology

At the level of histopathological diagnostic criteria, the pathologists can reliably distinguish between THCA and THCC. Malignancy is confirmed based on the presence of definitive capsular invasion, vascular invasion, or presence of lymph nodes or distance metastasis. A group of thyroid Hürthle cell neoplasms are considered as an intermediate group between THCA and THCC. This group is termed with different pathological nomenclature such as minimally invasive

Hürthle cell tumours, and Hürthle cell neoplasms of uncertain malignant behavior (UMB).¹³ These tumours are characterised morphologically by minimal capsular invasion. These histological criteria of this intermediate group are subjective due to interobserver and intra-observer variability, causing considerable controversy among surgical pathologists, and hence a dilemma for predicting the biological behavior. The management of such lesions is still uncertain. All cases diagnosed in our series as Hürthle cell carcinoma demonstrated definitive capsular and/or vascular invasion. It should be noted that pathologists should exercise some caution when dealing with Hürthle cell neoplasm to exclude the Hürthle cell (oncocyctic) variant of thyroid papillary carcinoma, by careful observation of the nuclear features of papillary carcinoma. In those suspected cases of Hürthle cell variant of papillary carcinoma, further immunohistochemistry can be useful adjunctive studies.¹⁴ None of our cases showed cytomorphic features of papillary carcinoma.

Roles of Frozen Section, Molecular Techniques, and Ultrasonography

The utilization of intraoperative frozen section was investigated for diagnosing Hürthle cell neoplasm, but the diagnostic value was limited.⁴ None of our cases had intraoperative frozen section consultation.

The contribution of recent molecular diagnostic techniques appears promising as ancillary studies,^{13,15} but has not been emerged yet as a handy and practical approach in many institutions around the world.

The role of ultrasound to predict risk of malignancy has been investigated. Presence of predominantly solid nodule with ill-defined outlines, hypoechogenicity and increased intra-nodular vascularity are ultrasonographic features, suggestive of malignancy.¹¹ The role of ultrasound is further complicated if the patient has a multinodular goiter in one or both lobes, as the differential diagnosis will include also hyperplastic dominant nodule. Multinodular goiter is relatively common in our region;¹⁶ therefore, preoperative ultrasonography was not helpful in most cases of our series.

Management

Hürthle cell carcinoma of the thyroid gland, which is both radioresistant and responds poorly to chemotherapy, should be treated with total thyroidectomy. In addition to total thyroidectomy, the Delphian, ipsilateral perithyroidal and central neck nodes should be excised. Patients with micro- or macrometastases in the regional lymph nodes are treated with a modified radical neck dissection. Post-operatively, suppressive doses of thyroid hormone should be administered because most THCC have thyrotropin receptors and produce thyroglobulin.^{17,18}

Conclusion

We believe that the combined approach involving clinical parameters such as age of the patient and size of the thyroid tumour nodule, in addition to FNAC, and ultrasonographic studies, will allow the surgeon to customize the management plan for each case. The histopathologic examination can give rise to a definitive subtyping for such uncommon thyroid tumours, and the surgeon can plan proper management for each case.

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Conflict of interest

None declared.

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Ethical approval

Ethical approval waived

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