

CASE REPORT

Hurthle cells in fine needle aspiration cytology of the thyroid: a potential diagnostic dilemma?

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Abstract

Hurthle cells are not uncommonly encountered in thyroid fine needle aspiration cytology (FNAC) smears. They are easily recognized by their distinct cytomorphology in cytological preparations, i.e. large, polygonal cells displaying uniform, rounded nuclei, often prominent nucleoli and abundant granular cytoplasm. Hurthle cells can be seen in both non-neoplastic and neoplastic thyroid lesions which can pose diagnostic dilemma to cytopathologists, especially when the lesions are focally sampled. We describe a case of solitary thyroid nodule in a 46-year-old male, whose aspirates comprised predominantly of Hurthle cells exhibiting nuclear features suspicious of papillary carcinoma, which turned out to be Hurthle cell carcinoma on subsequent histological sections. The potential diagnostic pitfalls of Hurthle cell lesions and associated conditions in thyroid FNA are discussed. The presence of Hurthle cell change in a wide variety of thyroid lesions can be diagnostically challenging. However, accurate diagnosis can still be made with careful observation of the predominant cell population, nuclear features and whether there is abundant colloid or lymphocytes in the background.

Keywords: Hurthle cells, thyroid, diagnostic pitfalls, fine needle aspiration

INTRODUCTION

Hurthle (oncocytic) cells are not uncommonly encountered in day-to-day practice of a cytopathologist. They are characterised by their uniform round nuclei, often with prominent central nucleoli and abundant granular, mitochondrial-rich cytoplasm.¹ Despite the ease of recognising these groups of cells on routine cytology smears, they can pose substantial diagnostic challenge to cytopathologists given the wide range of differential diagnosis with their presence, which varies from non-neoplastic to neoplastic conditions.² Histopathological examination of the entire lesion remains the gold standard for precise diagnosis.³

We describe a case of a 46-year-old male with a solitary thyroid nodule, whose aspirates comprised predominantly of Hurthle cells exhibiting nuclear features suspicious of papillary carcinoma, which turned out to be Hurthle cell carcinoma on subsequent histological sections. The potential diagnostic pitfalls of Hurthle cell lesions and associated conditions in thyroid FNA are discussed.

CASE REPORT

This is a case of a 46-year-old gentleman, who presented with a six-month history of gradually enlarging right thyroid nodule. He was clinically euthyroid. Physical examination revealed a six-centimetre, firm, non-tender solitary right thyroid nodule. It was fixed to the underlying tissue. Ultrasound of the nodule showed absence of halo sign, with mixed echogenicity and minimal calcification, suggestive of an underlying malignancy.

Pathological findings

FNA of the nodule showed an exclusive population of Hurthle cells arranged in cohesive sheets and loose clusters (Fig. 1a). The cells displayed nuclear enlargement with pale, powdery chromatin pattern with pin point nucleoli. Nuclear grooves were occasionally present (Fig. 1b). Obvious intranuclear pseudoinclusions were not identified. Inspissated colloid material was seen in the background. A differential diagnosis of oncocytic variant of papillary carcinoma and

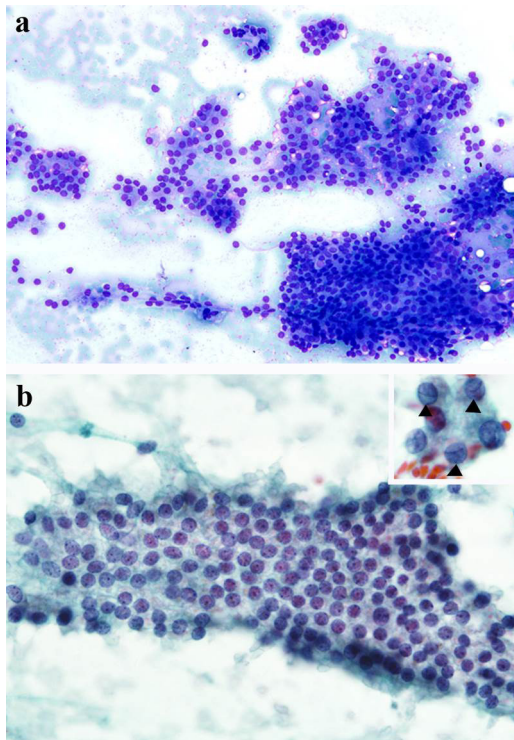


FIG. 1 Cytology smears. (a) Cellular smear comprising an exclusive population of neoplastic Hurthle cells arranged in loose cohesive sheets and clusters (MGG, x200). (b) The cells display nuclear enlargement with pale, powdery chromatin pattern, pin point nucleoli and abundant cytoplasm (Pap, x600). Inset shows nuclear grooves (arrow head) (Pap, x1000).

a follicular neoplasm, Hurthle cell type was made.

Right hemithyroidectomy was subsequently performed. Serial sections revealed an encapsulated, solid yellowish mass within the parenchyma measuring 55 mm in largest dimension. Microscopically, the mass comprised of sheets of neoplastic Hurthle cells arranged predominantly in trabecular pattern (Fig. 2a). In areas, follicular and insular patterns were also present. The malignant cells displayed uniform round to oval nuclei, inconspicuous nucleoli and abundant eosinophilic cytoplasm. Nuclear grooves and intranuclear pseudoinclusions were infrequently seen (Fig. 2b). Multifocal capsular and extensive vascular invasions were also noted. Immunohistochemically, the malignant cells were negative for CK19 (Fig. 2c) and affirmed the final histological diagnosis of follicular carcinoma, oncocyctic variant.

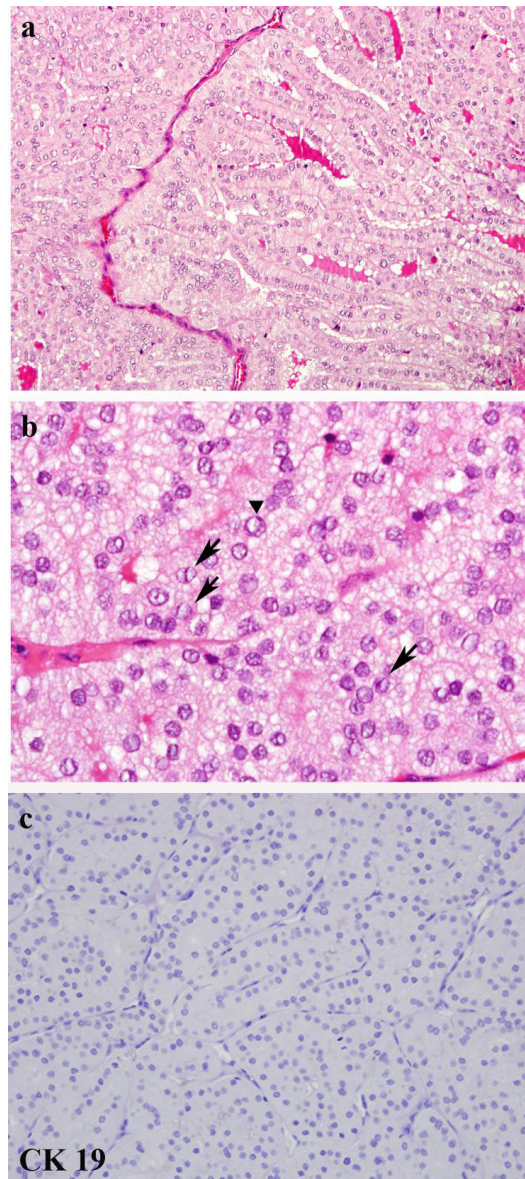


FIG. 2 Histological sections. (a) Sheets of neoplastic Hurthle cells arranged predominantly in a trabecular pattern (H&E, x200). (b) The neoplastic cells display fairly uniform, round pale nuclei with abundant eosinophilic cytoplasm. Nuclear grooves (arrows) and intranuclear pseudoinclusions (arrow head) were rarely seen (H&E, x600). (c) Immunohistochemically, the neoplastic cells display CK19 negativity (CK 19, x200).

DISCUSSION

Follicular-derived thyroid cells with abundant eosinophilic cytoplasm were first described in 1898 by a German Pathologist, Max Askanazy. Four years previously, similar-appearing cells of

parafollicular C cell in origin had been reported by his compatriot Karl Hurthle, whose name continues to be associated with these cells and their neoplasms.³

Hurthle cells can be present in a wide variety of thyroid lesions ranging from merely hyperplastic to malignant neoplastic lesions.² This include non-neoplastic conditions e.g. Hashimoto thyroiditis, multinodular goiter with Hurthle cell metaplasia and neoplastic conditions e.g. Hurthle cell neoplasm (Hurthle cell adenoma and carcinoma), variants of papillary carcinoma as well as oncocyctic variant of medullary thyroid carcinoma.² Rare metastatic malignancies to the thyroid particularly renal cell carcinoma should be considered in the differential diagnosis of a thyroid nodule in the right clinical context.

Diagnosis of Hashimoto thyroiditis (HT) in FNA is usually straightforward. In HT, a mixed heterogeneous population of lymphoid infiltrate is the prominent feature, with variable amount of Hurthle cells depending on chronicity of the disease state.² Gayathri *et al*⁴ reported a false-positive case of HT mistakenly diagnosed as Hurthle cell neoplasm (HCN) in a Hurthle cell-rich smear with scanty lymphocytes in the background. Potential sampling error can be minimised by improving sampling techniques with on-site immediate evaluation for sample adequacy and at least two passes per nodule in view of the heterogeneous nature of the lesions.⁵

Likewise, in a multinodular goitre with Hurthle cell metaplasia, Hurthle cells usually present as a minor constituent. One should carefully look for the presence of macrofollicular fragments with abundant thick and thin colloid in the background characteristically seen in colloid nodule. Some may find the presence of foamy and haemosiderin-laden macrophages useful.

In aspirates where the predominant cell population comprises of Hurthle cells, a diagnosis of Hurthle cell neoplasm (HCN) is favoured.² To date, Hurthle cell carcinoma (HCC) is separated from Hurthle cell adenoma (HCA) by the presence of capsular and/or vascular invasion on histological section. A few diagnostic criteria favouring HCC have been suggested, which include either architectural (dyscohesion, crowding) or cytological (small cell dysplasia, large cell dysplasia) abnormalities.⁶ However, the specificity of these criteria for HCC is dubious and not yet recommended for routine practice.

Some variants of papillary carcinoma (tall cell, Warthin-like, oncocyctic variants) potentially

masquerade as HCN. However, papillary carcinoma can be easily excluded by the absence of salient nuclear features, i.e. nuclear enlargement with irregular nuclear contour, powdery chromatin pattern, nuclear grooves and intranuclear pseudoinclusions. Ancillary studies e.g. immunocytochemistry can be performed on cell block material. Typically, papillary carcinoma is immunoreactive for CK19, Galectin-3 and HBME-1, distinguishing them from other differentiated thyroid malignancies.⁷

Neoplastic cells of oncocyctic variant of medullary thyroid carcinoma (MTC) are usually singly dispersed and exhibit plasmacytoid appearance mimicking HCN. One useful observation distinguishing MTC from HCN is the red cytoplasmic granules in MTC as compared to those of HCN which is usually blue with Romanowsky stains.² Also noted is that in MTC, the nucleoli are frequently inconspicuous compared to those in HCN.² In difficult cases, immunocytochemistry markers are useful, with MTC displaying calcitonin immunoreactivity and negativity for thyroglobulin and thyroid transcription factor-1 (TTF-1). The latter two are typically positive in HCN.⁷ Clinical information of a raised serum calcitonin is also valuable in diagnosing MTC.⁸

Similarly, metastatic renal cell carcinoma (RCC) is a 'great mimicker' for HCN in cytology. Classically, the cells of RCC are arranged in sheets or are singly dispersed and have abundant fine cytoplasmic vacuoles. Application of immunocytochemistry panel can be helpful in the right clinical context, since RCC is immunoreactive for CD10 and RCC markers, and is negative for thyroglobulin and TTF-1.²

Conclusion

The presence of Hurthle cell change in a wide variety of thyroid lesions can be diagnostically challenging. However, accurate diagnosis can still be made with careful observation of the predominant cell population, nuclear features and whether there is abundant colloid or lymphocytes in the background.

ACKNOWLEDGMENTS

We are grateful for Professor Dr. Alfred Lam, senior consultant pathologist from Griffith University, Australia for reviewing the case and confirming the histological diagnosis. Technical assistance from the laboratory staff of Universiti Kebangsaan Malaysia Medical Centre is also thankfully acknowledged.

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