Journal of Neonatal Surgery
ISSN (Online): 2226 -0439
Vol. 14, Issue 8s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Traps, Troubles, And Triumphs In A Case Series Of Thyroid Cytology

Seema Goel[1*], Kanak Atri[2], Kangana Sengar[3], Anshu Gupta Devra[4]

[1*]Professor, Department of Pathology, School of Medical Sciences & Research, Sharda University, Greater Noida, Uttar Pradesh, India
[2]Postgraduate student, Department of Pathology, School of Medical Sciences & Research, Sharda University, Greater Noida, Uttar Pradesh, India
[3]Associate Professor, Department of Pathology, School of Medical Sciences & Research, Sharda University, Greater Noida, Uttar Pradesh, India
[4]Professor and Head, Department of Pathology, School of Medical Sciences & Research, Sharda University, Greater Noida, Uttar Pradesh, India

***Corresponding Author:**
Dr Seema Goel
Email ID: drseemagoel222@gmail.com

Cite this paper as: Seema Goel, Kanak Atri, Kangana Sengar, Anshu Gupta Devra, (2025) Traps, Troubles, And Triumphs In A Case Series Of Thyroid Cytology. *Journal of Neonatal Surgery*, 14 (8s), 990-994.

Abstract
Background: Fine-needle aspiration cytology (FNAC) is a widely employed tool for evaluating thyroid lesions, giving high sensitivity and specificity. However, cytologic-histopathologic discordance can occur due to overlapping cytomorphologic features and interpretative challenges, likely affecting patient management.
Methods: This case series presents three challenging cases of thyroid lesions where FNAC results were at variance with subsequent histopathologic diagnoses. Each case was examined for cytological features, sampling adequacy, radiologic correlation, and clinical findings to identify sources of diagnostic discrepancies.
Results: Case 1 involved a thyroid nodule diagnosed as benign on FNAC but later confirmed as papillary thyroid carcinoma on histopathology. Case 2 presented as a benign colloid nodule with cystic changes, which histopathologic examination revealed as follicular variant of papillary thyroid carcinoma. Case 3 was initially classified as suspicious for malignancy on FNAC but was confirmed as a benign adenomatous nodule postoperatively. The discordance in these cases resulted from overlapping cytological features, inadequate sampling, and interpretative variability.
Conclusion: FNAC remains an important first-line diagnostic modality for thyroid lesions; however, cytologic-histopathologic discrepancy highlights the limitations of relying solely on cytology. A multimodal approach including clinical correlation, radiologic evaluation, and, when necessary, repeat FNAC or molecular testing can improve analytical accuracy. Cognizance of potential pitfalls in cytological interpretation is essential to reduce errors and enhance patient management

INTRODUCTION

Thyroid nodules are a frequent clinical finding, with a reported prevalence of 4%–7% in the general population. Their incidence increases with iodine deficiency and age . FNAC is the primary diagnostic tool for evaluating thyroid nodules, differentiating benign and malignant lesions, and guiding clinical management. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has standardized FNAC reporting, enhancing diagnostic reliability and ensuring a uniform approach to thyroid cytopathology [1,2].
Despite FNAC's high sensitivity (97%–99%) and specificity (72%–100%), it has some limitations like cytomorphologic overlaps, sample adequacy issues, and interobserver variability [3,4]. Certain histological subtypes, such as follicular-patterned lesions and oncocytic tumors, present considerable diagnostic challenges due to their overlapping cytological features. These challenges can lead to FNAC-histopathology discordance, where cytological features do not correlate with final histopathological diagnosis.
In this case series, we present three instances of FNAC-histopathology discordance to illustrate these diagnostic challenges. These cases emphasize the importance of meticulous cytological assessment, comprehensive sampling, and close histopathological correlation. Addressing these challenges is vital for improving diagnostic accuracy and promoting better patient management.

Case 1.
Hurthle Cell Adenoma Misclassified as Suspicious for Papillary Carcinoma
Clinical Presentation:
A 35-year-old female presented with a progressively enlarging midline thyroid swelling. On physical examination, a firm, non-tender nodule was palpated in the right thyroid lobe. Ultrasonography (USG) revealed a hypoechoic lesion with irregular margins, raising suspicion for malignancy.

Cytology Findings:
Fine-needle aspiration cytology (FNAC) yielded hypocellular smears composed of follicular cells exhibiting occasional oncocytic changes. Some nuclei demonstrated mild elongation with occasional intranuclear inclusions. (Figure 1a,1b) Given these nuclear changes, which suggested papillary thyroid carcinoma (PTC), the case was classified as Bethesda V (suspicious for malignancy) [1,2].

Histopathology Findings:
Right thyroid lobectomy showed an encapsulated follicular-patterned tumor composed of large polygonal cells with abundant eosinophilic cytoplasm and prominent nucleoli. Psammoma-like calcifications without lamination are noted in the lumen of few follicles were present, but no sign of capsular or vascular invasion was noted. (Figure 1c, 1d) These findings confirmed a diagnosis of Hurthle cell adenoma [3,4].

DISCUSSION
The misclassification in this case arose from oncocytic changes and nuclear alterations that mimicked features of PTC. Hurthle cell neoplasms often reveal prominent nucleoli and eosinophilic cytoplasm, leading to diagnostic pitfalls, particularly in paucicellular cases The presence of intranuclear inclusions further contributed to the misdiagnosis. Adequate sampling is critical to distinguish Hurthle cell adenomas from malignancies and avoid unnecessary surgical intervention [5,6]. Awareness of oncocytic features and their overlap with PTC-like nuclear changes is essential for enhancing diagnostic accuracy. [7,8]

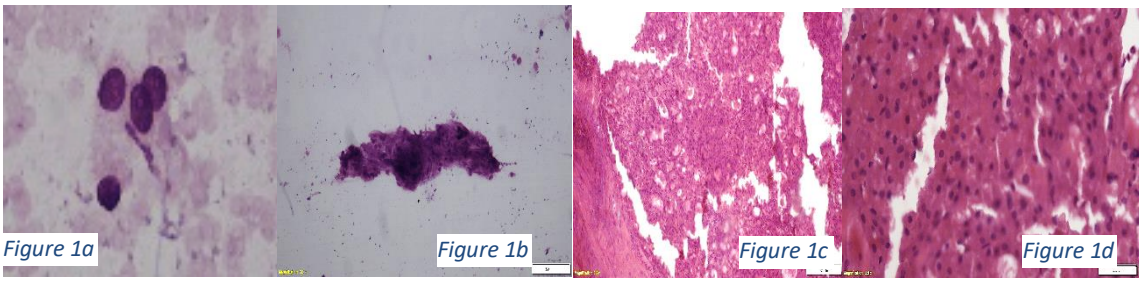

Figure 1: (a) &b MGG 400X: elongated nuclei with intranuclear inclusions; papillary cluster of tumor cells (c)& (d) H&E 100X, 400X respectively: Hurthle cell adenoma

Case 2
Follicular Variant of Papillary Carcinoma Misclassified as Colloid Nodule
Clinical Presentation:
A 47-year-old female presented with a constant right-sided thyroid swelling for over a year. Ultrasonography (USG) revealed a cystic lesion with internal echoes and colloid components

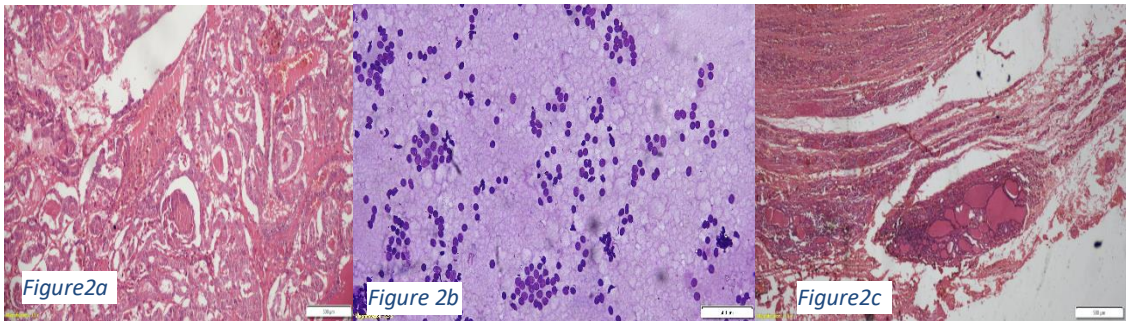

Figure 2: (a) MGG 400X; benign looking follicular epithelial cells (b) H&E 100X: capsular invasion (C) H&E 400X: follicular variant of papillary thyroid carcinoma.

Cytology Findings: Fine-needle aspiration cytology (FNAC) smears were sparsely cellular, displaying benign follicular epithelial cells, colloid, and numerous hemosiderin-laden macrophages. Based on these findings, the case was classified as Bethesda II, suggesting a benign colloid nodule with cystic changes. (Figure 2a)

Histopathology Findings:

Subsequent lobectomy measuring 4X4X2.5cm revealed a follicular-patterned tumor with nuclear inclusions, grooves, and occasional optically clear nuclei (Orphan Annie eye appearance). Few micropapillae were identified Capsular and vascular invasion identified. (Figure 2b,2c) which confirmed the diagnosis of follicular variant of papillary thyroid carcinoma (FVPTC).

DISCUSSION

The misdiagnosis resulted from the paucicellular aspirate and cystic degeneration, which masked the nuclear features characteristic of FVPTC. Cystic changes in thyroid lesions can obscure diagnostic cells, reducing FNAC sensitivity. [8,9] Recognizing subtle nuclear alterations, such as clearing, grooves and inclusions, is vital in cystic thyroid lesions to avoid misclassification. The diagnostic accuracy of FNAC can be improved through ultrasound-guided sampling and repeated aspiration in cases with inconclusive or paucicellular specimens. These measures upgrade the detection of nuclear features essential for differentiating FVPTC from benign lesions[1,2].

Case 3

Clinical Presentation:

A 32-year-old male came with a midline neck swelling that had persisted for six months. To diagnose the lesion, an ultrasound-guided fine-needle aspiration cytology (FNAC) was performed.

Cytology Findings:

The FNAC smears were hypercellular, displaying overlapping follicular cells arranged in microfollicles, mild to moderate anisonucleosis, and the presence of few macrophages andcolloid material. Based on these cytomorphologic features, the case was classified as Bethesda Category IV, indicating a follicular neoplasm. (Figure 3a)

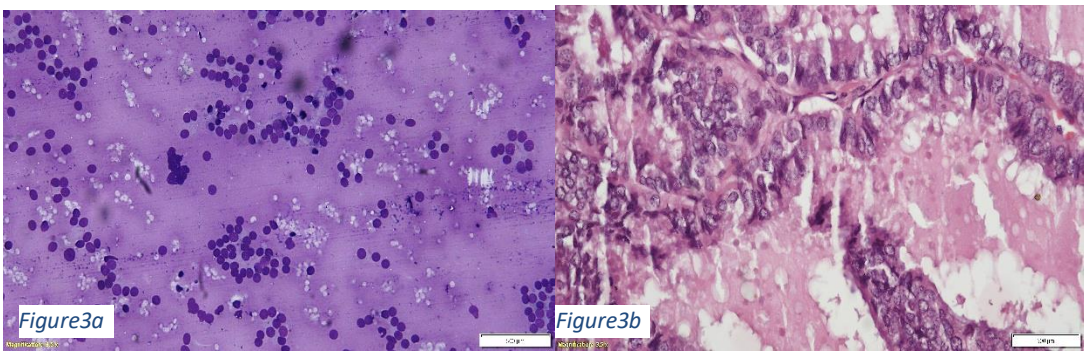

Figure 2: (a) MGG 400X; follicular neoplasm (b) H&E 400X: follicular variant of papillary thyroid carcinoma

Histopathology Findings:

A right hemithyroidectomy measuring 7X5X5cm was subsequently performed, revealing a well-encapsulated tumor with a follicular architectural pattern. Notably, the tumor revealed nuclear features characteristic of papillary thyroid carcinoma (PTC), such as nuclear grooving and optically clear nuclei. The presence of micropapillae, psamomma bodies, microcalcifications and focal capsular invasion led to the definitive diagnosis of encapsulated follicular variant of papillary thyroid carcinoma (FVPTC). (Figure3b). No angioinvasion or extrathyroidal extension seen

DISCUSSION

The encapsulated follicular variant of papillary thyroid carcinoma (FVPTC) presents considerable diagnostic challenges, particularly in distinguishing it from follicular adenomas or other benign follicular lesions. FNAC, although valuable, has limitations in differentiating between benign and malignant follicular-patterned tumors due to overlapping cytological features. The Bethesda System for Reporting Thyroid Cytopathology categorizes such indeterminate findings, with Category IV (follicular neoplasm/suspicious for follicular neoplasm) carrying an overall 15-30%. malignancy risk. However, definitive diagnosis often requires histopathological examination to search for capsular and vascular invasion, which are crucial for confirming malignancy. [10,11]

In this case, the FNAC findings led to a Bethesda IV classification, requiring surgical intervention. Histopathological analysis exhibited the encapsulated nature of the tumor with characteristic nuclear features of PTC and evidence of capsular invasion, confirming the diagnosis of encapsulated FVPTC. This emphasises the importance of thorough histopathological evaluation in cases where FNAC results are indeterminate.

The reclassification of non-invasive encapsulated FVPTC as non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is an effort to more accurately group tumors with low malignant potential, thereby reducing overtreatment. However, in cases with capsular invasion, as observed here, the label of carcinoma remains appropriate due to the accompanying risk of recurrence and metastasis.[12]

CONCLUSION

To enhance diagnostic accuracy, awareness and attention to nuclear features during cytological evaluation is essential. In addition, molecular testing for mutations, such as RAS or BRAF, can aid in distinguishing between benign and malignant follicular-patterned lesions. Thorough sampling and careful analysis of the tumor capsule are imperative to identify any invasion, thereby guiding appropriate clinical management and reducing the chances of misclassification.

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