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(CASE REPORT)

A TI-RADS 5 thyroid nodule with repeat Bethesda III cytology and final diagnosis of classic papillary thyroid carcinoma: A case report

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Abstract

Background: Bethesda category III thyroid nodules remain a diagnostic challenge because the risk of malignancy is intermediate and management should not rely on cytology alone. Ultrasound risk stratification is particularly important when cytological findings are discordant or persistently indeterminate.

Case presentation: We report the case of a 50-year-old woman presenting with swallowing discomfort. Thyroid ultrasound demonstrated a highly suspicious right thyroid nodule classified as ACR TI-RADS 5, together with a suspicious right level IV cervical lymph node. Initial fine-needle aspiration (FNA) of the thyroid nodule showed nodular hyperplasia, whereas repeat FNA after follow-up yielded Bethesda III cytology. Because of the persistently high-risk ultrasound appearance, the patient underwent total thyroidectomy with central neck dissection. Histopathology confirmed classic papillary thyroid carcinoma, while the dissected lymph nodes were inflammatory.

Conclusion: This case highlights the importance of integrating ultrasound findings, repeat cytology, and clinical judgment in the management of Bethesda III thyroid nodules. A benign or indeterminate FNA result does not exclude malignancy when sonographic features are strongly suspicious.

Keywords: Bethesda III; Atypia of Undetermined Significance; Thyroid Nodule; TI-RADS 5; Papillary Thyroid Carcinoma

1. Introduction

Thyroid nodules are common in adults, and only a minority are malignant. Ultrasonography is the main imaging modality for thyroid nodule evaluation because it is widely available, noninvasive, and effective for risk stratification and selection of nodules for fine-needle aspiration (FNA) [1-3]. Over the last decade, structured ultrasound classification systems and standardized cytopathology reporting have substantially improved the management of thyroid nodules.

The Bethesda System for Reporting Thyroid Cytopathology provides a standardized framework for interpreting thyroid FNA results and estimating the associated risk of malignancy [4,5]. Bethesda category III, currently termed atypia of undetermined significance (AUS), remains one of the most problematic categories in clinical practice because it represents a heterogeneous group of lesions with variable biologic behavior and an intermediate risk of malignancy [4,5]. Current international guidelines recommend individualized management for such nodules, including repeat FNA, surveillance, molecular testing, or diagnostic surgery depending on the ultrasound pattern, clinical risk factors, and local resources [1-3].

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Among indeterminate nodules, the role of ultrasound becomes especially important. Suspicious sonographic features such as marked hypoechogenicity, irregular margins, microcalcifications, and extrathyroidal contact increase the likelihood of malignancy and may justify more aggressive intervention even when cytology is benign or indeterminate [1-3,6]. Therefore, discordance between cytology and ultrasound findings should prompt careful reassessment rather than reassurance based on cytology alone [1-3,6].

We report a case of a highly suspicious thyroid nodule categorized as ACR TI-RADS 5, with an initial benign FNA result, repeat Bethesda III cytology, and final postoperative diagnosis of classic papillary thyroid carcinoma. This case underscores the importance of integrated decision-making in the management of indeterminate thyroid nodules.

2. Case presentation

A 50-year-old woman presented with a complaint of swallowing discomfort. She had no documented history of previous thyroid surgery, neck irradiation, or familial thyroid carcinoma.

Neck ultrasonography revealed a solid hypoechoic nodule in the upper pole of the right thyroid lobe, measuring 24 × 14 mm, with irregular margins, close contact with both the anterior and posterior thyroid capsule, multiple punctate echogenic foci suggestive of microcalcifications, and coarse calcification; Doppler examination showed no internal vascularity (Fig. 1). Based on the 2017 American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS), the lesion was classified as TI-RADS 5, indicating a highly suspicious thyroid nodule. Ultrasonography also demonstrated a right level IV cervical lymph node posterior to the carotid sheath, with loss of the fatty hilum and multiple internal echogenic foci, raising concern for nodal metastasis (Fig. 2).

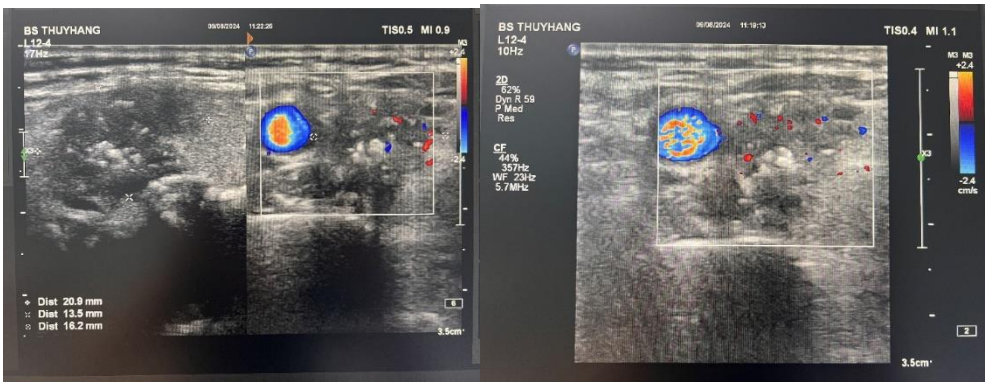

Figure 1 Ultrasound of the right thyroid lobe showing a solid hypoechoic nodule with irregular margins, punctate echogenic foci, and coarse calcification, categorized as ACR TI-RADS 5

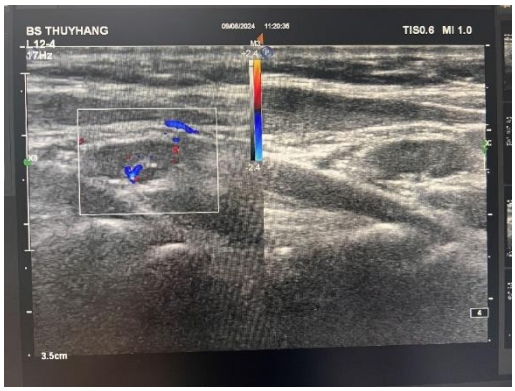

Figure 2 Ultrasound of the right level IV cervical lymph node showing loss of the fatty hilum and internal echogenic foci

Ultrasound-guided fine-needle aspiration (FNA) of the thyroid nodule and the cervical lymph node was performed. The initial cytology result of the thyroid nodule was reported as nodular hyperplasia, whereas the cervical lymph node was

interpreted as inflammatory. Because the sonographic pattern remained highly suspicious despite the non-malignant cytology result, the patient was scheduled for short-interval follow-up.

At 3-month reassessment, repeat ultrasound showed no significant interval change in the size or suspicious morphology of the thyroid nodule or the right cervical lymph node. In view of the persistent high-risk ultrasound pattern, repeat ultrasound-guided FNA was undertaken. Cytology of the thyroid nodule demonstrated atypical follicular cell groups with both architectural and nuclear atypia, corresponding to Bethesda category III (atypia of undetermined significance, AUS). The repeat aspirate from the cervical lymph node again showed inflammatory change without cytological evidence of metastasis.

Given the discordance between the persistently suspicious ultrasound findings and the indeterminate cytology, surgical treatment was recommended. The patient underwent total thyroidectomy with central neck dissection. Histopathological examination confirmed classic papillary thyroid carcinoma, while the resected lymph nodes showed inflammatory changes without metastatic involvement. The postoperative course was uneventful, and the patient was referred for endocrinology and oncologic follow-up.

3. Discussion

This case demonstrates a clinically important challenge in thyroid nodule management: a nodule with persistently high-risk ultrasound features, an initial benign FNA result, repeat Bethesda III cytology, and final confirmation of classic papillary thyroid carcinoma. Such cases illustrate the limitations of relying on cytology alone and support a more integrated approach combining ultrasound, repeat sampling, and clinical judgment [1-5].

Bethesda III is widely recognized as one of the most difficult cytologic categories because it includes a heterogeneous group of lesions that do not meet definitive criteria for either benignity or malignancy [4,5]. In the updated Bethesda system, this category remains associated with an intermediate but variable risk of malignancy, influenced by institutional thresholds, operator technique, cytopathologist experience, and whether certain borderline lesions such as NIFTP are considered malignant [4,5]. For this reason, Bethesda III should not be interpreted as a uniform diagnostic or management category [4,5,7].

In our patient, the ultrasound phenotype was highly suspicious from the outset. The lesion was solid, hypoechoic, irregular, and associated with punctate echogenic foci and coarse calcification. These features are classically associated with papillary thyroid carcinoma and are incorporated in major risk stratification systems such as ACR TI-RADS and ATA sonographic patterns [1-3,6]. Current international guidelines emphasize that when cytology and ultrasound findings are discordant, especially in a highly suspicious nodule, clinicians should not rely on a single reassuring cytology result [1-3]. Instead, further evaluation is warranted.

The initial benign FNA result in this case most likely reflected sampling limitations. False-negative FNA results may occur because of suboptimal sampling, partial calcification, intranodular heterogeneity, or focal malignant transformation within a larger lesion [4,5]. This explains why a benign cytology result may occasionally coexist with a highly suspicious ultrasound appearance. In such situations, repeat FNA is recommended by several guidelines and remains a practical next step in many clinical settings [1-3,8].

Repeat FNA in our patient yielded Bethesda III cytology with both architectural and nuclear atypia. This finding carries more weight than a nonspecific indeterminate result because several studies have shown that AUS with nuclear atypia is associated with a higher malignancy risk than AUS with isolated architectural atypia [4,5,7]. Yoo et al. reported that the malignancy rate of Bethesda III nodules varies substantially when both ultrasound risk stratification and cytological subtype are taken into account, and that combining these parameters improves decision-making [7]. Similarly, more recent work has confirmed that integration of cytologic subcategory, nodule size, and sonographic suspicion can better identify which Bethesda III nodules should proceed to surgery [9,10].

This case also underscores the central role of ultrasound after an indeterminate cytology result. Ultrasound is not simply a tool for selecting nodules for biopsy; it continues to influence management after FNA. Ahmadi et al. demonstrated that ATA and ACR TI-RADS classifications can serve as adjunctive predictors of malignancy in indeterminate thyroid nodules [6]. Other studies have also shown that combining repeat FNA with ultrasound-based risk stratification provides a more robust estimate of malignancy risk than repeat FNA alone [9,10]. In practical terms, a TI-RADS 5 nodule with repeat AUS should be approached more cautiously than a low-suspicion nodule with the same cytologic diagnosis.

Molecular testing has become an increasingly important adjunct in the management of indeterminate thyroid nodules, particularly Bethesda III and IV lesions [11-13]. Commercial tests such as Afirma GSC and ThyroSeq v3 may help identify nodules suitable for surveillance or surgery, especially in healthcare systems where these platforms are available and validated [11-13]. However, their usefulness depends on access, cost, local cancer prevalence, and clinical context. In resource-limited settings, repeat FNA and careful ultrasound reassessment remain more feasible than routine molecular testing [2,3,8]. In the present case, surgery was selected without molecular analysis because the persistently high-risk imaging pattern and repeat indeterminate cytology already supported a substantial suspicion of malignancy.

Another interesting aspect of this case is the suspicious cervical lymph node. On ultrasound, loss of the fatty hilum and internal echogenic foci may suggest nodal metastasis in patients with papillary thyroid carcinoma. However, inflammatory or reactive nodes can sometimes mimic malignant features on imaging. In our patient, both cytology and final pathology showed inflammatory change rather than metastatic involvement. This emphasizes the need for pathologic confirmation whenever possible before extending surgical management based solely on nodal ultrasound findings.

The final diagnosis of classic papillary thyroid carcinoma validates the decision to proceed with thyroidectomy. More importantly, this case supports a broader clinical message: a benign initial FNA or even repeat Bethesda III cytology does not exclude malignancy when the ultrasound pattern remains strongly suspicious [1-3,6,7,9,10]. In such cases, the overall integrated risk profile should guide management. Delayed intervention based on cytology alone may postpone definitive diagnosis and treatment.

Overall, this case highlights the need for individualized management of Bethesda III thyroid nodules. While many such nodules can be safely monitored, a subset with persistent high-risk sonographic features warrants a lower threshold for diagnostic or therapeutic surgery. This principle is particularly relevant in routine practice, where molecular testing may be unavailable and clinicians must rely on repeat cytology, imaging, and careful clinical judgment [1-3,8,11].

4. Conclusion

This case illustrates that a highly suspicious thyroid nodule may ultimately prove malignant despite an initial benign FNA result and repeat Bethesda III cytology. Management of Bethesda III thyroid nodules should not rely on cytology alone. Instead, ultrasound risk stratification, repeat FNA findings, and clinical judgment should be integrated to guide treatment decisions. In nodules with persistent TI-RADS 5 features, surgical management may be justified even when cytology remains indeterminate.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

Ethical approval was waived for this single case report according to institutional policy, provided that patient anonymity was preserved.

Statement of informed consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

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