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## Diagnostic Dilemma Of Follicular Tumor Of Unknown Malignant Potential: A Rare Case Report With Review Of Literature.

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### ABSTRACT

Thyroid cancer is one of fast-growing cancer with a female preponderance. The investigation of choice in a patient who present with a thyroid nodule is Fine Needle Aspiration Study (FNAC) along with Ultrasound and TSH profile. A major limitation of fine needle aspiration is its inability to distinguish a follicular adenoma from a follicular carcinoma as it is differentiated based on presence or absence of capsular/vascular invasion. Follicular cell-derived neoplasms are categorized into benign tumors, low-risk neoplasms, and malignant neoplasms according to 2022 WHO classification of Endocrine and neuroendocrine tumors. Tumors of UMP are described as “well-differentiated thyroid tumors with follicular architecture that can be encapsulated or unencapsulated but well-circumscribed, and invasion remains questionable after thorough sampling and exhaustive examination”. We present here a case of 60-year-old female with neck swelling who was cytologically diagnosed with atypia of undetermined significance and on microscopic examination was reported as Follicular Tumor of Undetermined potential. We present this case due to its rarity and prognostic significance. Absence of unequivocal capsular/vascular invasion as in this patient provides a better prognosis and increased survival rate compared to other follicular tumors.

**Keywords:** Atypia of undetermined significance, Follicular tumor of unknown malignant potential, thyroidectomy.

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## INTRODUCTION

Thyroid cancer currently ranks as the 13th most common cancer diagnosis overall and the 6th most common among women [1]. Globally, in 2020, the age-standardized incidence rates of thyroid cancer were 10.1 per 100 000 women and 3.1 per 100 000 men [2]. Among the major histologic types, almost 90% are papillary thyroid carcinomas (PTC), 4% follicular thyroid carcinomas (FTC), 2% Hürthle-cell carcinomas, 2% medullary thyroid carcinomas (MTC), and 1% anaplastic thyroid carcinomas (ATC) [3].

The investigation of choice in a patient who present with a thyroid nodule is Fine Needle Aspiration Study (FNAC) along with Ultrasound and TSH profile. A major limitation of fine needle aspiration is its inability to distinguish a follicular adenoma from a follicular carcinoma as it is differentiated based on presence or absence of capsular/vascular invasion. Some patients with a follicular adenoma or follicular carcinoma may show smears that consist of follicular cells with abnormal architecture and atypia that is more significant than usually seen with benign lesions but not sufficient enough to label it a follicular neoplasm. According to the Bethesda classification system, these patients are as having “atypia of undetermined significance” (AUS) [4]. Whereas there are other cases where cytological figures are strongly suspected of malignancy but not sufficient enough for a conclusive diagnosis. They have higher suspicion of malignancy than AUS but lower than malignant. They are reported as suspicious for malignancy (SM) Bethesda category V. Risk of malignancy is 60-80% and management is usually lobectomy [5]. Follicular cell-derived neoplasms are categorized into benign tumors, low-risk neoplasms, and malignant neoplasms according to 2022 WHO classification of Endocrine and neuroendocrine tumors. Tumors of UMP are described as “well-differentiated thyroid tumors with follicular architecture that can be encapsulated or unencapsulated but well-circumscribed, and invasion remains questionable after thorough sampling and exhaustive examination”.

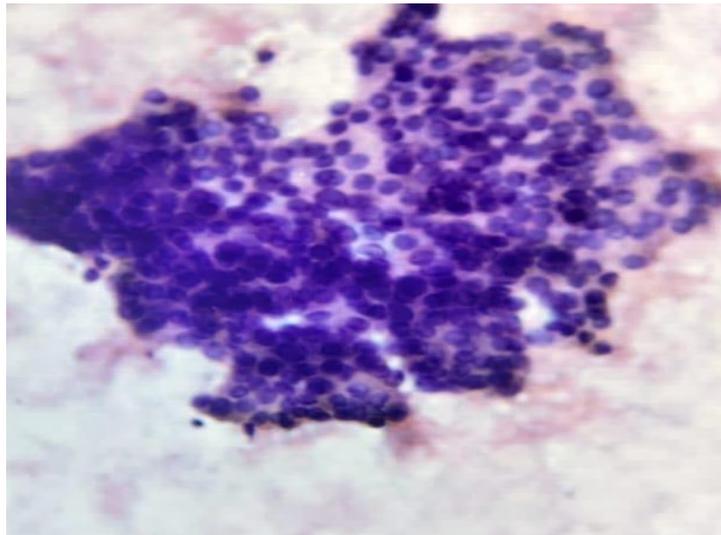
### Case report

A 60-year-old female attended surgery outpatient department of our hospital with a 1-month history swelling in the front part of the neck. On examination, there was a swelling in the anterior part of the neck more on the right side which moves on deglutition. USG neck of the right lobe showed a well-defined nodule measuring about 4x1cm without calcification with TIRADS 2 score. Left lobe showed a hypoechoic nodule measuring 1.7x1.6 mm with peripheral calcification with TIRADS 4 score. Fine needle aspiration cytology (FNAC) was suggestive of “Suspicious of malignancy” (BETHESDA CATEGORY V) (Figure 1). The patient underwent total thyroidectomy and the specimen was sent to our department of pathology for histopathological examinations. Thorough grossing of the specimen was done according to College of American Pathologists (CAP) protocol. On cut section of the right lobe, it was spongy brownish in color. One white solid nodule was seen in the upper pole measuring about 1 cm in max dimension. On cut section of the left lobe, a whitish nodule was found measuring 1.8 cm in max dimension (Figure 2). Routine tissue processing was done, hematoxylin and eosin slides were prepared and examined under the microscope. Microscopic examination showed presence of normal thyroid parenchymal tissue along with tumor tissue showing the following features: There was a thick capsule. Follicular cell predominantly arranged in fetal and trabecular pattern. Focal areas showed high cellularity, nuclear pleomorphism and mitotic figures. Secondary changes such as hemorrhage calcification and inflammatory cells also seen. Focal areas also showed features suggestive of mushroom shaped capsular invasion (Figure 3). Unequivocal capsular or vascular invasion was not seen. The final diagnosis was given as Follicular tumor of unknown malignant potential (FT-UMP).

## DISCUSSION

The incidence of thyroid cancer has exponentially increased worldwide during the last decade, with thyroid surgery becoming one of the most common surgical procedures mainly due to an increasing use of neck ultrasonography and fine needle aspiration cytology. To ease the communication and understanding between pathologists and clinicians for thyroid nodule treatment, in 2009, The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced which was modified further and the latest modification was done in 2023. TBSRTC 2023 recommends the following as the 6 reporting category names: (i) nondiagnostic; (ii) benign; (iii) atypia of undetermined significance (AUS); (iv) follicular neoplasm; (v) suspicious for malignancy (SFM); and (vi) malignant [6]. Even after the introduction of these criteria, pathologists face challenges in unique cases. In case of SFM, morphology is suspicious but not definitive for a malignant diagnosis as it lacks either qualitative or quantitative morphology [7].

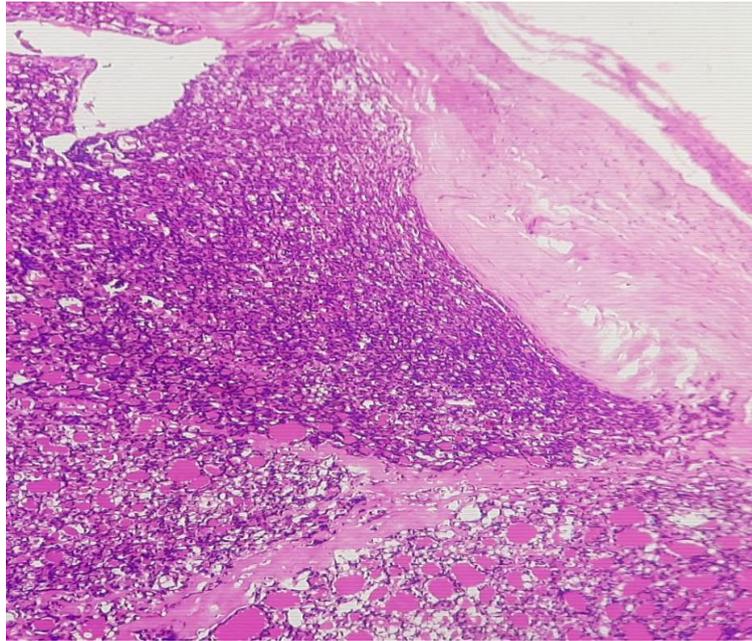
Management is usually thyroidectomy/lobectomy. In our case the patient underwent thyroidectomy and microscopic report revealed Follicular tumor of unknown malignant potential. Thyroid tumors of UMP are classified into two subtypes based on their nuclear alterations: follicular tumor of uncertain malignant potential (FT-UMP) that lacks PTC-like nuclear features (nuclear score of 0–1) and well-differentiated tumor of uncertain malignant potential (WDT-UMP) that has more or less pronounced nuclear features of PTC (nuclear scores of 2–3) [8]. FT-UMP usually have a questionable capsular and / or vascular invasion with equivocal papillary nuclear features. When questionable findings of capsular and/or vascular invasion are detected, it is wise to routinely perform re-examination by deep cut or additional preparations. Most cases are indolent and prognosis is excellent with lobectomy.[8]. A Multi dynamic approach involving imaging characteristics, molecular genetics ,clinical factors ,histopathological diagnosis contributes to management, as a greater understanding of these features can allow for a more organized management approach.



**Figure 1: FNAC smear showing crowded cell cluster with scant colloid and few cells showing nuclear enlargement and membrane irregularities (PAP stain,400x)**



**Figure 2: Gross specimen of thyroidectomy.**



**Figure 3: Showing mushroom shaped capsular invasion of neoplastic thyroid follicular cells (H&E,100X)**

#### CONCLUSION

To conclude, FT-UMP is generally an indolent disease but some cases show distant recurrence. Routine mutational screening in these patients aids in detecting relapse prone tumors. The findings of such mutation could motivate adjuvant treatment modalities and in the absence of such mutation, careful follow up of these patients after surgery is recommended.

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