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HOBNAIL VARIANT OF PAPILLARY THYROID CARCINOMA: A CASE REPORT - CLINICOPATHOLOGICAL FEATURES, HISTOMORPHOLOGY, AND PROGNOSTIC IMPLICATIONS

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ABSTRACT

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy, accounting for approximately 70–85% of all thyroid cancers. Although classical PTC is associated with an excellent prognosis, certain histopathological variants demonstrate aggressive biological behavior and poorer outcomes. The hobnail variant of papillary thyroid carcinoma (HV-PTC) is a rare and aggressive subtype characterized by distinctive cytomorphological and architectural features. This study aims to describe the clinicopathological profile, histomorphological characteristics, immunohistochemical findings, and prognostic significance of the hobnail variant of PTC, based on institutional experience and a detailed case analysis. Clinical history, cytological findings, histopathology, and immunohistochemistry were reviewed. HV-PTC accounted for a small proportion of PTC cases but demonstrated aggressive features including loss of polarity, micropapillary architecture, extrathyroidal extension, and association with adverse molecular alterations such as BRAF and TERT promoter mutations. Recognition of this entity is crucial for accurate diagnosis, prognostication, and optimal patient management.

INTRODUCTION-

Thyroid carcinoma constitutes approximately 1% of all malignancies and contributes to nearly 0.2% of cancer-related deaths worldwide. Among thyroid malignancies, papillary thyroid carcinoma (PTC) is the most common histological type, accounting for nearly 80–85% of cases. PTC typically exhibits an indolent course with excellent long-term survival; however, this favorable prognosis does not uniformly apply to all histological variants.

Several variants of PTC have been recognized in the World Health Organization (WHO) classification, including tall cell, columnar cell, diffuse sclerosing, oncocytic, and hobnail variants. These variants differ significantly in terms of morphology, molecular profile, and clinical behavior. The hobnail variant of papillary thyroid carcinoma (HV-PTC) is a relatively rare subtype, representing approximately 1% of all PTCs, and is associated with a more aggressive clinical course and poorer prognosis compared to classical PTC.

HV-PTC is characterized by a predominance of neoplastic cells exhibiting a "hobnail" appearance, defined by apically placed, bulging nuclei and a loss of cell polarity. Architecturally, tumors frequently display micropapillary patterns, discohesiveness, and increased mitotic activity. Clinically, HV-PTC is often associated with extrathyroidal extension, lymph node metastasis, distant metastasis, and resistance to radioactive iodine therapy.

Given its rarity and aggressive nature, HV-PTC poses diagnostic challenges, particularly on fine-needle aspiration cytology (FNAC). A thorough histopathological examination supplemented with immunohistochemistry and molecular analysis is essential for accurate diagnosis. This article presents a comprehensive analysis of HV-PTC based on institutional data and a detailed case report, highlighting its clinicopathological features and prognostic implications.

AIM AND OBJECTIVES-

AIM:

To study the hobnail variant of papillary thyroid carcinoma and evaluate its clinicopathological, histomorphological, and prognostic features.

Objectives:

- To describe the histomorphological features of HV-PTC
- To correlate cytological, histological, and immunohistochemical findings
- To assess clinical behavior and prognostic significance
- To emphasize the importance of recognizing HV-PTC as an aggressive variant

MATERIALS AND METHODS-

Clinical information was retrieved from the ENT Department of Hi-Tech Medical College and Hospital, Bhubaneswar. Relevant FNAC findings, radiological investigations, surgical pathology specimens, and follow-up data were reviewed. FNAC was performed prior to surgery, and cytological smears were evaluated using the Bethesda System for Reporting Thyroid Cytopathology.

Following surgical excision, specimens were subjected to routine histopathological processing and stained with hematoxylin and eosin (H&E). Immunohistochemical analysis was performed using markers including thyroid transcription factor-1 (TTF-1) and VE-1 antibody for detection of BRAF V600E mutation. Post-operative clinical information was obtained during follow-up visits and telephonic interviews.

RESULTS-

Between 2023 and 2024, a total number of papillary thyroid carcinoma cases were diagnosed at our institution. Among these, one case (approximately 1%) demonstrated hobnail features and fulfilled the diagnostic criteria for HV-PTC. Diagnostic criteria included the presence of hobnail morphology in at least 30% of neoplastic cells, micropapillary architecture, and loss of cellular polarity.

Clinical Findings-

A 42-year-old female patient presented with complaints of weight gain, tremors, and a solitary thyroid nodule measuring approximately 4 cm in diameter. The nodule was firm and

moved with deglutination. The patient had been on medical treatment for hyperthyroidism for five years without significant clinical improvement.

Cytological Findings-

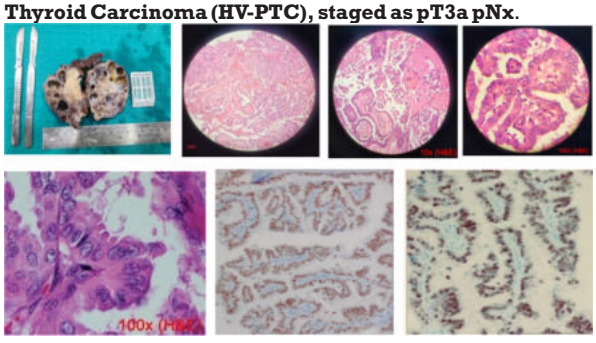
FNAC revealed cytomorphological features suggestive of atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), corresponding to **Bethesda Category III**. Based on these findings, the patient underwent right hemithyroidectomy.

Gross and Histopathological Findings-

Gross examination of the right thyroid lobe revealed a well-encapsulated mass measuring 6.5 × 3.5 × 2 cm with a greyish-brown friable cut surface. Histopathological examination showed features of papillary thyroid carcinoma with hobnail morphology in more than 30% of tumor cells. The tumor displayed micropapillary architecture, discohesiveness, loss of polarity, apically placed bulging nuclei, nuclear grooves, pseudoinclusions, and focal necrosis. Psammoma bodies were also identified.

Immunohistochemistry-

Immunohistochemical analysis demonstrated positivity for TTF-1.VE-1 antibody showed positive staining, indicating the presence of **BRAF V600E mutation**. Based on histopathological and immunohistochemical findings, the tumor was diagnosed as **Hobnail Variant of Papillary Thyroid Carcinoma (HV-PTC), staged as pT3a pNx**.



DISCUSSION-

The hobnail variant of papillary thyroid carcinoma is a distinct and aggressive entity within the spectrum of thyroid malignancies. The hallmark feature of HV-PTC is the predominance of hobnail-shaped cells, characterized by apically placed nuclei and a loss of cell polarity. These cells are often arranged in micropapillary patterns, contributing to the aggressive behavior of the tumor.

Several studies have demonstrated that HV-PTC shares molecular features with poorly differentiated thyroid carcinoma, including frequent mutations in **BRAF, TP53, and TERT promoter genes**. These molecular alterations are associated with tumor aggressiveness, increased recurrence rates, and decreased overall survival. In the present case, immunohistochemistry using VE-1 antibody confirmed the presence of BRAF V600E mutation, supporting the aggressive nature of the tumor.

Clinically, patients with HV-PTC often present with larger tumors, extrathyroidal extension, lymph node involvement, and distant metastasis. Compared to classical PTC, HV-PTC responds poorly to radioactive iodine therapy, further contributing to unfavorable outcomes. FNAC diagnosis can be challenging, as cytological features may overlap with other follicular-patterned lesions, leading to indeterminate Bethesda categories, as observed in the present case.

Accurate recognition of HV-PTC requires meticulous histopathological examination and awareness of its diagnostic criteria. Immunohistochemistry and molecular studies play a supportive role in confirming the diagnosis and guiding risk stratification.

CONCLUSION-

The hobnail variant of papillary thyroid carcinoma is a rare but highly aggressive subtype of PTC with distinct histomorphological and molecular features. Although it represents a small proportion of thyroid cancers, its association with poor prognosis, extrathyroidal extension, and molecular alterations necessitates early recognition and aggressive clinical management. Pathologists should be vigilant in identifying hobnail features, particularly when they constitute more than 30% of tumor cells. Integration of histopathology, immunohistochemistry, and molecular findings is essential for accurate diagnosis and optimal patient care.

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