



CYTOLOGY OF TALL CELL VARIANT OF PAPILLARY THYROID CARCINOMA - A RARE, AGGRESSIVE VARIANT.

Dr. Pradnya Kiran Ladkat*

DNB Gr. II Teacher, Consultant Pathologist, K. B. Bhabha Hospital, Bandra (West), Mumbai *Corresponding Author

Dr. Kalpana Arora

DNB Gr. I Teacher, Consultant Pathologist, K. B. Bhabha Hospital, Bandra (West), Mumbai

Dr. Shalaka Anand Deshpande

Senior Resident, Department Of Pathology, HBTMC And Dr. RN Cooper Municipal General Hospital.

Dr. Yasmeen Khatib

Additional Professor, Department Of Pathology, HBTMC And Dr. RN Cooper Municipal General Hospital. Vile Parle (West), Mumbai.

ABSTRACT

Tall cell Variant of Papillary thyroid carcinoma(TCV-PTC) is a rare and aggressive tumour with more than 30% cells having a height more than 3 times the width with oncocytic change and nuclear features of classical PTC. We present a case of 30 year female who came with a midline neck swelling with bilateral neck nodes of 3 months duration. FNAC showed the cytological features of TCV-PTC. Patient underwent thyroidectomy with neck dissection. The diagnosis of tall cell variant was confirmed on histopathology. One needs to be aware of the cytological features and criteria for the diagnosis of this tumour for optimum management as it has an aggressive course.

KEYWORDS : TCV-PTC, rare, aggressive, height three times the width

INTRODUCTION

Papillary thyroid cancer (PTC) accounts for nearly 90% of all thyroid cancers and has a good prognosis^[1]. It has several variants in addition to classical PTC with variable prognosis^[2]. Cytological features of classical PTC are well documented and include papillary architecture, enlarged nucleus with intranuclear grooves and inclusions with nuclear crowding and overlapping^[3]. Tall cell variant of PTC exhibits these characteristic cytological features along with presence of tall cells with height 3 times the width in at least 30% of the cells, abundant eosinophilic cytoplasm and basally placed nuclei^[4]. FNAC is a reliable tool in the preoperative diagnosis of PTC with accuracy of about 94%.⁵ It is important to identify the cytological features of TCV-PCV on FNAC as it is a more aggressive tumour with extrathyroidal extension and presence of metastasis at the time of presentation.^[6,8] This will lead to better and more aggressive patient management with better outcome. We report the cytological features in a case of TCV-PTC which was confirmed on histopathology.

Case History-

A 30 year female presented with a painless midline neck swelling along with bilateral cervical swellings since 3 months. Ultrasonography of thyroid revealed a heterogenous lesion measuring 2.1×1.5×1cm with few foci of microcalcification. FNAC smears of thyroid swelling showed tumor cells arranged in papillary groups, monolayered sheets with few singly scattered cells.

(fig. 1&2). The height of tumor cells was twice their width along with basally situated nuclei. Cells showed abundant cytoplasm with pale oval nuclei, some showing intranuclear grooves and intranuclear cytoplasmic inclusions (fig 3&4). FNAC from right cervical swelling showed metastasis. Diagnosis given was suspicious of Tall cell variant of Papillary thyroid carcinoma with metastasis to right cervical lymph node. Patient underwent right hemi thyroidectomy with right cervical lymph node dissection. Cut surface showed a well defined tumor measuring 2.5cm in diameter, grey white in colour. On microscopy, tumor showed architectural and cytological features of papillary carcinoma with presence of papillae lined by tall columnar cells with eosinophilic cytoplasm and nuclear features of PTC. (fig5) 6 cervical lymph nodes dissected showed metastasis of PTC. A diagnosis of

TCV-PTC with metastasis to cervical lymph nodes was given.

DISCUSSION-

TCV-PTC is an aggressive variant of PTC comprising 4-16% of all PTC cases^[7].

Hawk and Hazard first described TCV in 1976 and defined it as PTC composed of at least 30 % tall cells whose height to width ratio is 2.1 to 3.1.^[3,5] This variant presented with large tumour size in elderly men with extrathyroidal extension and metastasis and had a poor prognosis unlike the classical type of PTC.^[7] Our patient presented with nodal metastasis even though the tumour was small. The cytological features were first described by Harach and Zusman in 1992 followed by Kaw et al and Gamboa et al.^[8] Tall cells had oxyphilic cytoplasm well defined borders basal nuclei and appeared as tail like cells or tadpole cells^[9] However the percentage of tall cells required for diagnosis varied from 10% to 75% and the ratio of height to width from 2:1 to 3:1.² However according to recent WHO classification of thyroid tumours and Bethesda system of reporting thyroid cytopathology the height of the cells should be 3 times the width with at least 30% tall cells.^[4,7]

Aki Tanaka et al^[2] analysed smears of 19 TCV –PTC and 50 conventional PTC cases in their study. They included cases with more than 50% tall cells in their study. They considered five cytological findings indicating TCV-PTC (1) palisaded pattern, (2) tall columnar cells with the heights of at least three times their widths, (3) tombstone appearance, (4) spindle-like carcinoma cells with tapering ends (5) cytoplasmic elongation. Distinct cell borders with dense cytoplasm was seen.^[3] Similar findings were seen in the present case where cells showed moderate amount of cytoplasm, distinct cell borders, cytoplasmic tails, basal nuclei with palisading nuclear pseudoinclusions and intranuclear grooves. Diagnosis was confirmed on histopathology which showed features of papillary carcinoma with >30% tall cells consistent with TCV-PTC with metastasis to cervical lymph nodes.

The differential diagnosis is with other variants like columnar cell variant which characterised by lack of dense cytoplasm and presence of nuclear pseudostratification^[8,10,11] oncocytic variant which has dense cytoplasm but lacks tall cells and warthin like variant which shows lymphocytes in the

background^[1, 3, 6]

Jayaram et al also found larger thyroid follicular cells than usual cells of PTC with abundant granular cytoplasm with arrangement of cells in rows resembling respiratory epithelium in the smears of 3 cases of TCV-PTC.^[12]

Ganly et al recommended >30% presence of tall tumor cells. They observed same biological aggressive features and poor prognosis in PTC cases with 30%-49% tall cells and cases with $\geq 50\%$ tall cells than PTC cases with < 30% tall cells^[13].

Gamboa et al. studied 229 cases of PTC of which 19 cases were diagnosed as TCV-PTC on histology. FNA of 6 patients out of these 19 cases showed tall cell morphology, cohesive cells with respiratory epithelium like arrangement, singly scattered tadpole shape tumor cells on cytology and associated with aggressive behaviour.^[14] The characteristic cytological findings of TCV-PTC is not yet fully defined.^[2]

Recently molecular testing is being done and shows different profile in TCV-PTC as compared to classical PTC. About 90% of TCV-PTCs harbor the BRAF V600E mutation while 31% TCV-PTC are associated with TERT promoter mutations as compared to conventional PTC in <10% cases explaining the worse outcome in TCV-PTC.^[7, 15]

CONCLUSION-

The cytological characteristics of PTC have been thoroughly discussed in the literature, and when used by experienced cytopathologist, FNAC has a commendable diagnostic accuracy. However, some PTC variants including TCV-PTC pose a diagnostic challenge. Understanding the variations in cytomorphological characteristics and detecting the presence of tall cells may help with correct diagnosis and more aggressive treatment, which can improve patient outcome as they are associated with the bad prognosis.^[6]

Figures

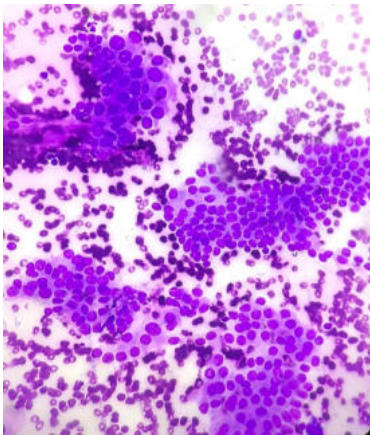


Figure 1). (Field stain 10X)

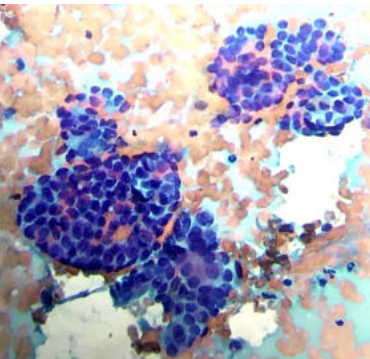


Figure 2) (Pap stain 10X)

Figure 1 Carcinoma cells in papillary pattern Figure 2 cells with nuclear pallisading, overlapping

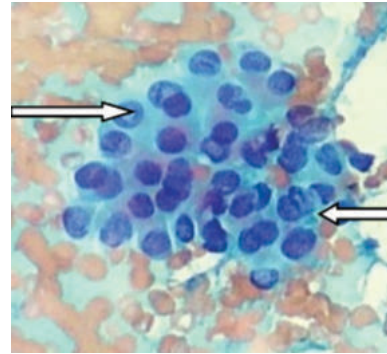


Figure 3). (Pap stain 40X)

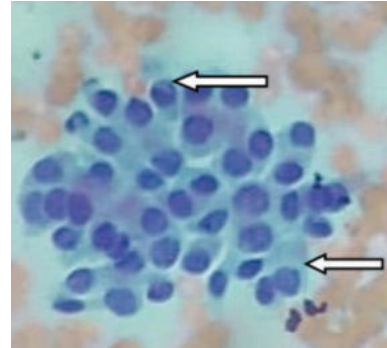
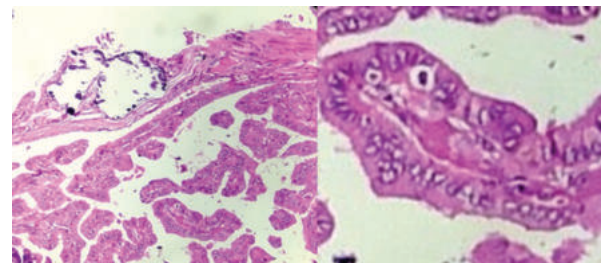


Figure 4) (Pap stain 40X)

Figure 3 Carcinoma cells showing intranuclear groove and pseudoinclusion with moderate to abundant cytoplasm Figure 4 showing cytoplasmic elongation with basally situated nuclei



A) (H&E4X)

B) (H&E 40X)

Figure 5 A) TPC with papillary architecture B & C) Cells with moderate to abundant dense cytoplasm with optically clear nuclei with height : width ratio 2:1.

REFERENCES

1. Zhang, J. , Xu, S. High aggressiveness of papillary thyroid cancer: from clinical evidence to regulatory cellular networks. *Cell Death Discov.* 10, 378 (2024).
2. Tanaka A, Hirokawa M, Higuchi M, Suzuki A, Yamao N, Hayashi T, Kuma S, Miyauchi A. Diagnostic clues indicating tall cell variants of papillary thyroid carcinoma in fine needle aspiration. *Diagn Cytopathol.* 2019 May;47(5):452-7.
3. Monappa V, Kudva R. Cytomorphologic diversity of papillary thyroid carcinoma. *J Cytol* 2017;34:183-7.
4. Oh WJ, Lee YS, Cho U, Bae JS, Lee S, Kim MH, Lim DJ, Park GS, Lee YS, Jung CK. Classic papillary thyroid carcinoma with tall cell features and tall cell variant have similar clinicopathologic features. *Korean J Pathol.* 2014 Jun;48(3):201-8.
5. Longheu, A. ; Canu, G. L. ; Cappellacci, F. ; Erdas, E. ; Medas, F. ; Calò, P. G. Tall Cell Variant versus Conventional Papillary Thyroid Carcinoma: A Retrospective Analysis in 351 Consecutive Patients. *J. Clin. Med.* 2021, 10, 70.
6. Solomon A, Gupta PK, LiVolsi VA, Baloch ZW. Distinguishing tall cell variant of papillary thyroid carcinoma from usual variant of papillary thyroid carcinoma in cytologic specimens. *Diagn Cytopathol.* 2002 Sep;27(3).
7. Ali SZ, Baloch ZW, Cochand-Priollet B, Schmitt FC, Vielh P, VanderLaan PA. The 2023 Bethesda system for reporting thyroid cytopathology. *Thyroid.* 2023 Sep 1;33(9):1039-44.
8. Urano M, Kiriya Y, Takakuwa Y, Kuroda M. Tall cell variant of papillary thyroid carcinoma: Its characteristic features demonstrated by fine-needle aspiration cytology and immunohistochemical study. *Diagn Cytopathol.* 2009

- Oct;37(10):732-7.
9. Sen A, Nalwa A, Mathur SR, Jain D, Iyer VK. Cytomorphology of columnar cell variant of papillary carcinoma thyroid: A case report and review of the literature. *Cytojournal*. 2014 Oct 21;11:27.
 10. Kini H, Pai RR, Kalpana S. Solitary parotid metastasis from columnar cell carcinoma of the thyroid: a diagnostic dilemma. *Diagn Cytopathol*. 2003 Feb;28(2):72-5.
 11. Jayaram G. Cytology of columnar-cell variant of papillary thyroid carcinoma. *Diagn Cytopathol*. 2000 Apr;22(4):227-9.
 12. Jayaram, n md; tambwekar, shubhangi md; prasad, sujay r md, dnb; ramprasad, av md. tall cell variant of papillary carcinoma of Thyroid. Report of Three Cases Diagnosed by FNAC. . *Journal of Cytology* 15(2):p 41-44, Apr-Jun 1998.
 13. Ganly I, Ibrahimpasic T, Rivera M, Nixon I, Palmer F, Patel SG, Tuttle RM, Shah JP, Ghossein R. Prognostic implications of papillary thyroid carcinoma with tall-cell features. *Thyroid*. 2014;24:662-70.
 14. Gamboa-Domínguez A, Candanedo-González F, Uribe-Uribe NO, Angeles-Angeles A. Tall cell variant of papillary thyroid carcinoma. A cytohistologic correlation. *Acta Cytol*. 1997 May-Jun;41(3):672-6.
 15. Wang X, Cheng W, Liu C, Li J. Tall cell variant of papillary thyroid carcinoma: current evidence on clinicopathologic features and molecular biology. *Oncotarget*. 2016 Jun 28;7(26):40792-9.