



EXPRESSION OF p53 AND BETACATENIN IHC MARKERS IN PREINVASIVE LESIONS OF GALL BLADDER-A CASE SERIES STUDY

Dr Sreelekshmi KT Assistant Professor, Malabar Medical college, Ulliyeri, Calicut.

Dr Deeshma T Associate Professor, Malabar Medical college, Ulliyeri, Calicut.

Dr Sily Sreedharan Professor, Malabar Medical college, Ulliyeri, Calicut.

ABSTRACT The relationship between p53 and beta-catenin is a dynamic and complex one, with implications for both normal cellular processes and cancer development. Their interplay is not always straightforward and can vary depending on the specific cellular context and genetic background. The aim of this study is to see the expression of the markers p53 and beta-catenin in preinvasive lesions of gall bladder.

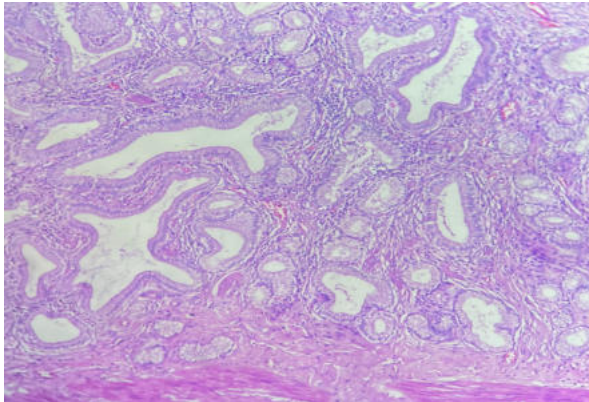
KEYWORDS : p53, Beta catenin, ICPN

INTRODUCTION

p53, also known as tumor protein p53 or TP53, is a crucial protein that acts as a tumor suppressor. It's a transcription factor, meaning it regulates the expression of other genes, and is often mutated in human cancers. p53 plays a vital role in preventing cancer formation by regulating cell division, DNA repair, and apoptosis (programmed cell death). (1) When p53 is functioning normally (wild-type), it can downregulate beta-catenin levels and activity. This is achieved through various mechanisms, including promoting beta-catenin's degradation via the ubiquitin-proteasome pathway. This interaction is often part of a negative feedback loop, where p53 activation can lead to a decrease in beta-catenin levels and signaling. (2) In many cancers, mutations in p53 can lead to its inactivation, allowing cancer cells to proliferate unchecked. Conversely, dysregulation of the Wnt/beta-catenin pathway, often due to mutations in genes like APC or beta-catenin itself, can also contribute to cancer development by promoting cell growth and survival. In some cases, p53 can negatively regulate beta-catenin levels and activity, while in others, beta-catenin can promote p53 accumulation and activity. This complex interplay between p53 and beta-catenin highlights their importance in cancer and their potential as therapeutic targets.(3).

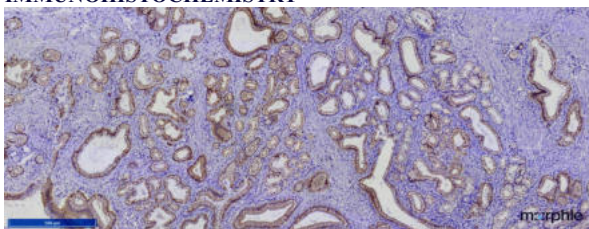
DISCUSSION

Case 1 57-year-old male who underwent cholecystectomy for cholelithiasis

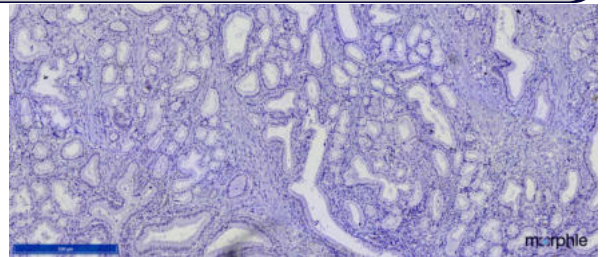


Microscopy-Adenomatous hyperplasia of gall bladder with pyloric gland metaplasia

IMMUNOHISTOCHEMISTRY



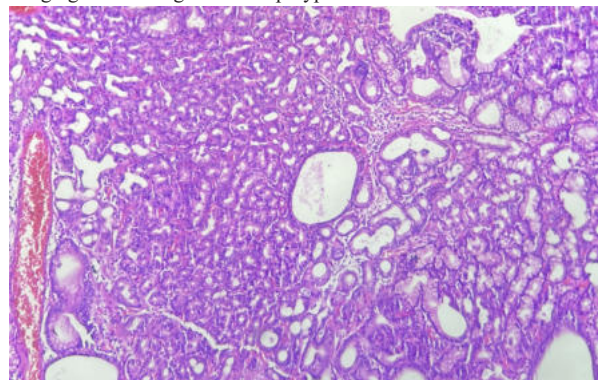
Beta Catenin- Membranous positivity



p53 - Negative

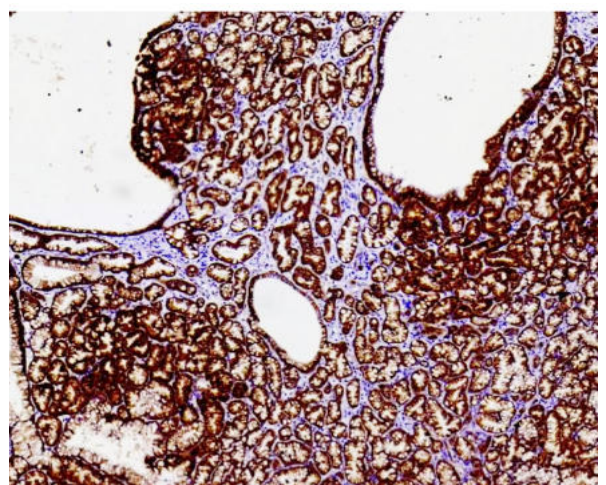
Case 2

37-year-old male who underwent laproscopic cholecystectomy, with imaging features of gall bladder polyp.

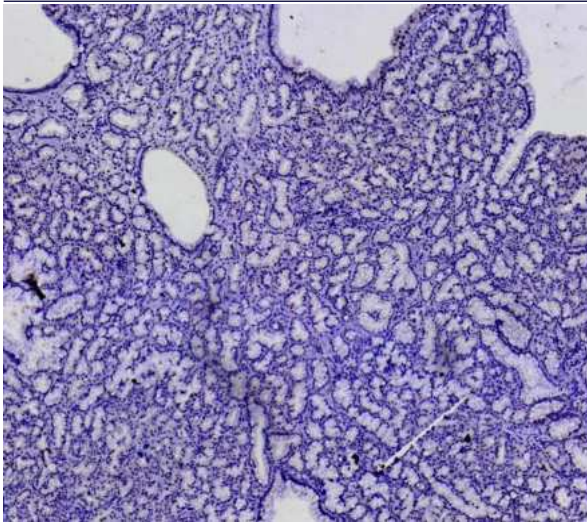


Microscopy - Pyloric gland adenoma

IMMUNOHISTOCHEMISTRY



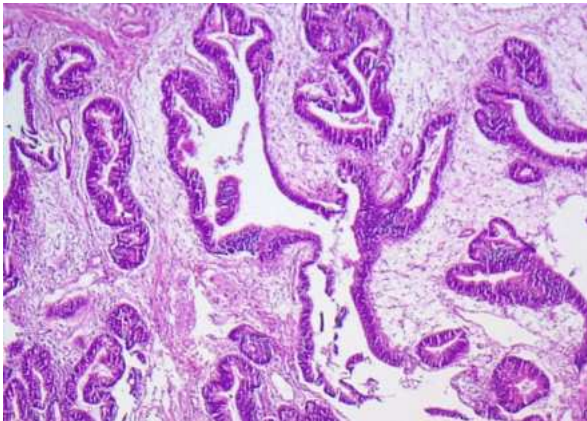
Beta catenin - Cytoplasmic and nuclear positivity



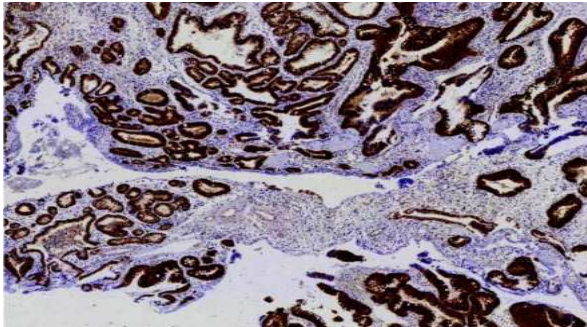
P53 -Negative

Case 3 63 year old male presented with upper abdominal discomfort, on imaging showed gall bladder polyp

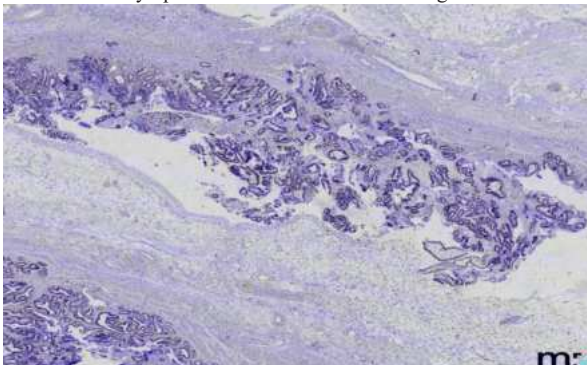
Microscopy - Intrahepatic papillary tubular neoplasm, high grade



IMMUNOHISTOCHEMISTRY



Beta catenin--Cytoplasmic and membranous staining



P53 - Wild type staining pattern

DISCUSSION

In the present study, we investigated expression patterns of beta-catenin and p53 in different gallbladder tissues to elucidate the role of p53 and beta-catenin in gallbladder carcinogenesis. We evaluated three preinvasive lesions of gall bladder.

Beta catenin was found to be mutated in pyloric gland adenoma of gall bladder where the IHC expression was in the nuclei and cytoplasm and there was a mutation in p53 which was found to be negative in IHC. Equivocal result was observed in ICPN in beta catenin, where p53 was found to have wild type expression. Beta catenin was found to be conserved in pyloric gland hyperplasia of gall bladder and p53 was found to be mutant where it was found to have negative expression. A positive association was found between p53 and beta catenin in pyloric gland adenoma of gall bladder. Intrahepatic papillary tubular neoplasm did not show any association between p53 and beta catenin. Pyloric gland hyperplasia of gall bladder showed no association between beta catenin and p53 where a mutant expression was observed in p53(4)

REFERENCES

- 1) Marei, H.E., Althani, A., Afifi, N. *et al.* p53 signaling in cancer progression and therapy. *Cancer Cell Int* **21**, 703 (2021)
- 2) Sadot E, Geiger B, Oren M, Ben-Ze'ev A. Down-regulation of beta-catenin by activated p53. *Mol Cell Biol*. 2001 Oct;21(20):6768-81.
- 3) Wang, H., Guo, M., Wei, H. *et al.* Targeting p53 pathways: mechanisms, structures and advances in therapy. *Sig Transduct Target Ther* **8**, 92 (2023)
- 4) Xiao, Q.; Werner, J.; Venkatachalam, N.; Boonekamp, K.E.; Ebert, M.P.; Zhan, T. Cross-Talk between p53 and Wnt Signaling in Cancer. *Biomolecules* **2022**, *12*, 453.
- 5) Bhattacharya I, Barman N, Maiti M, Sarkar R. Assessment of beta-catenin expression by immunohistochemistry in colorectal neoplasms and its role as an additional prognostic marker in colorectal adenocarcinoma. *Med Pharm Rep*. 2019 Jul;92(3):246-252.