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Pathology

Adenomatous Hyperplasia Mimicking Adenocarcinoma of the Gallbladder – Diagnostic Dilemma Resolved with Immunohistochemistry: A Case Report with Review of Literature

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Abstract **Case Report**

Adenomatous hyperplasia (AH) of the gallbladder is an uncommon and unique entity. AH is commonly confused with malignant GB neoplasms in the setting of chronic cholecystitis, gallstones or cholesterolosis. We herein report a case of AH with deep seated RA sinuses mimicking gallbladder cancer in a middle-aged female in the setting of symptomatic cholecystitis with cholelithiasis and cholesterolosis. In our case microscopy showed diffuse villous type of mucosal hyperplasia with proliferative, bland looking densely packed glands with numerous closely opposed R-A sinuses extending upto the peri muscular connective tissue. The whole microscopic picture closely simulating a well differentiated gall bladder carcinoma (GBC), hence warranted use of IHC to resolve the dilemma and to reach a definitive diagnosis. A literature search yields minimal information on these benign entities, thus suggesting the infrequency of its reporting, hence the need for this case report.

Keywords: Adenomatous hyperplasia, RA sinus, carcinoma, IHC.

INTRODUCTION

Benign neoplasms and tumor-like lesions of the gallbladder are infrequent, and diagnosis of these lesions is often difficult to establish on the basis of signs and symptoms [1]. Of these entities, adenomatous hyperplasia, with characteristic histopathological features of hyperplasia of glands and of deep-seated glands in the absence of cellular atypia of the gallbladder, is uncommon [1]. Adenomatous hyperplasia is considered a benign pseudotumor of the gallbladder and has no known malignant potential [2]. It can be diffuse or focal in its presentation. Given its benign character, cholecystectomy should be curative with regards to symptomatology, and no further diagnostic studies are warranted [2]. We present a case of a middle-aged female with diffuse adenomatous hyperplasia of gall bladder.

CASE REPORT

A 48-year-old female visited private hospital with complaints of mild upper abdominal pain. She had non-contributory past medical history.

Trans-abdominal ultrasound scan revealed cholecystomegaly, thickened gallbladder wall.

Cholecystectomy was done and specimen was sent for histopathological evaluation.

PATHOLOGICAL EVALUATION

GROSS: Specimen consists of cut opened gall bladder measuring 7x3cm. External surface is congested. Cut section – wall appears thickened measuring about 0.6cm and the mucos ais firm with granular texture and yellow streaks seen Multiple yellowish stones seen.

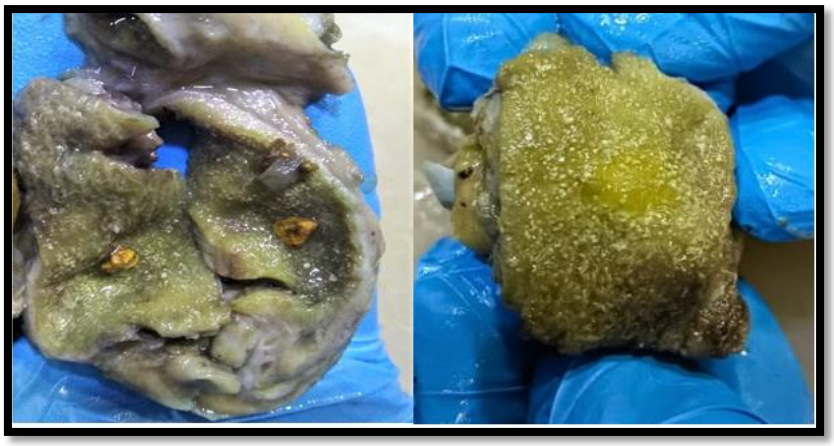

Figure 1: Gross image of gall bladder specimen with yellow stones and mucosa showing granular appearance and yellow streaks

MICROSCOPY

Sections showed diffuse villous type of mucosal hyperplasia with papillary folds and proliferative, bland looking densely packed glands with numerous closely opposed R-A sinuses extending upto the peri muscular connective tissue.Also subepithelial collections of foamy histiocytes seen, resulting in cholesterolosis. Transmural mononuclear inflammatory infiltrate consisting predominantly of lymphocytes also seen associated with fibrosis and congestion. There was no evident cellular atypia, dysplasia in the sections studied.

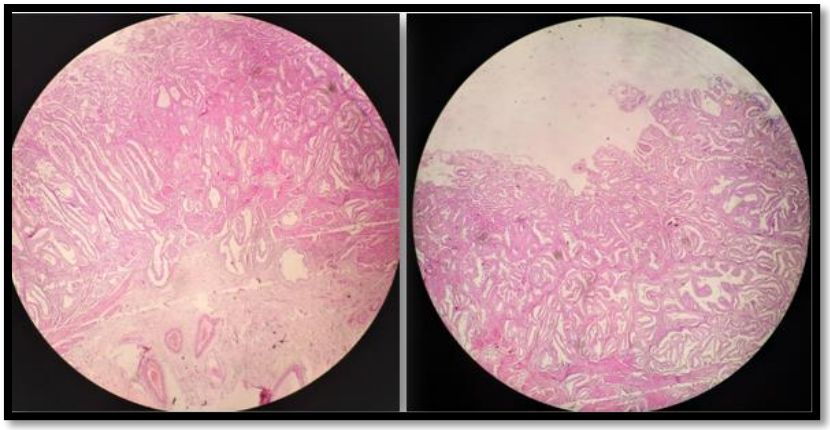

Figure 2: Low power view showing hyperplastic mucosa arranged in papillary pattern and closely arranged glandular structures

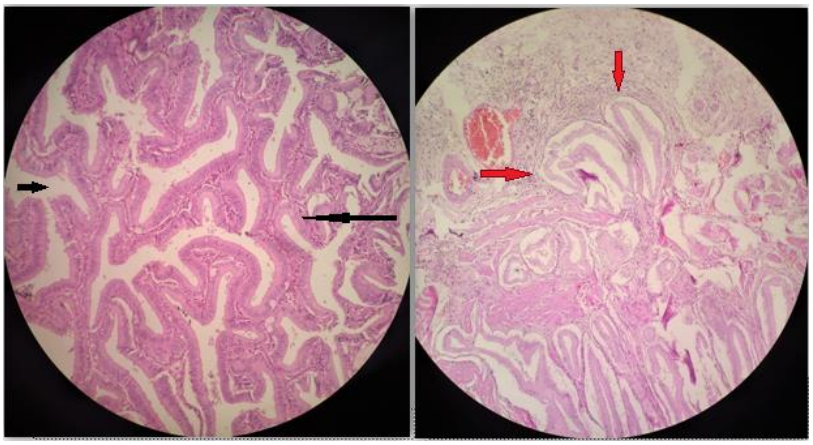

Figure 3: High power view showing closely apposed glands (Black arrows) showing bland looking nuclei. Also another micrograph showing deep seated R A sinuses (Red arrow) reaching up to the peri muscular stroma

The whole microscopic picture closely simulating a well differentiated GBC, hence warranted use of IHC to resolve the dilemma and to reach a definitive diagnosis.

The Immunohistochemistry Profile was as Follows,

CEA – Negative.
S100 – Negative.
CK 19 – Positive, diffuse.
CK 7 – Positive.
P^{53} – Positive, weak diffuse.
Ki67 – Moderate in high proliferating areas.

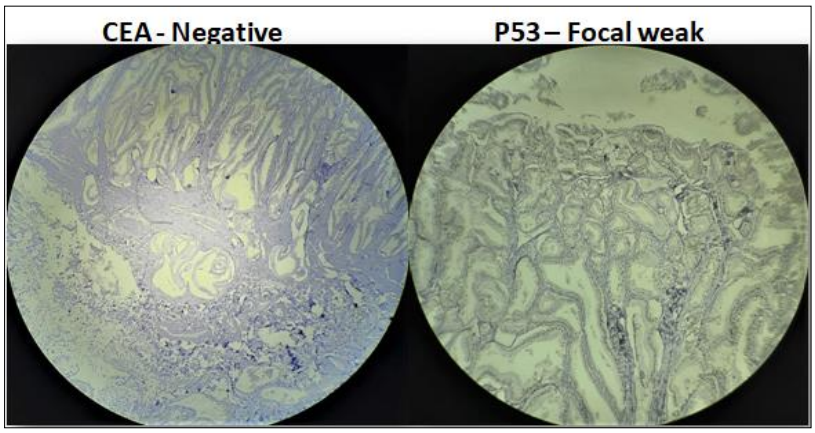

Figure 4: Images showing IHC staining for CEA is negative, where as staining for p53 is focal weak positivity seen in mucosa attributed to regenerative process

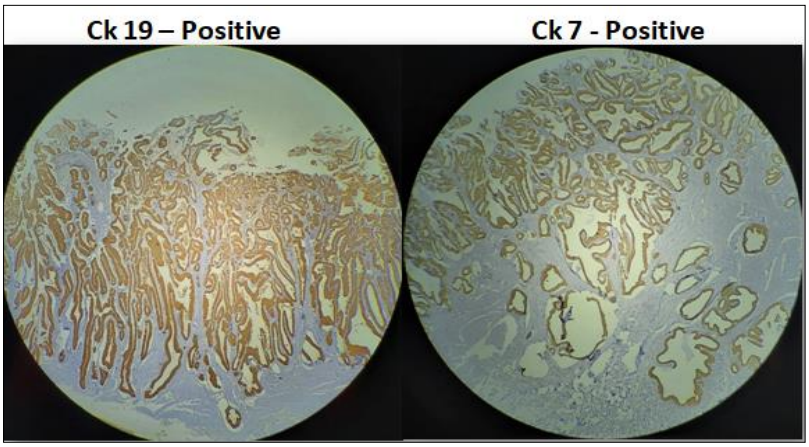

Figure 5: Imgaes showing IHC statining for CK 19 and CK 7 showing strong and diffuse positivity

The microscopic findings of absence of atypia or dysplasia and negative CEA on IHC helped us in confirming our diagnosis.

Hence a diagnosis of 'ADENOMATOUS HYPERPLASIA WITH DEEP SEATED R-A SINUSES AND CHOLELITHIASIS'' was given.

DISCUSSION

Adenomatous hyperplasia of the gallbladder is an uncommon benign lesion that should always be differentiated from malignant tumors of the gallbladder as surgical resection offers a complete cure for this unique disease entity [3]. Recent small and large case series have reported the prevalence of adenomatous hyperplasia to range between 0.8% and 12% of cholecystectomy specimens [3]. In comparison, the prevalence of malignancy has been reported to be as high as15%, particularly in association with polyps of less than 1 centimeter in dimension.

Adenomatous hyperplasia per se is not a premalignant lesion; however, previous studies have suggested a link between gallbladder carcinoma in the presence of gallstones, chronic inflammation, and metaplastic changes in patients with adenomatous hyperplasia [3].

Adenomatous hyperplasia of the gallbladder is characterized by a hyperplasia of metaplastic pyloric-type glands and of deep-seated glands in the absence of cellular atypia [4]. Macroscopically, this alteration presents in the form of a thick and nodular gallbladder mucosa, particularly in its diffuse form, but it can also produce polypoid lesions. The epithelial surface of the gallbladder and glandular epithelial can undergo focal to diffuse hyperplastic changes. In one rare form,

papillary hyperplasia is present, usually in a diffuse pattern [4].

Baig SJ *et al.,* and Aggarwal *et al.,* in their respective studies have found that adenomatous hyperplasia and Rokitansky-Aschoff sinuses may be seen in gallbladders containing mixed and cholesterol stones. Cholesterol may be a more potent stimulus for glandular hyperplasia [5].

Elfving *et al.,* reported that hyperplasia of the gallbladder was present in 22% of their 104 patients who presented with calculous cholecystitis. Two hypotheses were put forward in this paper. These authors suggested, in this study, that the hyperplastic mucosa absorbs more bile than normal and precipitation occurs with the increasing concentration, and this gives rise to stone formation. The other hypothesis proposed in this paper is that primary cholelithiasis causes secondary hyperplasia because of mechanical irritation by the calculi [6].

In our case also there was cholesterolosis with calculous cholecystitis present.

Dorantes-Heredia R *et al.,* in their study described 8 cases of cholecystectomy specimens with (R-A) sinuses that were misinterpreted as adenocarcinomas. 5 cases misinterpreted as adenocarcinomas consisted of densely packed, closely arranged R-A sinuses with little intervening stroma or surrounded by a desmoplastic stroma. They were lined by a single layer of cuboidal or columnar cells. There were also pseudostratified columnar cells with mucin-containing cytoplasm and hyperchromatic or vesicular nuclei but without mitotic figures [7]. In our case also RA sinuses were densely packed resembling gland like structures and had a laminar distribution. All the cases on IHC - R-A sinuses did not label with carcinoembryonic antigen or p53 and had very low proliferative activity as measured by the MIB1-labeling index. In our case also RA sinuses were negative for CEA and p53 with moderate ki 67 index [7].

Agrawal *et al*., reported that CEA immunostaining was observed in 42 of 51 GBC cases (82%). They found that CEA staining pattern was apical in 13/51 cases (25%), focal pattern in 15/51 cases (29%) to diffuse in 14/51 cases (27%). They also found CE Aexpression in 18 of 68 chronic cholecystitis cases (27%) and apical expression in all 18 cases along with focal cytoplasmic in nine cases. They concluded that diffuse cytoplasmic staining was found only in GBC [8].

Mondal *et al.,* reported that out of total 68 GBC cases, CEA immunostaining was seen in 62 GBC cases (91%). No expression in 6 cases (6/68), focal staining pattern was seen in 29 cases (29/68), i.e., 42% of GBC cases, and diffuse staining pattern was seen in 33 cases (33/68), i.e., 48% cases. In total 39 cases of benign diseases of GB with mild-to-moderate dysplasia, they found CEA expression in 12 cases (12/39), i.e., 30% of cases. CEA expression was apical in all 12 cases. They concluded that focal and diffuse CEA staining pattern was suggestive of GBC, and in the cases of benign GB diseases with dysplasia, either no CEA expression or apical CEA expression pattern is seen [9].

Albores-Saavedra *et al*., in their study on expression of CEA in GB epithelium concluded that from cases of dysplasia to invasive carcinoma, the amount of immunoreactive CEA progressively increases and shows a change in distribution. In malignant tumors, in addition to a stronger staining reaction, CEA could also been within the cytoplasm and even in gland secretions [10].

In our case there were absent CEA expression in gall bladder mucosa as well as RA sinuses. The p53 weak focal positivity was attributed to the regenerative process leading to mucosal hyperplasia.

CONCLUSION

Adenomatous hyperplasia of the gallbladder mimics malignant lesions, more so in the setting of chronic cholecystitis and gallstones. Also hyperplasia along with deep seated RA sinus may be misdiagnosed as GBC or vice versa many a times. CEA immune marker study may be helpful to resolve this diagnostic dilemma.

REFERENCES

1. Odongo, C. N., Dreque, C. C., Bongomin, F., Oyania, F., Situma, M., & Atwine, R. (2021). Adenomatous Hyperplasia of the Gallbladder in the Setting of Mirizzi Syndrome, Mimicking Adenocarcinoma of the Gallbladder. *International Medical Case Reports Journal*, *14*, 637-641. doi: 10.2147/IMCRJ.S326857. PMID: 34584463; PMCID: PMC8464327.
2. Stokes, M. C., Burnette, R., Ballard, B., Ross, C., & Beech, D. J. (2007). Adenomatous hyperplasia of the gallbladder. *Journal of the National Medical Association*, *99*(8), 959.
3. Mahajan, A., & Sripathi, S. (2016). Gallbladder adenomyomatosis mimicking carcinoma: a diagnostic dilemma. *Journal of global oncology*, *2*(5), 341. . doi:10. 1200/JGO.2016.005249
4. Baba, H., Wakabayashi, M., Oba, A., Tsubomoto, T., Nakamura, H., Sanada, T., ... & Goseki, N. (2014). Primary papillary hyperplasia of the gallbladder mimicking gallbladder cancer. *International Surgery*, *99*(3), 247-251. Doi: 10.9738/INTSURG-D-13-00252.1. PMID: 24833147; PMCID: PMC4027908.

5. Baig, S. J., Biswas, S., Das, S., Basu, K., & Chattopadhyay, G. (2002). Histopathological changes in gallbladder mucosa in cholelithiasis: correlation with chemical composition of gallstones. *Tropical gastroenterology: official journal of the Digestive Diseases Foundation*, *23*(1), 25-27. PMID: 12170916.
6. Elfving, G., Teir, H., Degert, H., & Mäkelä, V. (1969). Mucosal hyperplasia in the gallbladder demonstrated by plastic models. *Acta Pathologica Microbiologica Scandinavica*, *77*(3), 384-388.
7. Dorantes-Heredia, R., Chablé-Montero, F., Henson, D. E., & Albores-Saavedra, J. (2013). Rokitansky-Aschoff sinuses mimicking adenocarcinoma of the gallbladder: a study of 8 cases. *The American Journal of Surgical Pathology*, *37*(8), 1269-1274. doi: 10.1097/PAS.0b013e318286bd39. PMID: 23715158.
8. Agrawal, V., Goel, A., Krishnani, N., Pandey, R., Agrawal, S., & Kapoor, V. K. (2010). p53, carcinoembryonic antigen and carbohydrate antigen 19.9 expression in gall bladder cancer, precursor epithelial lesions and xanthogranulomatous cholecystitis. *Journal of postgraduate medicine*, *56*(4), 262. doi: 10.4103/0022-3859.70933. PMID: 20935395.
9. Mondal, S. K., Bhattacharjee, D., Mandal, P. K., & Biswas, S. (2017). Histopathological study of gallbladder carcinoma and its mimics with role of carcinoembryonic antigen immunomarker in resolving diagnostic difficulties. *Indian Journal of Medical and Paediatric Oncology*, *38*(04), 411-415. doi: 10.4103/ijmpo.ijmpo_230_15. PMID: 29333003; PMCID: PMC5759055.
10. Albores-Saavedra, J., Nadji, M., Morales, A. R., & Henson, D. E. (1983). Carcinoembryonic antigen in normal, preneoplastic and neoplastic gallbladder epithelium. *Cancer*, *52*(6), 1069-1072. doi: 10.1002/1097-0142(19830915)52:6<1069::aid-cncr2820520623>3.0.co;2-1. PMID: 6349777.