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Case report

A Case of Intracholecystic Papillary Neoplasm of Gall Bladder-A Rare Entity

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Background: Intracholecystic Papillary Neoplasm is a rare epithelial neoplasm originating in the gallbladder mucosa. It usually presents as gallbladder mass and is associated with varying degree of dysplasia or invasiveness needing high index of suspicion for proper management.

Case Presentation: A 48-year-old female presented with complaints of vague upper abdominal pain for last 10 days.Ultrasound abdomen revealed polypoidal mass filling gall bladder lumen measuring 7x3.8 cm. MRCP revealed hypointense mass lesion within gallbladder lumen with its stalk at the hepatic surface of gall bladder. CT abdomen revealed heterogeneously enhancing gall bladder mass with no regional lymphadenopathy. Serum tumor markers of CEA, CA19.9 were normal. Patient underwent en bloc resection of 2 cm segment IVB liver along with gallbladder. Intraoperative frozen section specimen revealed exophytic polypoidal papillary lesion in distal body of gallbladder measuring 5x4x3 cm. Microscopic features revealed intracholecystic papillary neoplasia with low-grade dysplasia. Regional lymphadenectomy was not performed. Final diagnosis of Intracholecystic papillary neoplasm,gastric type was confirmed and patient was kept on close follow up.

Conclusion: Intracholecystic papillary neoplasm of gall bladder is a rare entity presenting as intraluminal growth which require proper histopathological diagnosis. Clinical features and imaging modalities are non-specific. They have variable morphological subtypes like papillary or tubular growth patterns and may have underlying varying degree of dysplasia or invasive foci making it pertinent to perform surgical resection.They are relatively indolent with better prognosis as compared to gallbladder carcinomas. Further studies are required to precisely diagnose it and manage the various subtypes appropriately.

Introduction

Incidence of cancer is rising worldwide with India ranking third in cancer incidence as of 2020, from GLOBOCAN estimates with a study showing lung, oral, prostate, and gallbladder cancer exhibiting the rising trend in the age-standardised rates in males in Northern part of India [1]. It is therefore pertinent to diagnose these cancers at an early stage for appropriate management to provide better cure rates and improved survival. Intracholecystic Papillary Neoplasm (ICPN) is a rare preinvasive epithelial neoplasmof the gallbladder originating in the gallbladder mucosa. The incidence of all gallbladder polyps in the general population is 5-7% while the incidence of ICPN itself is much rarer (04-0.6% of cholecystectomies) [2, 3]. According to World Health Organisation (WHO) 2019 classification for the tumours of gall bladder, ICPN has been proposed as the ‘preinvasive neoplasm of the gall bladder’[4]. There are very few case reports reported in literature on this rare entity. A study has highlighted the significance of detailed and meticulous macroscopic examination of gallbladder intraoperatively to look for any abnormalities and to perform proper histopathological examination in the cases where gallbladder examination abnormality is found on macroscopic examination [5]. We hereby present a rare challenging case of intracholecystic

papillary neoplasm of gallbladder and highlight the importance of detailed and meticulous macroscopic examination of gallbladder intraoperatively, intraoperative frozen section and detailed histopathological examination to diagnose them.

Case Report

A 48-year-old female presented with vague upper abdominal pain for last 10 days. On evaluation, ultrasound abdomen revealed polypoidal mass filling gallbladder lumen measuring 7x3.8 cm (Figure 1).

Figure 1. USG Abdomen Showing Polypoidal Mass Filling Gall Bladder Lumen Measuring 7x3.8 cm.

On further evaluation, MRCP revealed hypointense mass lesion within gallbladder lumen measuring 79x32 mm in size with its stalk at the hepatic surface of the gall bladder and suspected focal fat plane loss with liver surface (Figure 2).

Figure 2. MRCP Abdomen Showing Hypointense Mass Lesion within Gallbladder Lumen with no Intrahepatic Bile Duct Dilatation and Regional Lymph Nodes Enlargement.

CECT chest and abdomen revealed heterogeneously enhancing gallbladder contents while CT chest was normal (Figure 3).

Figure 3. CECT Abdomen Revealed Heterogeneous Enhancement of the Mass within the Gallbladder Lumen without Evidence of Frank Hepatic Invasion.

Serum tumor markers CEA, CA19.9 were normal. Case was discussed in multidisciplinary tumor board and plan to perform surgery was made.In view of suspicious radiological findings along with the intraoperative findings suggestive of palpable hard mass within gallbladder body region and possible hepatic invasion, she underwent en bloc wedge resection of 2 cm segment IVB liver along with gallbladder to achieve negative margins and adequate oncological clearance.

Intraoperative frozen section of resected specimen revealed a grey-white exophytic, polypoidal papillary lesion in distal body region of gallbladder measuring 5x4x3 cm on cut section with microscopic features suggestive of intracholecystic papillary neoplasia with features of low-grade dysplasia and no invasiness seen (Figure 4, 5).

Figure 4. Intraoperative Cut Surface of Gallbladder Specimen Showing Exophytic Growth Arising from GB Body Filling almost Complete GB Lumen. Cystic duct (marked with silk suture) is away from the tumor.

Figure 5. Histopathology of the Mass on Microscopy Showed Back to Back Mucinous Glandular Units Intubulopapillary Configuration with Low-grade Dysplasia.

Plan to do regional lymphadenectomy was deferred. Her postoperative recovery was uneventful. Final histopathology revealed microscopic appearance of back to back mucinous glandular units intubulopapillary configuration with low-grade dysplasia. Final diagnosis of ICPN, gastric phenotype was made (Figure 5). Patient was advised to remain on close follow up with no adjuvant

therapy advised for her.

Discussion

ICPN is a pre-invasive, papillary, endoluminal growth arising from the gallbladder mucosa. Owing to its rarity, the diagnostic criteria are ill-defined, making it difficult to diagnose from other polypoidal lesions of gallbladder. A study described in 2012 analyzed 123 cholecystectomy specimens with well defined exophytic mass and found ICPN in 0.4% of cholecystectomies while in 6.4% cases,gallbladder carcinoma was associated with ICPN. They found the average tumour size of 2.6 cm and majority were solitary lesions located mostly in the body and fundus of gallbladder.Incidence was more common in females with mean age of 61 years and nearly half of them were symptomatic [3]. There were few more case reports reported in literature on ICPN but no randomized control trials have been done so far [6]. In the present case, ICPN tumor was large, solitary lesion and diagnosis was made on intraoperative frozen section and final histopathology. Hypothesis for ICPN development is based on an “adenomacarcinoma”sequence [3,7-9]. It was found that 43% cases were papillary in nature while 26% cases had tubular pattern, and 31% as combined pattern [3]. On the basis of dominant morphological features histopathologically, it may be biliary (most common), gastric, intestinal and oncocytic type [3, 4]. Smaller lesions less than 1 cm in size are less likely associated with invasiveness while larger size tumors have high propensity towards neoplastic transformation [3, 7-9]. Other risk features for presence of invasive foci are papillary type pattern, presence of high-grade dysplasia, and non pyloric cell line ICPN [8]. In our case study,the tumor size was 5x4 cm in size with papillary pattern growth with some gallbladder serosa tethering over hepatic surface side making it high risk for malignancy. We performed cholecystectomy en bloc with resection of 2 cm liver resection of segment IVB based on high index of suspicion and sent it for frozen section which revealed ICPN with low-grade dysplasia only. We did not perform regional lymph node dissection in this case as there was no evidence of invasive foci or presence of malignancy in the gallbladder mass. Most of the invasive carcinomas in ICPNs are gallbladder adenocarcinoma but other types like neuroendocrine tumors, may be seen [3]. In most cases, simple cholecystectomy for completely intraluminal growth or more radical cholecystectomy was performed when the imaging modality shows suspicious features for malignancy [10]. The 5-year survival rate of patients treated for ICPN was 78% as compared to gallbladder carcinoma [3]. It is therefore imperative to have proper collaboration with pathologists as proper histopathological study is essential to define this entity with its various subtypes and hence determining the prognosis of different pathological subtypes of ICPN after offering appropriate management.

In conclusion, ICPN of gallbladder is a rare entity presenting as intraluminal growth which require histopathological diagnosis. Microscopically, it may show papillary or tubular growth patterns with varying degree of dysplasia or sometimes with underlying invasive foci making it imperative to do surgical resection for final diagnosis. ICPNs have a relatively indolent course and better prognosis as compared to gall bladder carcinomas. Further studies are required to define clinico-radiological features, pathological features to aid in diagnostic precision as well as there is a need to do future studies for assessing their pattern of behaviour with various subtypes determining the prognosis in different subtypes of this entity.

Acknowledgments

Statement of Transparency and Principals

• Author declares no conflict of interest

• Study was approved by Research Ethic Committee of author affiliated Institute.

• Study’s data is available upon a reasonable request.

• All authors have contributed to implementation of this research.

Originality Declaration for Figures

All figures included in this manuscript are original and have been created by the authors specifically for the purposes of this study. No previously published or copyrighted images have been used. The authors confirm that all graphical elements, illustrations, and visual materials were generated from the data obtained in the course of this research or designed uniquely for this manuscript.

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