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A Tale of Two Primaries: Synchronous Gallbladder Adenocarcinoma and Breast DCIS

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Abstract: ***Multiple primary malignancies are uncommon, and synchronous dual primaries diagnosed in the same surgical setting are exceptionally rare. We report an unusual case of synchronous gallbladder invasive adenocarcinoma arising from intracholecystic papillary neoplasm (ICPN) and ductal carcinoma in situ (DCIS), comedo type, of the breast in a 75-year-old woman. The patient presented with acute abdominal pain and a right breast lump, and radiological evaluation revealed a polypoidal gallbladder mass along with a suspicious breast lesion. Cholecystectomy and breast wide local excision specimens were received simultaneously for frozen section. Histopathology confirmed invasive gallbladder adenocarcinoma arising from ICPN and high-grade DCIS without invasion. Distinct morphological and immune-histochemical profiles supported independent primary origins. This rare synchronous presentation underscores the importance of comprehensive clinical and pathological evaluation to ensure accurate diagnosis and appropriate multidisciplinary management.***

Keywords: DCIS of breast, Dual malignancies, ICPN, Invasive adenocarcinoma of gallbladder, Multiple primaries.

1. Introduction

Multiple primary malignancies are uncommon; although their overall frequency ranges from 2–17%, synchronous dual primary tumors diagnosed simultaneously in the same surgical setting are exceptionally rare (<1%) and diagnostically challenging.[1] Gallbladder carcinoma is an aggressive malignancy, most often adenocarcinoma, and is frequently detected at an advanced stage.[2,3] Intracholecystic papillary neoplasm (ICPN) is a recognized pre-invasive epithelial lesion of the gallbladder with papillary or tubular architecture and is regarded as a precursor to invasive adenocarcinoma in a subset of cases which represents about only 0.4-0.6% of cholecystectomy specimen.[4,5] Ductal carcinoma in situ (DCIS) of the breast is a non-invasive neoplasm confined to the ductal system, with the comedo pattern representing a high-grade variant characterized by central necrosis and increased malignant potential.[6] Synchronous gallbladder invasive adenocarcinoma arising from ICPN and breast DCIS diagnosed in the same surgical setting is exceedingly rare.[1,4] We report this unusual case to highlight its clinicopathological significance and diagnostic considerations.

2. Case History

A 75-year-old Indian female presented with acute intermittent colicky abdominal pain for two days, multiple episodes of vomiting, and a right-sided breast lump. She had hypertension for 30 years (on medication) and a remote history of pulmonary tuberculosis treated 40 years ago. Hemoglobin was 8.5 g/dL, while CBC, coagulation profile, and biochemical parameters were within normal limits. CA19-9 levels were normal.

Abdominal ultrasonography demonstrated a 2.8 × 2.1 cm hypoechoic, vascular polypoidal lesion arising from the anterior wall of the gallbladder, along with cholelithiasis. CT scan of the abdomen revealed a corresponding enhancing polypoidal mass measuring 2.8 × 2.0 × 1.5 cm. MRCP showed a multilobulated, T2-hypointense lesion measuring 27 × 23 × 30 mm, attached by a small pedicle and projecting into the gallbladder lumen, without evidence of hepatic invasion, findings suggestive of malignancy. A smaller hypointense filling defect in the fundus was noted, likely a calculus. Mammography identified a 1.2 × 0.8 cm heterogeneous hypoechoic lesion with lobulated margins at the 7 o'clock position (BIRADS IV-A), associated with subcentimetric right axillary lymph nodes, which were also demonstrated on CT scan of the chest.

For frozen section, cholecystectomy and right-sided breast wide local excision specimens were received simultaneously from the same surgical setup. The cholecystectomy specimen measured 8 × 3.5 × 1 cm, was cystic, yielded brownish hemorrhagic fluid on sectioning, and showed loss of rugosity with a 1 × 0.8 × 0.7 cm polypoidal mass. The breast specimen measured 7.5 × 7 × 1.5 cm and revealed a firm to hard, creamish-white lesion measuring 1 cm on cut surface.

3. Discussion

The coexistence of two distinct primary malignancies in a single patient is uncommon, and the synchronous occurrence of invasive gallbladder adenocarcinoma arising from intracholecystic papillary tubular neoplasm (ICPN) with comedo-type ductal carcinoma in situ (DCIS) of the breast is exceedingly rare. Each neoplasm has distinct histopathological and clinical features, and their simultaneous

presentation poses important considerations for pathogenesis, diagnosis, and management.

Intracholecystic papillary tubular neoplasm (ICPN) is a recently recognized, grossly visible (≥1 cm) preinvasive epithelial lesion of the gallbladder with papillary or tubular architecture and variable lineage differentiation, carrying malignant potential.[1,5] In this case, the lesion showed transition to invasive adenocarcinoma arising from the base and infiltrating the gallbladder wall.[Fig.1] Ductal carcinoma in situ (DCIS), comedo type, is a high-grade non-invasive breast carcinoma characterized by central necrosis and calcification, associated with a high risk of progression if untreated; however, absence of invasion in this patient indicates early detection.[7,8,Fig.2]

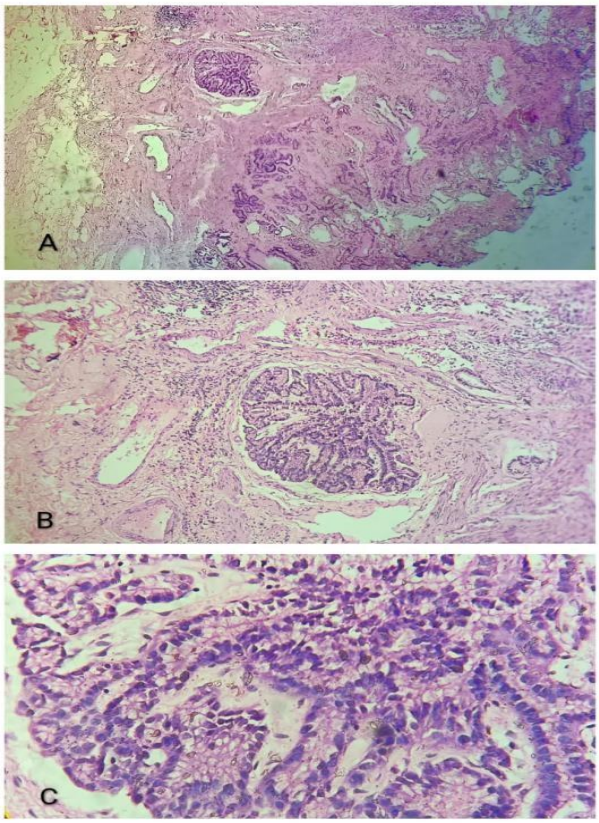

Figure 1: (A-4x, B-10x, C-40x view; H & E stain) Papillary tubular ICPN with dysplastic epithelium showing transition to invasive adenocarcinoma with atypical gland formation and desmoplastic stroma

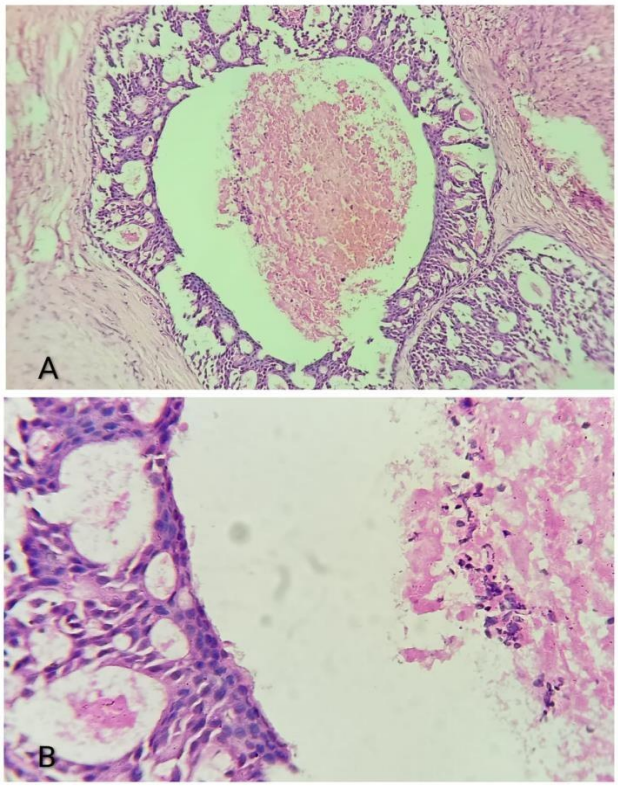

Figure 2: A-10x, B-40x view; H & E stain) Dilated ducts filled with pleomorphic epithelial cells and central comedo-type necrosis (DCIS)

The occurrence of synchronous malignancies in different organs can be attributed to several mechanisms, including genetic susceptibility, shared environmental or hormonal factors, chronic inflammation, due to any medication, food intake and random coincidence. Although no direct etiological link between gallbladder adenocarcinoma and breast DCIS has been established, hormonal and metabolic factors especially in postmenopausal women may contribute to the development of both. Additionally, mutations in genes such as TP53, KRAS, or PIK3CA have been implicated in both biliary and breast carcinogenesis, suggesting a possible molecular overlap.[8]

The diagnosis of both lesions in the same patient emphasizes the need for meticulous pathological examination and thorough clinical evaluation to distinguish synchronous primaries from metastatic disease. In this case, the distinct histopathological and immunohistochemical profiles- CK7, CK 8 & 18 positivity[Fig.3] in the gallbladder carcinoma, and estrogen receptor (ER)/progesterone receptor (PR) positivity[Fig.4] in DCIS- confirmed the independent origin of both malignancies.

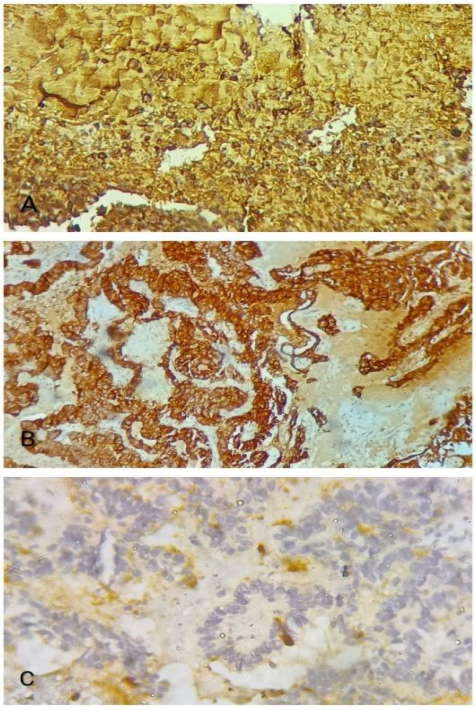

Figure 3: (A) CK7 demonstrating strong cytoplasmic positivity (B) CK8/18 demonstrating diffuse cytoplasmic positivity (C) CA19-9 demonstrating absence of staining in the tumor cells - supports a primary gallbladder adenocarcinoma

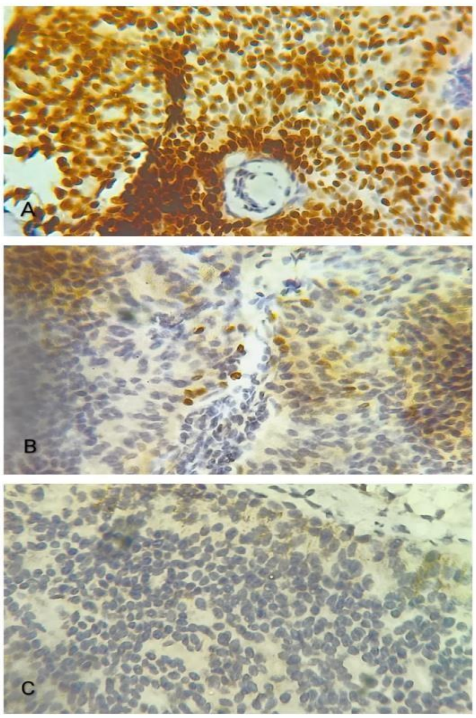

Figure 4: (A) Estrogen receptor (ER) demonstrating strong nuclear positivity (B) Progesterone receptor (PR) demonstrating weak nuclear positivity (C) HER2/neu demonstrating absence of membranous overexpression, consistent with HER2-negative status.

Management of synchronous primary malignancies requires a multidisciplinary approach based on tumor stage and biology. Surgical resection is the mainstay for gallbladder carcinoma arising from ICPN,[4] while DCIS is treated with breast conserving surgery or mastectomy depending on disease extent.[7,8] Prognosis primarily depends on the stage of gallbladder carcinoma and adequacy of DCIS excision.

4. Conclusion

This case emphasizes the importance of thorough diagnostic assessment when encountering multiple lesions, as synchronous primary malignancies, though rare in literature. Early recognition and multidisciplinary management are crucial for improving patient outcomes. Moreover, it highlights the need to evaluate underlying genetic hormonal or environmental risk factors that may predispose individuals to the development of dual primary malignancies simultaneously.

References

[1] Vogt A, Schmid S, Heinimann K, Frick H, Herrmann C, Cerny T, Omlin A. Multiple primary tumours: challenges and approaches, a review. ESMO Open. 2017 May 2;2(2):e000172. doi: 10.1136/esmoopen-2017-000172. PMID: 28761745; PMCID: PMC5519797.

[2] Albores-Saavedra J, Adsay NV, Crawford JM, et al. Carcinoma of the gallbladder and extrahepatic bile ducts. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, editors.WHO Classification of Tumours of the Digestive System. 4th ed. Lyon: IARC Press; 2010. p. 266–273.

[3] Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. Clin Epidemiol. 2014 Mar 7;6:99-109. doi: 10.2147/CLEP.S37357. PMID: 24634588; PMCID: PMC3952897.

[4] Adsay V, Jang KT, Roa JC, Dursun N, Ohike N, Bagci P, Basturk O, Bandyopadhyay S, Cheng JD, Sarmiento JM, Escalona OT, Goodman M, Kong SY, Terry P. Intracholecystic papillary-tubular neoplasms (ICPN) of the gallbladder (neoplastic polyps, adenomas, and papillary neoplasms that are ≥1.0 cm): clinicopathologic and immunohistochemical analysis of 123 cases. Am J Surg Pathol. 2012 Sep;36(9):1279-301. doi: 10.1097/PAS.0b013e318262787c. PMID: 22895264.

[5] Roa JC, Adsay NV, Aretxabala X, et al. Intracholecystic papillary neoplasm of the gallbladder: clinicopathological analysis of 15 cases. Histopathology. 2006;48(6):701–708.

[6] Lester SC, Bose S, Chen YY, Connolly JL, de Baca ME, Fitzgibbons PL, Hayes DF, Kleer C, O'Malley FP, Page DL, Smith BL, Weaver DL, Winer E; Members of the Cancer Committee, College of American Pathologists. Protocol for the examination of specimens from patients with ductal carcinoma in situ of the breast. Arch Pathol Lab Med. 2009 Jan;133(1):15-25. doi: 10.5858/133.1.15. PMID: 19123730.

[7] Allred DC. Ductal carcinoma in situ: terminology, classification, and natural history. J Natl Cancer Inst Monogr. 2010;2010(41):134-8. doi: 10.1093/jncimonographs/lgq035. PMID: 20956817; PMCID: PMC5161057.

[8] World Health Organization. WHO Classification of Tumours: Breast Tumours. 5th ed. Lyon: IARC; 2019.