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CASE REPORT

Pancreatic cancer associated with gallbladder malignancy: coincidence or common genetic pathway?

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ABSTRACT

The synchronous occurrence of pancreatic adenocarcinoma and other primary tumors is rarely reported in the literature. We present the case of a 51-year-old woman diagnosed with adenocarcinoma of the pancreatic head associated with a papillary tumor of the gallbladder. The coexistence of these tumors poses significant diagnostic and therapeutic challenges, particularly in determining the optimal management sequence and the indication for combined surgical resection. This case underscores the importance of thorough preoperative assessment and meticulous intraoperative exploration in patients with pancreatic malignancies, as synchronous neoplasms—although uncommon—may significantly impact prognosis and therapeutic strategy. Furthermore, this report raises questions regarding potential shared etiological factors, including genetic predisposition, environmental exposures, and chronic inflammatory conditions, which may contribute to the concurrent development of multiple primary tumors. Recognition and reporting of such cases are essential to enhance our understanding of tumor biology and to inform clinical decision-making in complex hepatopancreatobiliary oncology. The aim of this article is to emphasize both the rarity of this association and the technical challenges involved in its management.

Keywords: *papillary tumor of the gallbladder, head* pancreatic adenocarcinoma, The coexistence of these tumors, synchronous tumors, prognostic.

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1. INTRODUCTION

Synchronous cancers are defined as malignant tumors arising within six months of the diagnosis of a first primary malignancy, whereas metachronous cancers develop beyond this six-month period. The occurrence of synchronous tumors in a single patient presents a substantial therapeutic challenge, often requiring carefully coordinated multidisciplinary management. Surgical intervention in such cases is frequently extensive, technically demanding, and associated with prolonged operative times (1,2). Over the past decades, the reported incidence of multiple primary cancers has increased, a trend largely attributable to advances in diagnostic imaging, improved surveillance strategies, longer life expectancy, and enhanced long-term survival of patients with cancer. Recognizing and appropriately managing these complex cases is critical, as the presence of synchronous tumors can significantly impact treatment planning, surgical strategy, and overall prognosis (3,4).

Informed consent was obtained from the patient for the publication of this case report and the accompanying images.

2. CASE REPORT

A 51-year-old male patient, known to have type 2 diabetes mellitus treated with oral hypoglycemic agents for the past three years, initially presented with symptoms consistent with hepatic colic. Physical examination demonstrated mild tenderness localized to the right upper quadrant.

Abdominopelvic ultrasonography followed by magnetic resonance imaging (MRI) identified a tumoral lesion of the gallbladder, located at the junction between the body and fundus, measuring approximately 17 × 13 mm. This lesion was associated with multiple lymphadenopathies involving the celiac region, hepatic pedicle, and retroportal area. These lymph nodes appeared confluent, forming a tumoral mass encasing and narrowing the hepatic artery. A thoraco-abdominopelvic computed tomography (CT) scan was subsequently performed. The patient underwent surgical management consisting of a bisegmentectomy involving segments IVb and V. Histopathological analysis of the resected specimen confirmed the diagnosis of a papillary carcinoma of the gallbladder.

Two months after surgery, the patient was readmitted with a marked deterioration of general condition, accompanied by diffuse mucocutaneous jaundice and severe epigastric pain. Laboratory investigations revealed a cholestatic pattern, while serum lipase levels remained within normal limits. Follow-up MRI demonstrated the presence of a poorly demarcated, irregular mass located in the head of the pancreas, measuring 53 × 35 × 57 mm. The lesion exhibited heterogeneous signal intensity with a central necrotic component and was associated with dilatation of both the main pancreatic duct and the intra- and extrahepatic bile ducts (double duct sign) [Figure 1].

Locally, the tumor showed infiltration of the retroportal lamina, circumferential contact exceeding 180° with the celiac trunk, and complete occlusion of the portal vein, rendering the lesion unresectable. The patient underwent endoscopic biliary drainage with placement of a plastic stent. A CT biopsy of the pancreatic mass confirmed pancreatic adenocarcinoma, and the patient was subsequently referred to the oncology department for consideration of palliative chemotherapy.

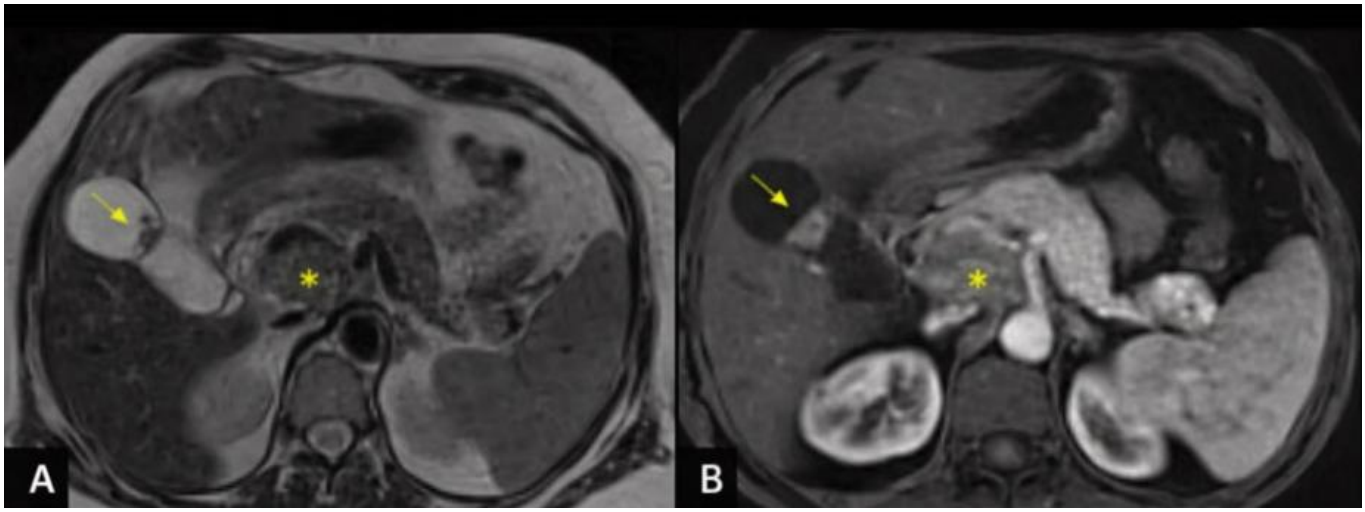

Figure 1. MRI of intracystic papillary neoplasm of the gallbladder (arrow) associated with pancreatic ductal adenocarcinoma (*) on T2 (A) and T1 with injection (B) sequences

3. DISCUSION

The synchronous occurrence of two primary malignancies within the hepatopancreatobiliary (HPB) system is uncommon and represents a significant diagnostic and therapeutic challenge. In particular, the association of gallbladder carcinoma and pancreatic ductal adenocarcinoma (PDAC) is extremely rare, with only isolated cases reported in the literature.

Multiple primary malignancies are generally classified as synchronous when diagnosed simultaneously or within six months and metachronous when diagnosed beyond this time interval (Warren and Gates criteria) (5). Synchronous tumors involving the pancreatobiliary tract account for a very small proportion of gastrointestinal cancers, reflecting both the relative rarity of these tumors and the complexity of their pathogenesis (6).

Gallbladder carcinoma is the most common malignancy of the biliary tract and is frequently associated with chronic inflammation related to gallstones, biliary infection, or congenital anomalies such as pancreaticobiliary maljunction (7). Histologically, several subtypes have been described, including adenocarcinoma, papillary carcinoma, and mucinous variants. Papillary carcinoma of the gallbladder represents a rare subtype, accounting for approximately 5–10% of gallbladder cancers, and is generally associated with a more favorable prognosis due to its exophytic growth pattern and lower propensity for deep invasion (8). In contrast, pancreatic ductal adenocarcinoma, particularly when located in the pancreatic head, remains one of the most aggressive gastrointestinal malignancies. It is characterized by early vascular invasion, rapid metastatic spread, and poor overall survival, with a 5-year survival rate typically below 10% in most series (9).

The coexistence of gallbladder carcinoma and pancreatic cancer raises several pathogenetic hypotheses. One possible explanation is the presence of a common carcinogenic pathway within the pancreatobiliary epithelium, which shares an embryological origin and similar exposure to bile and pancreatic secretions. Chronic inflammation and exposure to carcinogenic bile acids have been implicated in the development of malignancies along the biliary tree (10). Another proposed mechanism is the presence of pancreaticobiliary maljunction (PBM), a congenital anomaly characterized by an abnormal union of the pancreatic and bile ducts outside the duodenal wall. This condition allows reflux of pancreatic enzymes into the biliary system, resulting in chronic mucosal injury and increased risk of biliary tract cancers, particularly gallbladder carcinoma (11). However, PBM has also been associated with an increased incidence of pancreatic malignancies, suggesting a shared carcinogenic environment (12).

From a genetic perspective, pancreatobiliary cancers may share alterations in several oncogenic pathways, including KRAS, TP53, CDKN2A, and SMAD4, which are frequently mutated in pancreatic adenocarcinoma and have also been described in biliary tract cancers (13). These molecular similarities raise the possibility that synchronous tumors may arise through overlapping carcinogenic mechanisms rather than pure coincidence. Another explanation is the concept of field cancerization, whereby a large area of epithelium exposed to similar carcinogenic stimuli undergoes genetic alterations, predisposing it to the development of multiple independent tumors within the same anatomical region (14).

Clinically, the diagnosis of synchronous pancreatobiliary tumors can be difficult. Imaging studies such as contrast-enhanced CT, MRI, and endoscopic ultrasound may identify both lesions, but in many cases the second tumor is discovered incidentally during surgery or on histopathological examination (15). Distinguishing between synchronous primary tumors and metastatic disease is essential, as this distinction significantly impacts staging and therapeutic strategy.

Surgical management remains the cornerstone of treatment when both tumors are resectable. In selected cases, extended resections, including pancreaticoduodenectomy combined with radical cholecystectomy or hepatic resection, have been reported (16). However, such procedures are associated with increased operative complexity and require careful patient selection. The prognosis of patients with synchronous pancreatobiliary malignancies largely depends on the stage and biological behavior of the pancreatic cancer, which typically dictates overall survival. Nevertheless, early-stage papillary gallbladder carcinoma may have a relatively favorable outcome if completely resected (8,16,17).

4. CONCLUSION

The synchronous occurrence of papillary gallbladder carcinoma and pancreatic head adenocarcinoma is exceptionally rare. The association may reflect shared embryological origin, chronic inflammatory processes, genetic alterations, or field cancerization within the pancreatobiliary tract. Recognition of this rare entity is important for accurate diagnosis, appropriate surgical planning, and better understanding of the carcinogenesis of pancreatobiliary malignancies. We must maintain the highest level of preoperative vigilance by systematically searching for any associated lesions or locoregional extension in order to avoid underestimating the disease and to adapt the surgical strategy from the outset.

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