COLLISION TUMOUR: ADENOCARCINOMA OF GALLBLADDER WITH LEIOMYOSARCOMA

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ABSTRACT
Collision tumours, characterized by the synchronous growth of two distinct tumour types, are exceedingly rare. This report presents a case of a collision tumour involving adenocarcinoma of the gallbladder and leiomyosarcoma. A 75-year-old male presented with a 4-day history of vomiting, persistent hiccups, fever, and right upper abdominal pain. Physical examination revealed abdominal distension, tenderness, and positive Murphy's sign, with localized tenderness in the right hypochondrium. Ultrasound performed prior to admission identified multiple echogenic gallbladder calculi. Contrast-enhanced CT of the abdomen showed moderate ascites, multiple large radiopaque calculi, and bilateral mild perinephric fat stranding. During laparotomy, dense adhesions, necrotic tissue surrounding the gallbladder, and nodules on the omentum were observed. A subtotal cholecystectomy was performed. Histopathological examination revealed a well-differentiated adenocarcinoma of the gallbladder infiltrating all layers, along with leiomyosarcoma involving the omental nodules. This case underscores the rare coexistence of two distinct malignancies within a single clinical presentation, highlighting the importance of thorough histopathological evaluation in similar scenarios.

Introduction:

Collision tumours are an uncommon phenomenon characterized by the synchronous occurrence of two histologically distinct tumour types within the same anatomical region(1). While these tumours can arise in various organ systems, they are particularly rare in the gallbladder, where malignancies are predominantly represented by adenocarcinomas. Gallbladder adenocarcinoma is the most common biliary tract malignancy, acc(2)ounting for approximately 85-90% of cases. On the other hand, leiomyosarcomas are rare mesenchymal tumours, comprising only 5-10% of all soft tissue sarcomas. The simultaneous presentation of these two malignancies in the form of a collision tumour has not been documented before, making this case unique and clinically significant.

The gallbladder, an organ primarily associated with bile storage, is not typically a site for dual tumour pathology. Adenocarcinomas of the gallbladder often develop in the context of chronic inflammation, gallstones, or other risk factors(3). Leiomyosarcoma, however, is a soft tissue sarcoma originating from smooth muscle cells and is more commonly seen in the uterus, gastrointestinal tract, or retroperitoneum. The occurrence of these two distinct tumour types in close proximity suggests complex and as yet poorly understood pathogenic mechanisms(4). This case report highlights the first documented instance of a collision tumour involving gallbladder adenocarcinoma and leiomyosarcoma, underscoring the importance of histopathological evaluation in accurately diagnosing and managing such rare and intricate clinical entities.

Case History

A 75-year-old male presented with a 4-day history of vomiting, persistent hiccups, right upper abdominal pain, and fever. There was no history of loose stools. The patient reported difficulty in breathing over the past 10 days. He was a known case of diabetes for the last 10 years and hypertension for 5 years. On examination, the patient was conscious, oriented, and afebrile. His respiratory rate was 24/min, and blood pressure was 160/60 mmHg. Cardiovascular and respiratory system examinations revealed no abnormalities. The abdomen was distended and tender, with localized tenderness in the right hypochondrium. Murphy's sign was positive. Capillary blood glucose was 173 mg/dl, and arterial pO2 was 94% on room air.

An ultrasound conducted 4 days before admission revealed multiple echogenic gallbladder calculi ranging from 5 to 13 mm in size. The gallbladder wall was thickened and edematous, with pericholecystic fluid and free peritoneal fluid. Prostatomegaly was also noted. A diagnosis of acute calculous cholecystitis was made. On admission, CT of the abdomen showed moderate ascites and multiple large radio-opaque calculi clustered within the gallbladder lumen. Bilateral mild perinephric fat stranding was observed. The liver appeared normal. CT chest imaging revealed cystic bronchiectatic changes with associated fibrosis in the right upper and lower lobes. Echocardiography showed no regional wall motion abnormality, left ventricular ejection fraction of 63%, Grade I diastolic dysfunction, concentric left ventricular hypertrophy, and mild mitral regurgitation. A sclerosed aortic valve was noted.

Following anesthetic evaluation, the patient was taken up for laparoscopic cholecystectomy. During surgery, 500 ml of straw-colored fluid was aspirated and sent for analysis. Due to dense adhesions and extensive inflammation, laparoscopy was converted to an exploratory laparotomy. The abdomen appeared plastered with dense adhesions to the gallbladder, necrotic tissue adherent to the gallbladder, suspected empyema, and nodules over the omentum. A subtotal cholecystectomy was performed as dense adhesions surrounded the cystic duct. Post-operatively, the patient was shifted to the ICU and developed acute renal failure with serum creatinine of 2.4 mg/dl. After consultation with a nephrologist and adequate hydration, the creatinine levels dropped to 1.4 mg/dl. The patient was started on a liquid diet and shifted to the ward. However, on the fourth postoperative day, the patient experienced a seizure and was returned to the ICU. CT of the brain showed no significant abnormalities, and serum electrolytes were within normal limits. Following stabilization, the patient's relatives requested discharge. At discharge, the patient was conscious, oriented, and afebrile, with a pulse of 104/min, BP of 160/90 mmHg, SpO2 of 99% on 2 liters of oxygen/min, and a distended abdomen. Unfortunately, the patient succumbed to the illness on the 10th postoperative day.

Pathological analysis:

Cytopathology of ascitic fluid smears revealed predominantly lymphocytes, with no atypical cells identified. The histopathology laboratory received nine tissue samples of grey-brown color,

ranging in size from 5.2 × 3 × 1.5 cm to 1.1 × 0.5 × 0.3 cm. The largest specimen, suspected to be the fundus of the gallbladder, showed papillary excrescences. The gallbladder wall measured 0.6 cm in thickness, and multiple faceted pigmented gallstones were observed. Microscopic examination of the gallbladder wall revealed atypical glands lined by cells with vesicular nuclei, moderate cytoplasm, and marked pleomorphism. There was loss of polarity and areas of intestinal metaplasia. The tumour infiltrated all layers of the gallbladder, extending into the surrounding fat(figure 1). Tumour involvement of Rokitansky-Aschoff sinuses was noted. Mitotic activity was increased (2-3/hpf), and biliary calculi were present. Attached hepatic tissue appeared unremarkable. Other tissue samples revealed retroperitoneal fat infiltrated by spindle cells arranged in sheets and a storiform pattern(figure 2). These cells exhibited round-to-oval vesicular nuclei with blunt ends, prominent nucleoli, and moderate cytoplasm. Marked pleomorphism, raisinoid nuclei, bizarre cells, and multinucleated giant cells were observed, along with infiltrating lymphocytes(figure 3).

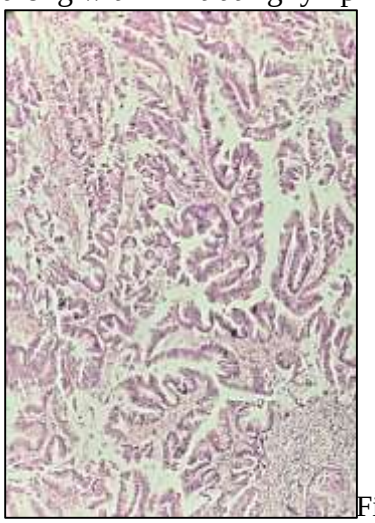

Fig 1-Haematoxylin and eosin stained slide (10X)-showing adenocarcinoma of the gall bladder.

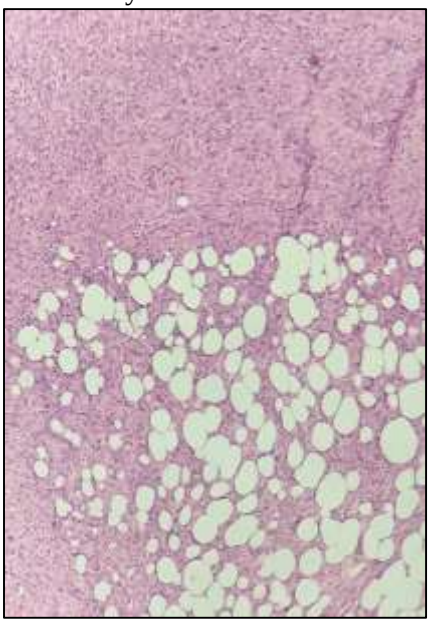

Fig2- Haematoxylin and eosin stained slide (10X)-showing adjacent omentum with a high grade leiomyosarcoma

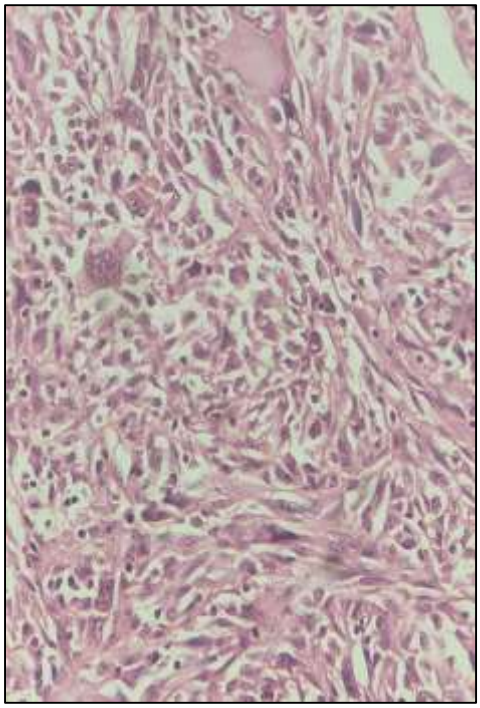

Fig 3-Haematoxylin and eosin stain(10X10 X) of Leiomyosarcoma

Fig 4-Immunohistochemistry for Epithelial membrane antigen(10X) showing positivity in the Adenocarcinoma component.

Fig 5-Immunohistochemistry for Desmin(10X) showing positivity in the leiomyosarcoma component

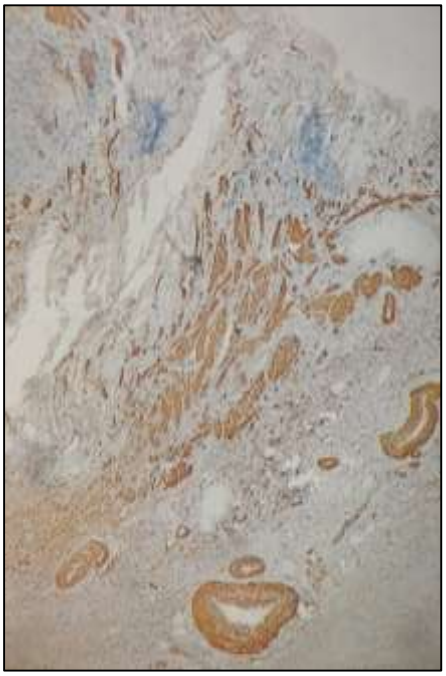

Fig 6-Immunohistochemistry for Smooth muscle cell actin(10X) showing positivity in the leiomyosarcoma component.

Histopathological examination concluded a diagnosis of poorly differentiated adenocarcinoma of the gallbladder infiltrating all layers, with pathological staging as pT4. Retroperitoneal fat showed an aggressive neoplasm composed of spindle cells. Both tumour types were separated by fibro-muscular tissue, suggesting distinct origins. A panel of immunohistochemical stains (figure 4,5,6) was conducted, including EMA, CK7, Vimentin, S100, SMA, and CD117. The gallbladder neoplasm was positive for EMA and CK7 but negative for SMA, S100, Vimentin, and CD117, confirming its epithelial origin. In contrast, the omental deposits were negative for EMA and CK7 but showed strong cytoplasmic staining for SMA, indicative of smooth muscle

origin. S100, Vimentin, and CD117 were negative in the omental neoplasm. These findings confirmed the diagnosis of leiomyosarcoma in the omental deposits. The final diagnosis was a rare collision tumour composed of gallbladder adenocarcinoma and leiomyosarcoma. This case underscores the importance of detailed histopathological and immunohistochemical evaluation to distinguish between coexisting neoplasms and determine appropriate management strategies.

Discussion

The histological findings in this case demonstrated two distinct malignant neoplasms, one located in the gallbladder and the other in the omentum. Determining whether these neoplasms represented a single entity or a collision tumour involving two different tumours required careful investigation, especially given their separation by fibro-muscular tissue. The morphological differences between the two tumours were striking: the gallbladder neoplasm was an adenocarcinoma, while the omental tumour exhibited features of an aggressive spindle-cell neoplasm. To ascertain their independent origins and exclude the possibility of a dedifferentiated gallbladder adenocarcinoma infiltrating the omentum, a panel of immunohistochemical stains(3,5,6) was performed. The results confirmed the gallbladder neoplasm as adenocarcinoma with positivity for epithelial markers EMA and CK7, while the omental tumour was negative for these markers. Conversely, the omental tumour showed strong cytoplasmic staining for SMA, confirming its smooth muscle origin and identifying it as leiomyosarcoma(7,8). Other markers, including S100, Vimentin, and CD117, were negative. This immunohistochemical profile established that the two neoplasms were distinct entities, supporting the diagnosis of a collision tumour.

Leiomyosarcoma originating from retroperitoneal fat is a rare finding, and in this case, no other primary site for the tumour could be identified radiologically or during surgery. The separation of the two tumours by fibro-muscular tissue further supported their independent origins. The presence of two distinct neoplasms in close proximity underscores the rarity of collision tumours, and to the best of our knowledge, this is the first documented case of a collision tumour involving gallbladder adenocarcinoma and leiomyosarcoma. This case highlights the importance of histopathological and immunohistochemical evaluations in accurately diagnosing such complex cases, as they provide essential insights into tumour differentiation, origins, and potential behaviour. The use of immunohistochemistry not only helped delineate the tumours' unique characteristics but also provided a clear framework for understanding their pathogenesis.

Collision tumours are uncommon and pose significant diagnostic and therapeutic challenges. A review of the literature reveals several examples of collision tumours, each involving distinct tumour types and sites. For instance, a case of pancreatic adenocarcinoma colliding with retroperitoneal liposarcoma was documented, where the pancreatic tail tumour was an adenocarcinoma, and the retroperitoneal mass demonstrated atypical lipomatous cells and lipoblasts confirmed as liposarcoma through MDM2 amplification(9). Another unique example involved hepatoid carcinoma and colonic adenocarcinoma, where the hepatoid carcinoma likely originated from ovarian remnants left behind after a prior hysterectomy(10,11). In both cases, the tumours were morphologically distinct and separated by fibrous tissue, emphasizing the importance of histological differentiation. Similarly, a collision tumour involving colonic adenocarcinoma arising in a sigmoid diverticulum and a recurrent ovarian granulosa cell tumour has been reported(12). The patient, unfortunately, succumbed to lung metastases from the ovarian tumour within six months of diagnosis, illustrating the aggressive nature of such tumours.

Other reports include mixed adenoneuroendocrine carcinoma (MANEC) of the pancreas, consisting of adenocarcinoma and neuroendocrine carcinoma components, coexisting with gastrointestinal stromal tumours (GISTs) in the duodenum(13,14). Immunohistochemistry revealed distinct profiles for the GISTs, confirming their unique origin and behaviour(15). Collision tumours involving mantle cell lymphoma with pancreatic adenocarcinoma and pancreatic ductal adenocarcinoma (PDAC) with neuroendocrine tumours (NET) have also been described(16,17). In one notable case, an axillary lymph node showed metastasis from two distinct tumours: malignant melanoma and leiomyosarcoma(18). Such cases emphasize the importance of distinguishing between primary tumours and metastases in clinical practice. Additional examples include a collision tumour of bile duct and pancreatic adenocarcinomas(19–21) and a rare case of intracranial collision tumours involving meningioma and glioblastoma at adjacent sites in the cerebral hemisphere(22). These reports underline the rarity and complexity of collision tumours, necessitating a multidisciplinary approach to diagnosis and management.

The growing body of literature on collision tumours highlights their diverse presentations and clinical implications. Cases such as collision tumours of gastric GIST and pancreatic adenocarcinoma, solitary concomitant endocrine tumours, and ductal adenocarcinoma of the pancreas further emphasize the complexity of diagnosing and managing such cases(23,24). The role of immunohistochemistry in delineating tumour types is crucial, as seen in our case, where markers like EMA, CK7, and SMA provided definitive insights into the nature of the neoplasms. This case not only contributes to the understanding of collision tumours but also emphasizes the importance of thorough histopathological evaluation, immunohistochemical studies, and detailed clinical correlation in reaching an accurate diagnosis(25). By documenting this rare case, we aim to provide a reference for future cases and expand the existing knowledge base on collision tumours, ultimately improving diagnostic accuracy and patient outcomes.

Conclusion:

This case highlights a rare occurrence of a collision tumour comprising gallbladder adenocarcinoma and omental leiomyosarcoma, emphasizing the importance of thorough histopathological and immunohistochemical evaluations in distinguishing between distinct neoplasms. The morphological and immunohistochemical differences observed in this case ruled out dedifferentiation and confirmed the independent origins of the two tumours. This is the first reported instance of such a collision tumour, contributing valuable insights to the understanding of its diagnosis and pathogenesis. Early recognition and accurate identification of collision tumours are critical for guiding appropriate therapeutic strategies and improving patient outcomes.

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Conflict of Interest: None declared

References:

1. Arora V, Yadav V, Aggarwal M, Mandal G, Chakraborty A, Dewan AK, et al. Collision Tumour of Combined Neuroendocrine and Squamous Cell Carcinoma of Nasal Cavity and Paranasal Sinus- Case Report and Review of Literature. Indian J Otolaryngol Head Neck Surg. 2023 Dec;75(4):3765–9.
2. Park G, Park WS, Lee SK, Kim JO. A rare collision tumor comprising intracystic papillary neoplasm associated with adenocarcinoma and angiosarcoma in the gallbladder. Korean J Intern Med. 2020 May;35(3):732–3.

3. Dedopoulou P, Rodis N, Lampropoulos C, Kitsou KS, Mpogiatzopoulos N, Kehagias I. Synchronous Primary Gallbladder and Colon Adenocarcinoma: A Case Report and Systematic Literature Review. Cureus. 2024 Sep;16(9):e69092.
4. El-Boghdadly SA, Alshareef AM, Almisfer AK, Momen IM. Diagnosis and management of sigmoid leiomyosarcoma presenting with intussusception: a case report. J Surg Case Rep. 2024 Dec;2024(12):rjae795.
5. Hirose K, Omori Y, Ono Y, Mizukami Y, Kaneko Y, Maruyama T, et al. Molecular comparison of concurrent components of high-grade dysplasia, adenocarcinoma, and sarcomatoid carcinoma in a case of sarcomatoid carcinoma of the gallbladder. Virchows Arch. 2023 Aug;483(2):261–6.
6. Yadav K, Agarwal P, Kumar M, Gupta S, Mishra M, Maurya MK, et al. Immunohistochemical appraisal of epithelial mesenchymal transition type III in gall bladder cancer. Indian J Pathol Microbiol. 2023 Jan-Mar;66(1):44–53.
7. Momeni-Boroujeni A, Nucci MR, Chapel DB. Risk Stratification of Uterine Smooth Muscle Tumors: The Role of Morphology, Immunohistochemistry, and Molecular Testing. Adv Anat Pathol. 2025 Jan 1;32(1):44–56.
8. Dudhe SS, Mishra GV, Parihar P, Nimodia D, Kumari A, Shinde D. Leiomyosarcoma of the Duodenum: A Case Report on a Rarely Encountered Tumor. Cureus. 2024 Jul;16(7):e65182.
9. Buchner D, Hieggelke L, Löser H, Bruns CJ, Quaas A, Ghadimi MPH. First reported case of a collision tumor composed of pancreatic adenocarcinoma and retroperitoneal liposarcoma: a case report. BMC Cancer. 2018 Dec 12;18(1):1243.
10. Gopaldas R, Kunasani R, Plymyer MR, Bloch RS. Hepatoid malignancy of unknown origin--a diagnostic conundrum: review of literature and case report of collision with adenocarcinoma. Surg Oncol. 2005 Jul;14(1):11–25.
11. Choi WK, Cho DH, Yim CY, Lee NR. Primary hepatoid carcinoma of the ovary: A case report and review of the literature. Medicine (Baltimore). 2020 May;99(19):e20051.
12. Brahmania M, Kanthan CS, Kanthan R. Collision tumor of the colon--colonic adenocarcinoma and ovarian granulosa cell tumor. World J Surg Oncol. 2007 Oct 20;5:118.
13. Ferrando Marco J, Pallas Regueira A, Moro Valdezate D, Fernández Martínez C. [Collision tumor of the ampulla of Vater: carcinoid and adenocarcinoma]. Rev Esp Enferm Dig. 2007 Apr;99(4):235–8.
14. Williams IM, Williams NW, Stock D, Foster ME. Collision tumour of the ampulla of Vater: carcinoid and adenocarcinoma. HPB Surg. 1997;10(4):241–4.
15. Aigner B, Kornprat P, Schöllnast H, Kasparek AK, Mischinger HJ, Haybaeck J. A Case of Focal Small-cell Neuroendocrine Carcinoma in the Vicinity of the Extrahepatic Bile Duct, Adjacent to an Extensive Biliary Intraepithelial Neoplasm: A Diagnostic Challenge with Major Clinical Implications. Anticancer Res. 2015 Sep;35(9):4821–8.
16. Serafini S, Da Dalt G, Pozza G, Blandamura S, Valmasoni M, Merigliano S, et al. Collision of ductal adenocarcinoma and neuroendocrine tumor of the pancreas: a case report and review of the literature. World J Surg Oncol. 2017 May 2;15(1):93.
17. Dasanu CA, Shimanovsky A, Rotundo EK, Posteraro AF, Cooper DL, Atienza JA. Collision tumors: pancreatic adenocarcinoma and mantle cell lymphoma. JOP. 2013 Jul 10;14(4):458–62.
18. Ul-Mulk J, Rasmussen H, Breiting L, Siim E. A case of collision tumor or transdifferentiation between malignant melanoma and leiomyosarcoma. Indian J Pathol Microbiol. 2012 Oct-Dec;55(4):538–9.

19. Izumi H, Furukawa D, Yazawa N, Masuoka Y, Yamada M, Tobita K, et al. A case study of a collision tumor composed of cancers of the bile duct and pancreas. Surg Case Rep. 2015 Dec;1(1):40.
20. Haratake J, Hashimoto H. An immunohistochemical analysis of 13 cases with combined hepatocellular and cholangiocellular carcinoma. Liver. 1995 Feb;15(1):9–15.
21. Porcell AI, De Young BR, Proca DM, Frankel WL. Immunohistochemical analysis of hepatocellular and adenocarcinoma in the liver: MOC31 compares favorably with other putative markers. Mod Pathol. 2000 Jul;13(7):773–8.
22. Chamberlin K, Chamberlin G, Saunders K, Khagi S. Next-generation sequencing reveals novel mutations in a collision tumor of glioblastoma and meningioma. CNS Oncol. 2021 Jun 1;10(2):CNS70.
23. Abbas N, Zahreddine L, Tawil A, Natout M, Shamseddine A. An Atypical Case of Pancreatic Cancer with Mesenchymal Differentiation in a Patient with Primary Lung Adenocarcinoma: Insights into Tumor Biology and Novel Therapeutic Pathways. Diagnostics (Basel) [Internet]. 2024 Nov 9;14(22). Available from: http://dx.doi.org/10.3390/diagnostics14222512
24. Read C, Hughes M, Itani O. Presentation of Gastrointestinal Stromal Tumor, Pancreatic Adenocarcinoma, and Gastric Adenocarcinoma in a Woman With No Identifiable Genetic Abnormalities. Am Surg. 2023 Dec;89(12):6393–5.
25. Wang X, Zhou Y, Zhang W, Li Y, Ma Y, Liu P. A Rare Collision of Endometrioid Adenocarcinoma and Second Recurrent Low-Grade Endometrial Stromal Sarcoma 8 Years After Hysterectomy: A Case Report and Literature Review. Int J Surg Pathol. 2024 Nov 18;10668969241295356.