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## LETTER TO THE EDITOR

## Recurrence of gallbladder carcinoma 12 years after laparoscopic cholecystectomy

**KEYWORDS**

Incidental gallbladder cancer;  
Recurrence;  
Colon cancer;  
Differential diagnosis;  
Surgery

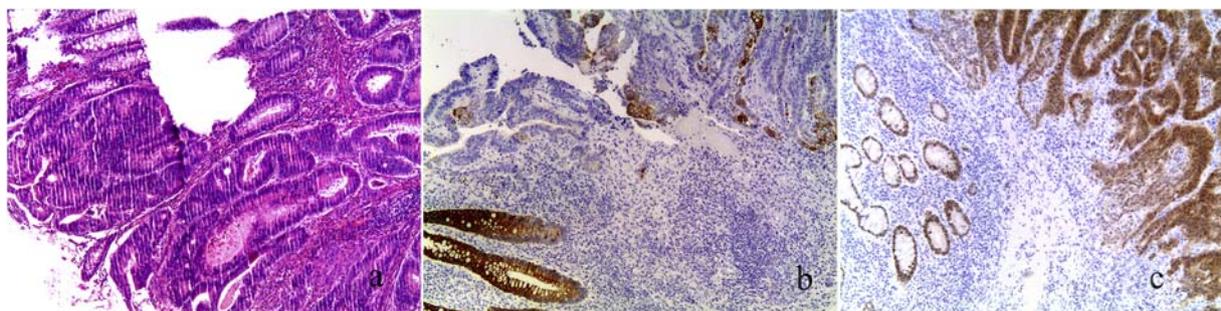
Dear editor,

Owing to the widespread diffusion of laparoscopic procedures, an increasing number of unexpected gallbladder cancer has been reported. In order to improve outcome, re-resection may be required depending on the depth of invasion. Development of recurrences is usually an early event associated with poor prognosis but those occurring several years after surgery are extremely rare. In these cases, the synchronous discovery of a colon cancer may pose difficulty in the differential diagnosis of metastatic lesions. Radical surgical resection is the only chance to relieve symptoms and prolong survival in selected cases. We report a case of abdominal recurrence following resection of incidental gallbladder carcinoma (IGC), occurring 12 years after laparoscopic cholecystectomy in a patient with synchronous right colon adenocarcinoma (ADC).

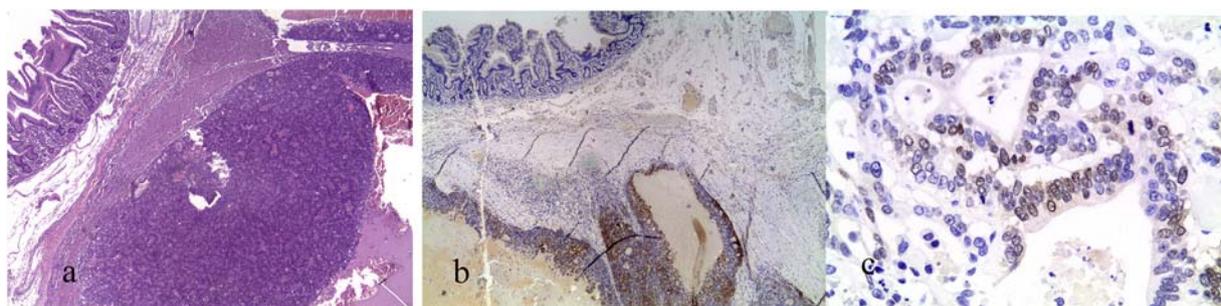
A 78-year-old woman was referred to our department with a two-month history of enlarging, painless mesogastric mass and fatigue. Past medical history included laparoscopic cholecystectomy for cholelithiasis twelve years before. Histology revealed papillary IGC, spreading to the submucosal layer (pT2). Open liver bed dissection and hepato-duodenal ligament lymphadenectomy were performed one month later, without evidence of residual disease. At admission, physical examination revealed a firm and fairly well-circumscribed mesogastric lesion. Laboratory data including tumor markers were within the normal range. Computed tomography (CT) scan demonstrated a 5.5 cm

lobulated mass between the abdominal wall and transverse colon, showing partial necrosis and heterogeneous contrast enhancement, with few small satellite nodules. A similar 2.5 cm bilobated lesion within the incisional wound was also evident. Positron emission/computed tomography (PET/CT) showed increased focal uptake in the mass (SUV maximum 10), within the incisional scar (SUV maximum 8.2) and in the right colon (SUV maximum 8.1). Colonoscopy revealed a 3 cm ulcerated firm lesion in the cecum and biopsy was positive for ADC. A preliminary laparoscopy showed an omental mass located between the abdominal wall and transverse colon with satellite nodules, the lesion in the abdominal scar and a small nodule located in the proximal small bowel, without evidence of peritoneal carcinomatosis and liver metastases. Peritoneal washing was negative for malignancy. One week later, the patient underwent right enlarged hemicolectomy, omentectomy, segmental small bowel resection and excision of the abdominal parietal nodule. Histology of the colon tumor revealed moderately differentiated ADC, infiltrating the muscular layer (pT2) with negative lymphnodes (Fig. 1A). Immunohistochemical staining was positive for CK 20 (Fig. 1B) and CDX2 (Fig. 1C) and negative for CK 7. The omental and other excised nodules were moderately differentiated papillary ADC at histology (Fig. 2A). Immunohistochemical staining was strongly positive for CK 7 (Fig. 2B), positive for CK 20, weakly positive for CDX2 (Fig. 2C) and negative for MUC 1, consistent with gallbladder origin. Postoperative course was uneventful and the patient was discharged 10 days after surgery. The patient received adjuvant chemotherapy with capecitabine and she is currently alive without evidence of disease at 6 months. Informed consent was obtained from the patient.

Laparoscopic cholecystectomy is the gold standard treatment for benign gallbladder disease. The diffusion of this procedure increased the number of IGC discovered with an estimated incidence of 0.2–3% of all cholecystectomies [1]. Revision surgery for definitive treatment depends on tumor stage. Approximately 53.4–66.9% of cases show perimuscular connective tissue involvement (pT2) [1,2]. Treatment of these patients includes bed excision or a more extensive liver resection and lymphnode dissection of the hepato-duodenal ligament. Beyond survival improvement, accurate stage of the disease is another target of surgery. Since up



**Figure 1** A. Histology showing moderately differentiated ADC (H&E  $\times 5$ ). B. Immunohistochemical analysis positive for CK20 ( $\times 5$ ). C. Immunohistochemical analysis positive for CDX2 ( $\times 10$ ).



**Figure 2** A. Histology showing moderately differentiated papillary ADC (H&E  $\times 10$ ). B. Immunohistochemical analysis strongly positive for CK7 ( $\times 10$ ). C. Immunohistochemical analysis weakly positive for CDX2 ( $\times 40$ ).

to 60% of these patients may have positive lymphnodes, without dissection adequate staging will be not possible [2]. The presence of residual disease (RD) after resection has been reported in up to 61% of cases and it is associated with poor disease-specific survival [1,2]. Other significant prognostic factors are tumor location, depth of invasion, lymph nodes status and lymphovascular or neural invasion. In absence of RD prognosis is good, with reported 5-year survival rates ranging from 64.6% to 81.6% [2,3]. Wound recurrence is an uncommon complication, usually occurring with a median time of 7 months and it associated with advanced disease and poor outcome. In the largest series reported, all patients with wound metastasis died, showing a median survival of 10 months [4]. Only sporadic cases of late type recurrence after GC resection have been described, with interval time between 4 and 11 years [5,6]. Since cell implants can survive, intraoperative careful handling of the specimen is mandatory to avoid this complication. Wound protection measures such as avoiding bile spillage and use of retrieval bags, should be employed to minimize tumor seeding. Complete surgical resection is the only chance to relieve symptoms and prolong survival in selected cases. Limited data support the use of neoadjuvant and/or adjuvant chemotherapy/radiotherapy in these patients [2].

Beyond the long interval of time, another feature unique to our patient is the incidental synchronous of a right colon ADC. In this event, the differential diagnosis of metastatic lesions could be challenging and should be obtained by a combination of morphologic and immunohistochemical data. Both the CK7–/CK20+ phenotype with the diffuse and strong expression of CDX2 are considered highly specific

and sensitive markers of colorectal origin. In comparison, the CK7+/CK20+ immunoprofile is commonly present in biliary tract tumors and the combination with focal and weak expression of CDX2 favours extra-intestinal origin [7]. Papillary ADC of the gallbladder accounts for approximately 5% of cases and it is associated with a better prognosis [8]. MUC 1 expression has been associated with significant decreased survival [9], while CDX2 expression has been associated with increased survival [10]. Papillary subtype, lack of MUC 1 expression and CDX2 expression may represent biologic features partially explaining the favourable clinical behaviour in our case.

In conclusion, recurrences occurring several years after IGC resection are extremely rare. The synchronous discovery of a colon ADC may pose a challenge in the differential diagnosis of metastatic lesions. The correct diagnosis could be obtained by a combination of morphologic and immunohistochemical data. Surgical resection may improve quality of life and provide a survival advantage in selected cases.

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## Authors' contribution

FC and MV designed the report and critically revised the manuscript; OF and MG searched literature data; FC, MV and MD analysed and interpreted data; FC drafted the manuscript. All authors have approved the final article.

## Disclosure of interest

The authors declare that they have no competing interest.

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