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Case Report

Gallbladder Cancer in a Liver Transplant Patient

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Abstract

Gallbladder cancers are relatively rare malignancies. While early-stage cases can achieve good outcomes with cholecystectomy, the 5-year survival rate in advanced stages is extremely low. Primary sclerosing cholangitis is a progressive liver disease characterized by inflammation of the bile ducts and is associated with an increased risk of gallbladder cancers.

A 32-year-old male patient with primary sclerosing cholangitis was referred for liver transplantation. Imaging revealed a suspicious polypoid lesion, 2.5 cm in diameter, in the gallbladder. With a Meld score of 30, the patient was placed on the transplant waiting list. After waiting period of one month a deceased donor liver transplant was performed. The hepatectomy specimen revealed T2 gallbladder cancer. No recurrence or metastasis was detected during 1 year of follow-up.

There is no consensus on the management of suspicious gallbladder lesions in patients with primary sclerosing cholangitis. Cholecystectomy in these patients carries a risk of decompensation in cirrhosis. Considering the decompensated liver cirrhosis and high Meld score, we preferred transplantation over cholecystectomy. Therefore, liver transplantation can be considered as primary treatment option instead of cholecystectomy.

Keywords: Gallbladder cancer, primary sclerosing cholangitis, liver transplantation.

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Gallbladder cancer (GBC) is the most common malignancy of the biliary tract and the fifth most common malignancy of the gastrointestinal system.[1] Except for those detected incidentally during elective cholecystectomies, the prognosis is generally poor. While gallstones and polyps are considered possible etiological factors, the exact causes remain unclear. Early-stage curative resections are effective, but oncological treatments in advanced stages have limited impact on overall survival.

Primary sclerosing cholangitis (PSC) is a chronic and progressive liver disease that affects the bile ducts. It is characterized by inflammation, strictures, and fibrosis in the intra- and extrahepatic bile ducts.[2] PSC is associated with hepatobiliary malignancies, colorectal cancer, and inflammatory bowel diseases. Liver transplantation (LT) is the most effective treatment for patients with cirrhotic livers due to PSC.[3]

There are limited reports in the literature of liver transplant patients with coexisting PSC and GBC. In this report, we present a patient with PSC and GBC who underwent LT.

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Case Report

A 32-year-old male patient who had been followed up in gastroenterology department due to PSC and ulcerative colitis for about 7 years was referred to our clinic for transplantation, with no history of other comorbidities or previous surgery with. He had a history of recurrent endoscopic retrograde cholangio pancreatography (ERCP) and stenting and was using ursodeoxycholic acid (UDCA) and azathioprine. Laboratory tests showed a Meld (Model for End-stage Liver Disease) score of 30. Ultrasonography (USG) showed an asymmetric increase in gallbladder fundus thickness up to 2.5 cm in addition to the findings of chronic liver disease. Computed tomography (CT) and magnetic resonance imaging (MRI) showed cirrhotic liver and suspicious polypoid lesions measuring 2.5 cm in size in the gallbladder (Fig. 1). A cholecystectomy was not considered because of the risk of decompensation due to high Meld score and poor liver parenchyma. The patient with an patent portal vein was placed on the deceased donor waiting list because of lack a living donor. After 1 month on the waiting list, the patient was hospitalized due to decompensation and was under medical treatment when a deceased donor organ was presented. With a Meld score 30, the patient underwent LT. The gallbladder appearance was normal. There were no early post-transplant complications and histopathologic examination of the liver revealed cirrhosis with an etiology compatible with PSC. The gallbladder showed adenocarcinoma with a size of 3.5x2.5x1.5 cm. The pathologic stage of the patient with clear surgical margins and no lymphovascular and perineural invasion was T2aN0Mx (Figs. 2 and 3). No distant organ metastasis was detected in the scans and no oncologic treatment was given. Due to malignancy, everolimus was started in addition to tacrolimus in immunosuppression treatment. The patient continued with dual treatment and no recurrence or metastasis was observed 1-year follow-up (Fig. 4).

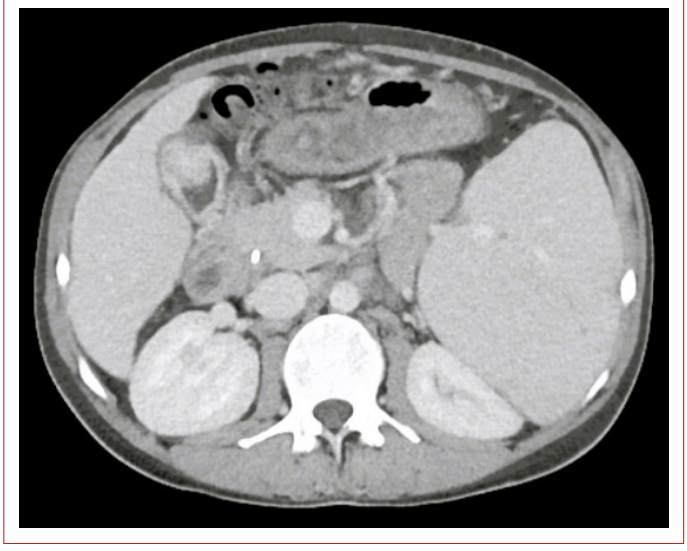

Figure 1. Preoperative polypoid lesion in the gallbladder.

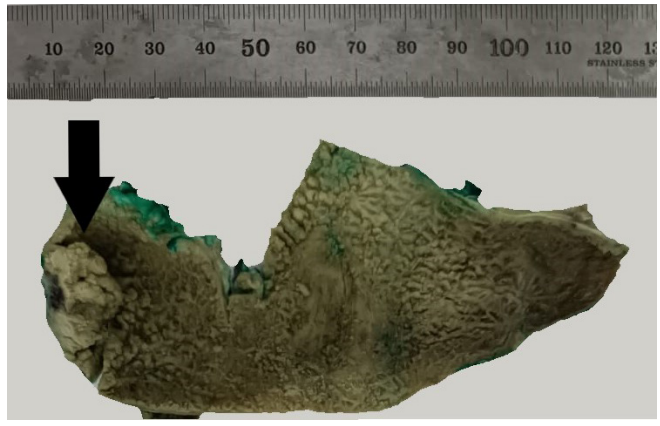

Figure 2. Polypoid tumoral lesion located in the fundus (arrow).

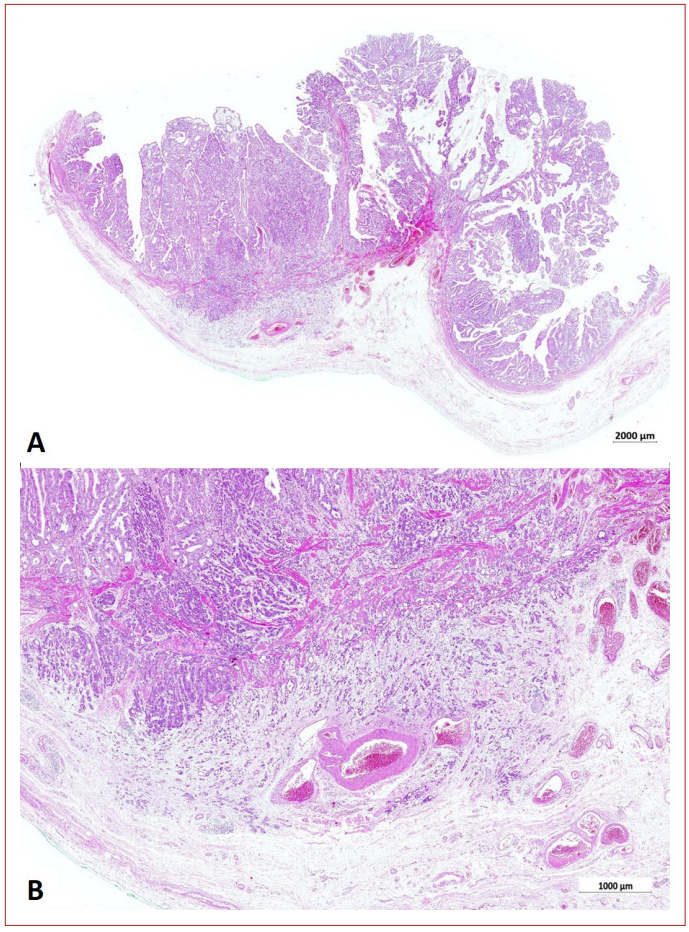

Figure 3. (a) Invasive adenocarcinoma (arrow) developing in the gallbladder on the background of intracholecystic papillary neoplasm with polypoid appearance (H&E; 10x). **(b)** Tumoral cells forming glandular structures invade the perimuscular connective tissue on the peritoneal side (H&E; 100x).

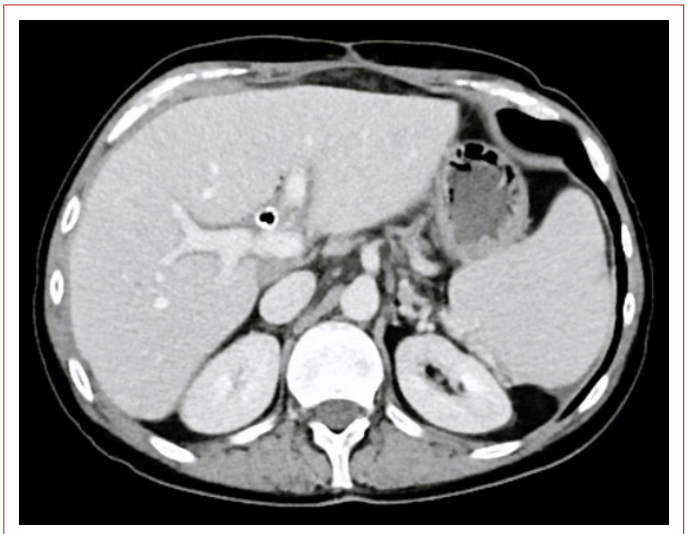

Figure 4. CT image of the patient 1 year after transplantation. Stent inserted due to biliary stricture.

Discussion

GBC is a malignancy with an aggressive course and poor prognosis. The 5-year survival of patients is between %5-15.[4] The worldwide incidence of this relatively rare disease is 2.5 per 100,000 people and is higher in women than in men. Gallstones are significantly associated with an increased risk of GBC. At the time of diagnosis, %90 of patients have stones.[5] Other risk factors include polyps and PSC disease. Especially in patients with PSC, the malignancy risk of gallbladder polyps has been found between %40-60.[6] In the early stage, patients mostly remain asymptomatic and are diagnosed as incidental in the imaging studies or elective cholecystectomies. Approximately %0.7 GBC has been reported in pathologic examination performed after cholecystectomy. The only curative treatment option for GBC is R0 resection.[7] While cholecystectomy is sufficient for T1 and T2 tumors, extensive resections and lymph node dissection are required for T3 and T4 tumors. It has been reported that depth of invasion and lymph node involvement are prognostic indicators for survival.[8]

PSC is a progressive liver disease involving the biliary tract and progressing to cirrhosis. It is known that the incidence of extrahepatic hilar cholangiocarcinoma and GBC are increased in PSC. The relationship between PSC and GBC has not been definitively established. Although the imaging studies performed at the diagnostic stage can put forth the diagnosis of GBC, the findings may be misleading due to the chronic cholecystitis in the background of PSC.

In the literature, cases who underwent LT due to PSC and incidentally found GBC have been presented. In the first report written in 1994, two patients underwent LT for PSC. They had T1N0M0 and T2N0M0 GBC.[9] Both patients survived for 2,5 years without the need for additional treatment. In another report, a 60-year-old patient who underwent LT due to PSC was found to have GBC and a 6-year disease-free survival was achieved.[10] The common point in the published reports is that cholecystectomy is avoided in patients with cirrhotic liver due to PSC in the diagnostic approach for suspicious masses in the gallbladder. On the other hand, in one report a cholecystectomy was performed in a 29-year-old patient who was followed up with PSC and an irregular mass of 11x13 mm in size was observed in the gallbladder. Histopathologic examination revealed GBC.[11] No distant metastasis was found and LT was performed 1 month later and a 24-month disease-free survival was reported. In another report, the association of LT and GBC was reported in four patients, three of whom had PSC and one had cryptogenic cirrhosis.[12] In one of the patients, cholecystectomy was performed before LT and T2N0M0 stage was diagnosed and the patient received radiotherapy and chemotherapy. LT was performed 11 months after cholecystectomy when liver function deteriorated. The other 3 patients were diagnosed in the hepatectomy specimen after LT. Disease-free survival was reported as the shortest 22 months and the longest 42 months.

LT seems to be the only option for these patients due to the risk of decompensation. And there have been no reports of early recurrence or metastasis after LT. One of the common features of these patients is the absence of nodal spread and early detection of tumors. Although lymph node involvement is an important prognostic factor in the literature, it has also been reported that residual disease in the lymph nodes of incidental GBCs has no effect on survival.[13] This makes the option of LT more attractive when a suspicious mass is seen in the gallbladder in patients with PSC. On the other hand, planning cholecystectomy because of the cirrhotic liver background in these patients is risky as it may lead to decompensation. In such a case, the patient's liver function should be well evaluated. Cholecystectomy should be avoided in patients with high Meld score.

Therefore, if early-stage GBC is considered in decompensated cirrhotic patients, LT should be done. There is no indication for LT in advanced-stage GBC. However, early-stage GBC should not be considered a contraindication for LT. The reported cases show favorable outcomes, making LT a viable treatment option for early-stage GBC, particularly in the setting of PSC or cirrhotic liver.

Conclusion

Since there is a risk of GBC in patients with PSC, the gallbladder should be examined especially in detail in perioperative imaging. As in our case, the result of LT in patients with T2 GBC are promising.

Disclosures

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

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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