



Isolated Peritoneal Recurrence After Liver Resection for Hepatocellular Carcinoma

Narendra Pandit¹ · Laligen Awale¹ · Sameer Chaudhary¹ · Rajan Shah² · Shailesh Adhikary¹

Published online: 9 May 2018

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Introduction

Hepatocellular carcinoma (HCC) continues to be the common and lethal malignancy worldwide that often arises in the setting of background liver disease [1]. Options for treating HCC have expanded dramatically over the last few decades from initially resection to liver transplantation (LT) with the expansion of tumor criteria and improved results [2]. Liver resection (LR) is the standard of care for patients without underlying liver disease, while LT is the gold standard for patients with Child-Pugh B/C cirrhosis and limited hepatic reserve within transplant criteria. Despite treatment, unfortunately around 70% of patients in LR group and only 10% in LT group develop recurrence over 5-year period [1].

Majority of recurrence when they occur are intrahepatic. Extrahepatic or peritoneal recurrences have been described in less than 3% of patients following LR, and only few data are available from a case series [3, 4]. We report a unique case of isolated peritoneal recurrence developing 2 years following successful resection of right liver HCC.

Case Report

A 78-year-old male presented with dull aching pain abdomen and lump in right lumbar region of 2 months duration. The patient denied any history of vomiting, anorexia, and weight loss. The past history was significant for right hepatectomy 2 years back for 8 by 8-cm size, segment 6 and 7 hepatocellular carcinoma in a non-cirrhotic and non B and C viral hepatitis background. Diagnosis at that time was made based on characteristic CT feature and percutaneous tumor biopsy. Histopathological report revealed hepatocellular carcinoma, moderately differentiated with absence of lymphovascular emboli and a tumor free resection margin (stage-pT1N0M0, American Joint Committee on Cancer (AJCC), 7th edition). The patient was under regular follow-up for last 2 years without any adjuvant chemotherapy.

On examination, there was a right subcostal scar of previous surgery with 8 by 7-cm, hard, non-tender lump in the right lumbar region. There was no pallor, jaundice, or left supraclavicular lymphadenopathy. Laboratory investigation was normal for hemoglobin, liver and renal function test, and serum chemistry. Serum alpha-fetoprotein (AFP) was 9.3 IU/ml (< 6.0), which was marginally raised. A contrast-enhanced computed tomography (CT) of the chest and abdomen revealed a well-defined (8 by 8-cm) soft tissue density intraperitoneal lesion with minimal heterogeneous enhancement in the right lumbar area, abutting and continuous with anterior abdominal wall (Fig. 1). The visualized left liver and caudate lobe was enlarged without any focal lesion. No peritoneal deposits, ascites, or other lesions were seen. A diagnosis of solitary intraperitoneal tumor recurrence was made and planned for upfront resection. Staging laparoscopy followed by open midline conversion was done. Intraoperatively, there was a tumor recurrence in the greater omentum, slightly adhered to the right side peritoneum. The tumor was excised in toto without any spillage. Cut section of the specimen showed a solid, grayish-white tumor containing necrosis (Fig. 2). Intraoperative and postoperative periods

✉ Narendra Pandit
narendrapandit111@gmail.com

Laligen Awale
lalijan@hotmail.com

Sameer Chaudhary
neveragain@yahoo.com

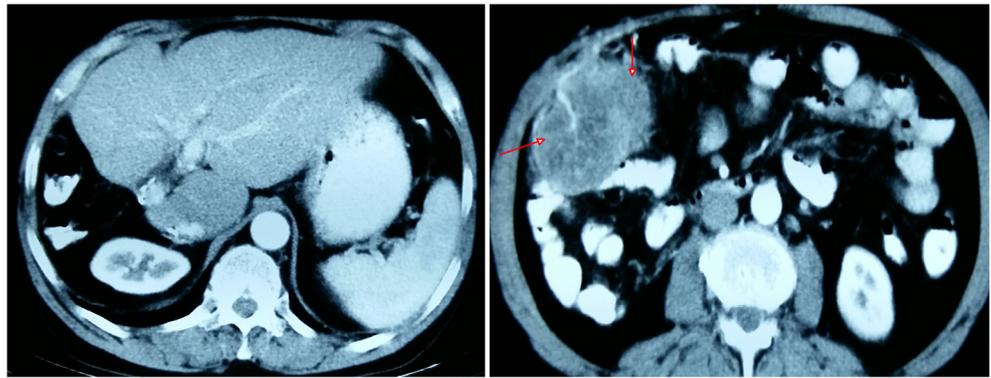
Rajan Shah
rajan.shah@bпкиhs.edu

Shailesh Adhikary
shaileshchina@yahoo.com

¹ Surgical Gastroenterology Division, Department of Surgery, B P Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal

² Department of Pathology, B P Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal

Fig. 1 Contrast CT abdomen showing a well-defined (8 × 8-cm), heterogeneously enhancing tumor lying intraperitoneally in the right lumbar region (arrow), with a normal remaining left liver



were uneventful, and the patient was discharged in a satisfactory condition on postoperative day 5. Histopathological report of the resected tumor revealed proliferation of atypical cells arranged in solid sheets, nests, and papillary pattern with few Mallory-Denk bodies suggesting deposits of hepatocellular carcinoma (Fig. 3). At 1-year of follow-up, patient is alive without any recurrence.

Discussion

Peritoneal recurrence (PR) in a patient with HCC is generally considered as an indicator of an advanced cancer not suitable for surgery. Most of the recurrences after LR are intrahepatic followed by the systemic metastases at the lungs, bone, and brain. Peritoneal recurrence, that also isolated is rare, occurring in less than 3% of cases of total recurrence. In terms of pattern of distribution of PR, omentum is the most common site as was seen in the present case [4, 5].

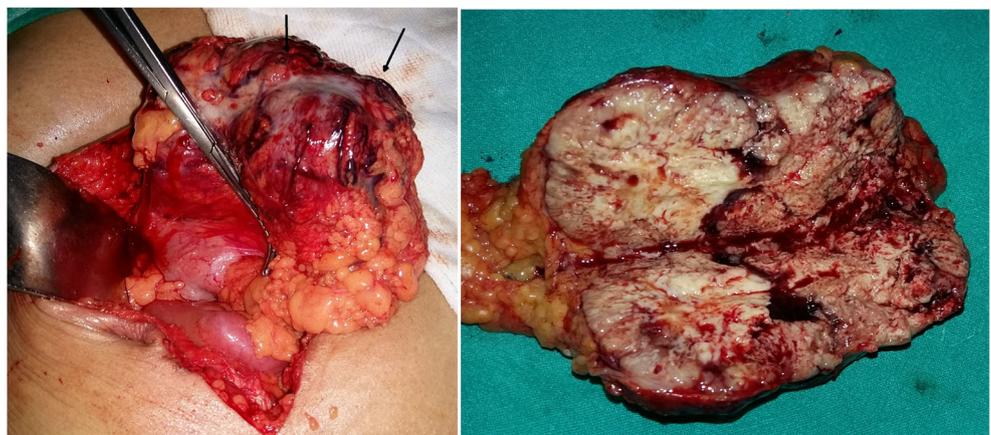
The main pathogenetic mechanism related to PR can be summarized as (1) passive transportation of the tumor cells from the liver capsule; (2) neoplastic seeding by violation of HCC integrity by percutaneous needle biopsy, ethanol injection (PEI), or radiofrequency ablation; (3) intraoperative manipulation and consequent tumor cell spillage during liver

resection, especially in large tumors; and (4) spontaneous rupture of HCC leading to spillage of tumor cells in the peritoneal cavity [6, 7].

Above all, the most important factor for the PR is the previous surgery tumor-related histological factors. The adverse factors for PR and survival are the tumor size > 5 cm, presence of microvascular emboli or satellites, bile duct invasion, positive resection margin, and poorly differentiated HCC [5]. In contrast, the presence of an intact tumor capsule especially for large tumors (> 5 cm) is associated with a protective effect. Patients with an intact tumor capsule had nearly 50% reduction in the risk of recurrence versus patients with a disrupted capsule [8]. Our case was unique in the sense that recurrence occurred long after liver resection in spite of absence of all the tumor-related adverse prognostic factors as described. The presumed risk factor for PR in our case was the percutaneous tumor biopsy from the liver at first surgery, which was done at outside center, leading to possible tumor spillage along the needle tract.

Currently, there is no standardized treatment for HCC patients with peritoneal recurrence; however, surgical resection should be attempted in every patient with isolated PR, provided that the surgical risk is acceptable, no other distant metastases is present, and radical resection could be attempted [9, 10]. At surgery, staging laparoscopy should be done to

Fig. 2 Intraoperative (arrow) and cut section view of the tumor



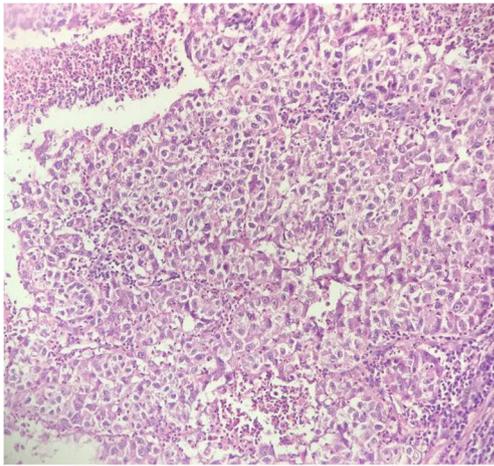


Fig. 3 Photomicrograph (H&E, $\times 100$) showing atypical cells arranged in nests with Mallory-Denk bodies suggesting hepatocellular carcinoma deposits

exclude other peritoneal recurrences, not detected on peroperative imaging modality. A further peritoneal recurrence is not rare (50% in one study) and can be considered for further resection in selected patients with favorable long-term survival [11]. Postoperatively, these patients should be kept under multimodality approach, with initiation of oral sorafenib [12]. However, our patient refused for it because of its high cost, toxicity, and modest survival benefit of 3 months.

Good long-term survival can be achieved after excision of PR following resection of HCC [13]. A retrospective analysis reported that surgical resection of peritoneal recurrence from HCC in selected patients improved long-term survival with 1-, 3-, and 5-year overall survival rate of 71, 44, and 39%, respectively [14]. The positive prognostic factors for survival in these patients are the longer time interval between hepatectomy and detection of PR (> 6 months) and low-level of serum AFP level at detection of PR [10]. Indeed, appearance of PR after longer interval between hepatectomy (at 2 years) with low level of AFP level in our patient can be explained due to better tumor biology, which took longer time to become clinically evident.

To conclude, isolated peritoneal resection after resection of HCC is a rare event. Tumor-related factor of previous liver resection is the main determinant for recurrence. Surgical resection is the best option for selected patients without any distant metastases with acceptable long-term survival.

Compliance with Ethical Standards

Conflict of Interests The authors declare that they have no conflict of interest.

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