Hepatic Metastasis 12 Years after Nephrectomy for Renal Cell Carcinoma

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Abstract
We report a case in which hepatectomy was performed to treat a patient with metastatic liver cancer 12 years after nephrectomy for renal cell carcinoma. The patient was a 56-year-old man. Abdominal CT and MRI showed tumors with diameters of 8.5 cm and 2.5 cm in S2 and S4, respectively, of the liver, and many nodules with a diameter of 1 cm or less, all in the left hepatic lobe. FDG-PET/CT revealed a SUVmax of the tumors of 35, suggesting very high accumulation of FDG. Based on the history of renal cell carcinoma and normal hepatitis virus marker values a diagnosis of metastatic liver cancer from renal cell carcinoma was made. Distant metastasis was found only in the liver. Extended left hepatectomy was carried out, and the histologic findings confirmed metastasis by renal cell carcinoma. The patient had a good surgical postoperative course and was discharged on postoperative day 7. No signs of recurrence were observed at the 20 month follow-up examination. Hepatic metastasis by renal cell carcinoma generally has a poor prognosis, and since no specific, effective pharmacotherapy has been established, hepatectomy is an option, if the safety of surgery can be assured.

Key words: hepatic metastasis, renal cell carcinoma, hepatectomy

Introduction
Metachronous hepatic metastasis often occurs in advanced stage of renal cell carcinoma, and hepatectomy is rarely an introduction option\textsuperscript{1}. When hepatectomy is taken, the multiple metastasis is not included in adaptation. The prognosis after the hepatectomy is said to be very poor, and active treatment is not generally performed for hepatic metastasis of renal cell carcinoma.

The clear policy cannot show even a guideline of National Cancer Institute for hepatic metastasis from renal cell carcinoma treatment and tends it to be taken off.

However, we report a case in which hepatectomy was used to treat a patient diagnosed with multiple liver metastases 12 years after nephrectomy, and the outcome was successful.

Case Report
The patient was a 56-year-old male who had been diagnosed with renal cell carcinoma and undergone nephrectomy 12 years previously. The results of a routine health check-up 12 years after the operation indicated a hepatic tumor, and he was referred to our hospital because liver metastasis was suspected.

Blood chemistry showed normal liver function. Hepatitis virus markers were negative, and tumor marker levels were within normal limits. Abdominal computed tomography (CT) showed tumors having a diameter of 8.5 cm and 2.5 cm in S2 and S4, respectively, of the liver (Fig. 1a, b). Both appeared as low density areas on plain CT images and very dark shadows in the early-phase contrast-enhanced CT images (Fig. 1a). In the portal venous and equi-
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Fig. 1a, b Abdominal CT showing tumors measuring of 8.5 cm and 2.5 cm in diameter in S2 and S4, respectively, of the liver. Both appeared as low density areas on plain CT images, and were very dark areas in the early phase of contrast-enhanced CT (a). In the portal venous and equilibrium phases, the contrast rapidly decreased, and the tumors appeared as low density areas (b).

librium phases, the contrast rapidly decreased, and the lesion sites appeared as low density areas (Fig. 1b). In addition to these two tumors, many nodal images 1 cm or less in diameter were observed in the left hepatic lobe. Magnetic resonance imaging (MRI) of the tumors in S2 and S4 showed low-intensity and high-intensity imaging on the T1WI images and T2WI images, respectively, with contrast in the early contrast-enhanced phase, but the margins were distinct in the late phase due to wash-out. Contrast-enhanced sonography with Sonazoid showed abundant blood flow in the tumors beginning in the early contrast-enhanced phase. Positron emission tomography-CT (PET-CT) showed that the tumors had a maximum standardized uptake value (SUVmax) of 35, suggesting a very high accumulation of $^{18}$F-fluorodeoxyglucose (FDG) (Fig. 2).

In view of the history of renal cell carcinoma, normal hepatitis virus marker values, the fact that hepatocellular carcinoma and focal nodular hyperplasia (FNH) had been ruled out based on the diagnostic imaging findings, a diagnosis of metastatic liver cancer by renal cell carcinoma localized in S2 and S4 and the left lobe of the liver was made. No distant metastases were found outside the liver, and the patient was young and had good activities of daily living (ADL) level. Because of these reasons, the liver was resected.

Extended left heptectomy was carried out, and intraoperatively a solid tumor having a diameter of approximately 80 mm was found together with many micronodules 1 cm or less in diameter in the surrounding area (Fig. 3). There were no palpable or sonographically detectable lesions in the right lobe.

Histologic examination revealed a variety of nuclear sizes and karyotypes in the tumors and alveolar proliferation by tumor cells containing eosinophilic bodies. Papillary and tubular proliferation was observed in some parts of the tumors, and alveolar and papillary proliferation by tumor cells with relatively clear cell bodies was observed in other parts (Fig. 4). Immunostaining showed that the tumor cells were negative for CD10, CK19, and Hep-Par1, but diffusely CK7-positive and partly vimentin-posi-
Fig. 3 Examination of the resected specimen showed a solid tumor having a maximum diameter of approximately 80 mm and many micronodules around it having a diameter of 1 cm or less.

tive, findings consistent with those of most likely renal cell carcinoma.

The postoperative course was favorable, and the patient was discharged on postoperative day 7. No signs of recurrence were observed at the 20-month follow-up examination.

**Discussion**

Renal cell carcinoma initially metastasizes 10 or more years after the initial surgery more often than other carcinomas. David et al. reported recurrence 10 years or more after nephrectomy in 11% (18/158) of Discussion patients. Moreover, hepatic metastasis by renal cell carcinoma frequently occurs in the advanced stage, generally suggesting a poor outcome. Neves et al. studied the outcomes of patients with metastatic renal cancer and found no difference in survival rate according to metastatic organ site, but the patients with hepatic metastases had an exceptionally poor outcome. Consequently, hepatic metastases of renal carcinoma are generally not treated aggressively. A response rate of renal carcinoma to cytokine therapy with interferon alpha of approximately 15% has been reported, similar to the response rate to interleukin 2 (IL-2). No efficacy has been obtained with combined therapy consisting of interleukin alpha and IL-2, and the response rate to chemotherapy was less than 10%. Therefore, as for the case that is judged if we cannot expect these treatment if resectable, what we hepatectomy positively should be reviewed. Overall 5-year survival rates of 26-38.9% after hepatectomy for hepatic metastases of renal cell carcinoma have recently been reported, and long-term survival can be expected after hepatectomy. In terms of the safety of surgery, a study showed that 31% of patients who underwent extended left hepatectomy died of complications. However, the technique of hepatectomy has improved, and it has recently been established as a safe form of treatment. Maldalys et al. showed that higher survival rates of patients treated for renal cell carcinoma with remote metastasis were related to a long relapse-free period between nephrectomy and metastatic occurrence, good performance status, limited metastatic lesion, and removal of the primary cancer lesion. Golimbu et al. resected metastatic renal cell carcinoma in 21 cases and reported that the patients who survived 5 or more had a longer relapse-free period than those who died within 5 years after the operation, and that the patients who developed metastasis 2 years or more after nephrectomy survived longer than those who developed metastasis within 2 years. Therefore, surgery is not necessarily contraindicated in patients with a long disease-free period between the time of the initial nephrectomy and metastatic tumor development, if the patient has sufficient residual liver function and the surgeon is confident of a safe operation. Schwartz proposed
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that resection of metastatic liver cancer from renal carcinoma should be performed in accordance with the same criteria as metastatic for liver cancer from colon cancer\(^{10}\). Our patient had many small metastatic lesions in addition to the main metastatic lesion. We thought that the tumors could be completely and safely removed by hepatectomy and that the patient would have a good outcome because the recurrence was diagnosed 12 years after the nephrectomy. There have been many reports on surgery for metastasis to the lung, bone, soft tissue, and brain, but there have been few reports on hepatic metastasis. The results of future operations for hepatic metastases of renal carcinoma should be accumulated and evaluated.

Promising pharmacotherapy approaches include antiangiogenic therapy with sorafenib\(^{14}\), bevacizumab\(^{15}\) and sunitinib\(^{16}\), but its efficacy needs to be demonstrated by clinical trials.

In our patient, preoperative FDG-PET/CT showed a SUV\(_{\text{max}}\) of 35, suggesting high accumulation of FDG. PET is generally useful for the diagnosis of metastatic liver cancer, and Abdel-Nabi et al. showed that it was a sensitivity and specificity of 88% and 98%, respectively, for metastatic liver cancer from colon cancer, substantially higher than the 38% and 81% for CT, indicating higher sensitivity of PET for metastatic liver cancer\(^{17}\). A sensitivity of 84.6% and specificity of 97% have been reported for PET in metastatic liver cancer from pancreatic cancer, of figures that are also superior to those of CT\(^{18}\). Kinkel et al. conducted a meta-analysis of diagnostic methods for metastatic liver lesions from gastrointestinal cancer and concluded that PET is a more sensitive method of detecting metastatic liver cancer than US, CT, or MRI\(^{19}\). However, few studies have reported evidence for the efficacy of PET/CT in the diagnosis of metastatic liver cancer, except for metastasis from colorectal cancer. Thus, further cases need to be accumulated to establish the efficacy of PET/CT in renal cell carcinoma, however, the results in over case indicate that it can be highly effective, and FDG-PET/CT can be an effective means of detecting recurrence in the early stage of postoperative follow-up after surgery for renal cell carcinoma.

References

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