Case report

Experience of gastric cancer in a patient who had received a living-donor liver transplantation

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Abstract

A 57-year-old woman had previously undergone a living-donor liver transplantation (LDLT) for end-stage liver disease related to hepatitis B virus. The liver graft had been donated by her husband. Her postoperative course had been uneventful. In the course of postoperative surveillance, she was incidentally found to have gastric cancer by an endoscopic examination 2 years after the liver transplantation. A gastric resection was the treatment choice, and the results were successful. The tumor, which was moderately differentiated adenocarcinoma, was limited to the mucosal layer, with no metastasis. In addition, a *Helicobacter pylori* infection was observed. This is the first reported case of a gastric cancer after LDLT. We report this case because of its importance regarding the need to carry out close surveillance in transplant recipients who are treated with immunosuppressive drugs, in order to make a timely identification of the occurrence of common malignancies.

Key words Living-donor liver transplantation · Gastric Cancer · *Helicobacter pylori*

Introduction

Malignancy after transplantation has become a serious problem. Because outcomes after transplantation are becoming better, patients are able to survive for a long time. The overall incidence of malignancy in the transplant recipient has been estimated to be as high as 20% in the 10-year period after transplantation [1]. Most conditions in which a state of profound immunosup-

pression exists are thought to be associated with an increased risk of malignancy. Gastric cancer is uncommon in the United States; however, an increase in the number of gastric cancer cases has been recognized after liver transplantation [2].

In Japan, because the availability of organs from deceased donors remains extremely limited, living-donor liver transplantation (LDLT) has therefore become a common treatment. By the end of 2004, 3218 cases of LDLT had been entered in the Japanese Liver Transplantation Society registry [3]. However, little is known about the occurrence of malignancies after LDLT. We herein present a report of a patient who had gastric cancer after LDLT, who was successfully treated by a distal gastrectomy.

Case report

The patient was a 57-year-old woman with a diagnosis of gastric cancer. Two years previously, at our department, she had undergone LDLT for end-stage liver disease related to hepatitis type B virus. She also had a history of a perforated duodenal ulcer 1 year before the transplantation, which had been cured without any surgery. *Helicobacter pylori* eradication therapy had failed because of severe diarrhea.

The liver graft was donated by her husband. The weight of his right hepatic lobe was 720 g. The graft's right hepatic veins were anastomosed to the stump of the recipient's right hepatic vein and inferior vena cava (IVC) directly. The graft's portal vein was anastomosed to the recipient's portal vein in an end-to-end fashion. The graft's right hepatic artery was anastomosed to the recipient's right gastroepiploic artery under microscopic observation. Both the anterior and posterior branches of the biliary duct were reconstructed by duct-to-duct anastomosis to the common bile duct. The vagal trunk was preserved. The operation time was 26 h and 47 min,

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Received: January 29, 2007 / Accepted: May 19, 2007

Fig. 1. Three-dimensional computed tomography (CT), showing vessels around the stomach. The arrow indicates the right gastroepiploic artery (RGEA) anastomosed to the right hepatic artery in the right lobe of the liver graft

Fig. 2. The right gastroepiploic artery (RGEA) was carefully conserved. The right gastroepiploic vein (RGEV) around the greater curvature was transected using a vessel-sealing device

and the total amount of bleeding was 10650g. The postoperative course was uneventful. An immunosuppressive agent, FK-506, was maintained at the optimal level. There was no problem regarding routine monitoring of various parameters, including the liver function.

Two years after the transplantation, without any complaints, the patient underwent upper gastrointestinal endoscopy for the first time after the LDLT. It revealed chronic gastritis without any bile reflux and an elevated lesion in the lower part of the stomach. A histological examination proved the lesion to be moderately differentiated adenocarcinoma. On physical examination, her abdomen was soft and flat. There were surgical scars on her upper abdomen. Neither a mass nor ascites was felt. Laboratory test results, including biochemical examination, were within the normal limits. There was no evidence of distant metastasis. Under an ultrasound evaluation through endoscopy, the depth of the tumor was estimated to be within the submucosal layer. An evaluation of the vessels around the stomach was then performed by three-dimensional computed tomography (CT; Fig. 1). The stomach appeared to be fed from the left gastric artery, the left gastroepiploic artery, the short gastric artery, and the posterior artery of the stomach. The veins around the stomach were slightly dilated.

Based on the imaging findings as noted above, an operation was performed, on December 9, 2005. The incision was made on the previous scar without a median incision. No ascites was encountered. Blunt dissection of the adhesions between the transplanted liver and duodenum was done. The right gastroepiploic artery, which fed the graft, was identified (Fig. 2). First, the proximal side of the stomach was transected, with an

adequate margin from the tumor. Next, the distal side of the stomach was transected at the pylorus while preserving the gastroduodenal artery. The resected stomach showed a depressed peripherally raised lesion in the antrum (Fig. 3). Histopathologically, the tumor consisted of moderately differentiated adenocarcinoma, limited to the mucosal layer, with no metastasis (Fig. 4). The neoplastic and non-neoplastic gastric mucosa showed chronic inflammation associated with lymph follicles. *H. pylori* itself was identified microscopically; however, Epstein-Barr virus could not be detected by in situ hybridization.

The patient's postoperative course was uneventful except for a transient elevation of her liver transaminase levels. On ultrasonography, both the arterial and the portal flows in the liver were found to be normal after the operation. The immunosuppressive agent (FK-506) was resumed on the day after the surgery, through an enterostomy tube. She was discharged 3 weeks after the surgery. At the time of this writing, no recurrence has been observed for a year after the gastric surgery.

Discussion

Malignancy after transplantation has been an important topic since the inception of this therapy. Newer immunosuppressive agents have steadily reduced the incidence of acute rejection, thus extending the life expectancy of allograft recipients. However, following initial studies in the immunosuppressed transplant-recipient population, the risk of cancer has been reported to have increased from threefold to fourfold

Fig. 3. The tumor was located in the anterior of the lower part of the stomach. The macroscopic type was classified as the superficial depressed type

Fig. 4. Histopathologically, the tumor cells formed moderately differentiated tubular structures. The depth of invasion was limited to within the mucosal layer. H&E, $\times 100$

[4]. Regarding liver transplantation, post-transplant malignancy has become an important cause of mortality. In the United States, nongraft-related deaths in liver transplant patients are due to, first of all, cardiovascular disease and then malignancies [5]. Except for lymphoid tumors, such as post-transplant lymphoproliferative disorders, skin cancer has been identified as the most common solid tumor post-transplant. Sarcoma and prostate and colon cancers have also been reported to be common transplant-related malignancies [6]. In the United States, 33 gastric cancers were identified among

7000 malignancies reported to the Israel Penn International Transplant Tumor Registry, and 3 of the 33 were observed after liver transplantation [2].

The number of LDLTs has dramatically increased in Japan. However, until now, there has been no survey regarding malignancy after liver transplantation. Our patient had undergone LDLT 2 years before the detection of the gastric cancer, and subsequently a curative operation was performed for the gastric cancer. Before transplantation, she had a history of a perforated duodenal ulcer, and eradication therapy for *H. pylori*

infection had failed because of adverse events. In the screening before transplantation, no tumor was detected in the stomach.

For a gastrectomy, we have to pay attention to the unusual variation caused by the conversion of vessels at the time of transplantation. Before laparotomy, it is necessary to obtain reasonable information in order to avoid any serious problems. For superficial gastric cancer, endoscopic submucosal dissection may be another option. However, complications associated with this technique, such as bleeding, perforation, or an inadequate resection, have to be avoided.

To our knowledge, this is the first reported case of a gastric cancer after LDLT. The condition of immunosuppression is strongly associated with the occurrence of tumors. However, it is still unclear whether a relationship exists between the immunosurveillance systems used for cancer patients and immunocompetent hosts [7, 8]. In our patient, massive infiltration of lymphocytes was seen around the tumor, but their function was unclear. It is also possible that *H. pylori* infection may promote carcinogenesis.

In the United States, gastric cancer tends to be discovered at an earlier stage in transplant recipients in comparison with the general population, and excellent survival can be achieved. Close surveillance in such patients treated with immunosuppressive drugs is therefore essential. So far no consensus on the optimal interval for screening of the gastrointestinal tract in transplant recipients. Further data accumulation and analyses are called for before any definitive conclusions can be made in this regard.

Conclusion

Once a malignancy is identified in a transplant recipient, aggressive and adequate management, including appropriate surgical modalities, is thus called for. A prospective study is therefore required to determine whether transplant recipients should be routinely screened for gastric cancer.

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