Metachronous liver and bone metastasis from small early gastric carcinoma without lymph node involvement: A case report

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Abstract. A 65-year-old man was referred to our Hospital for examination of gastric cancer initially diagnosed by medical check-up. Esophagogastroduodenoscopy demonstrated a superficial depressed-type gastric cancer in the antrum, and abdominal computed tomography showed no evidence of distant metastases. A tumor measuring 11 mm in diameter was removed by endoscopic submucosal dissection (ESD). Since histological examinations of ESD specimens showed a well-differentiated adenocarcinoma invading the submucosal layer with lymphatic invasion, the patient subsequently underwent laparoscopy-assisted distal gastrectomy with regional lymph node dissection, resulting in no residual carcinoma and no lymph node metastasis. The patient developed solitary liver metastasis one year later and was treated with trastuzumab plus capecitabine/cisplatin since results of the immunohistochemical analysis of the resected specimens demonstrated overexpression of the human epidermal growth factor receptor 2 (HER2). The patient was alive 12 months after surgical resection of the liver metastasis and subsequently developed bone metastasis. Controversy remains over the role of HER2 status as a prognostic factor in gastric cancer. However, it has been generally reported that HER2 overexpression correlates with aggressive biological behavior and poor prognosis. HER2 overexpression is a potentially useful predictive factor for tumor recurrence and poor prognosis even in early gastric cancer cases.

Introduction

Early gastric cancer (EGC) is defined as the presence of a lesion confined to the mucosa or submucosa, regardless of the presence of regional lymph node metastasis, and has a good prognosis with appropriate treatment (1). Although the outcome of patients with EGC following curative surgery is excellent, cancer recurrence is a rare event and could occur even after curative gastrectomy with an incidence of 1.4-2.7% (2-5).

Endoscopic resection with endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is widely accepted as the standard treatment for EGC without lymph node metastasis and enables a clinician to resect a target lesion en bloc (6,7). Most EGC confined to the mucosa can be curatively treated by endoscopic resection, since lymph node metastasis is rare in such cases. Endoscopic resection is currently considered appropriate for the treatment of intestinal-type gastric cancer cases without central ulceration that are <2 cm in diameter, according to guidelines for EMR/ESD established by the Japanese Gastric Cancer Association (7). However, gastrectomy with lymph node dissection should be performed in patients with submucosal invasion with or without margin involvement following endoscopic resection (8,9).

In this study, a case of metachronous liver and bone metastasis after laparoscopy-assisted distal gastrectomy is described, following initial treatment by ESD for small EGC without lymph node metastasis, showing human epidermal growth factor receptor 2 (HER2) overexpression. All diagnostic procedures and therapy concerning the patient were performed after obtaining written informed consent.

Case report

A 65-year-old man was referred to our hospital for examination of gastric cancer initially diagnosed by medical check-up. The patient’s medical and family history were unremarkable. The laboratory findings were almost within normal range, as were levels of serum carcinoembryonic antigen and cancer antigen 19-9. Esophagogastroduodenoscopy (EGD) demonstrated a superficial depressed-type gastric cancer in the antrum that proved to be a well-differentiated adenocarcinoma on biopsy (Fig. 1). Abdominal computed tomography (CT) demonstrated no evidence of distant metastases and endoscopic ultrasound (EUS) identified tumor invasion of the antral mucosa.

Following a clinical diagnosis of EGC confined to mucosa, ESD was performed. The macroscopic findings of the resected specimen showed that the tumor was an irregularly shaped
depressed lesion, 11 mm in diameter (Fig. 2). Histological analyses revealed that the tumor was a well-differentiated adenocarcinoma that had invaded the submucosal layer to a depth of >500 µm at the center of the lesion with positive lymphatic and negative venous invasion (Fig. 3). Therefore, according to the extended criteria for endoscopic resection, the patient underwent laparoscopy-assisted distal gastrectomy with regional lymph node dissection, resulting in no residual carcinoma and no lymph node metastasis. The post-operative course was uneventful, and the patient was discharged on post-operative day 14.

The patient underwent periodic follow-up physical examinations, and 1 year after the operation, abdominal CT showed a ring-enhanced, well-defined mass measuring 4.8 cm in diameter located in the liver (Fig. 4). Since there was no evidence of further metastatic lesions in other organs, the patient...
underwent surgical resection of the liver tumor. Histological examination confirmed the diagnosis of a well-differentiated adenocarcinoma originating from the previous gastric cancer and immunohistochemical analysis of the tumor showed strong reactivity for HER2 (Fig. 5). Therefore, the patient was administered trastuzumab in combination with chemotherapy consisting of capecitabine plus cisplatin.

However, eight months after the second operation, the patient developed metastasis of the third lumbar vertebrae, which was detected using 18F-2-deoxy-2-fluoro-D-glucose positron emission tomography combined with CT imaging (FDG-PET/CT) (Fig. 6). Therefore, the patient was treated with trastuzumab plus irinotecan/docetaxel and was alive 12 months after the second operation.

Discussion

Solitary liver metastasis from EGC after curative gastrectomy is rare, with a reported incidence of 0.4-0.7%. A significant correlation between liver metastasis from gastric cancer that has invaded the submucosal layer and venous invasion has been reported (2,3,11). This clinical case emphasizes the risk of metachronous distant metastasis even after curative treatment for small EGC infiltrating the submucosa.

In the present case, bone metastasis appeared despite complete removal and disappearance of the liver metastasis. Additional case reports are therefore needed in order for the poor prognosis of EGC recurrence to be improved.

Liver resection for hepatic metastases from gastric carcinoma is, however, not a common procedure due to poor prognosis. Therefore, there is still no widespread agreement regarding surgical resection of synchronous or metachronous liver metastases from gastric cancer (23,24). In the present case, as the first recurrence was limited to the liver, surgical resection was the chosen treatment, followed by a chemotherapy regimen consisting of trastuzumab in combination with capecitabine plus cisplatin. However, in the present case, bone metastasis appeared despite complete removal and disappearance of the liver metastasis. Additional case reports are therefore needed in order for the poor prognosis of EGC recurrence to be improved.

Despite the generally excellent outcome of EGC patients following curative surgery, a strong malignancy potential remains, which is associated with an extremely poor prognosis even in cases of small-sized tumors. Therefore, clinicians should take this possibility into consideration in follow-up management after curative treatment to treat recurrent disease earlier. Determination of the HER2 expression status in addition to conventional pathological diagnoses, such as lymph node metastasis as well as lymphatic and venous involvement may be helpful in predicting the risk of EGC recurrence.

References