

Isolated Splenic Metastases of Her2+++ Gastroesophageal Junction Adenocarcinoma

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Key Words

Gastric adenocarcinoma · Isolated splenic metastases · Her2

Abstract

Isolated metastases from gastric adenocarcinoma to the spleen are very infrequent. Usually, there are multiple metastases from gastric cancer, and isolated splenic metastases are very rare [Lam and Tang: Arch Pathol Lab Med 2000;124:526–530] because of certain anatomical and physiological characteristics (e.g., angulation between the splenic artery and celiac trunk, paucity of afferent lymph flow toward the spleen, contractility of the spleen and major immune content). Here, we report 2 cases of isolated splenic metastases from an adenocarcinoma of the gastroesophageal junction, both with long-term survival outcome and overexpression of Her2.

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Introduction

Isolated metastases from gastric adenocarcinoma to the spleen are very infrequent. Usually, there are multiple metastases from gastric cancer, and isolated splenic metastases are very rare [1] because of certain anatomical and physiological characteristics (e.g., angulation between the splenic artery and celiac trunk, paucity of afferent lymph flow toward the spleen, contractility of the spleen and major immune content). Here, we report 2 cases of isolated splenic metastases from an adenocarcinoma of the gastroesophageal junction, both with long-term survival outcome and overexpression of Her2.

Case Report 1

A 41-year-old man who presented with dysphagia was diagnosed with adenocarcinoma of the gastroesophageal junction. No metastasis was detected. The patient was given 3 cycles of an EOC chemotherapy regimen (epirubicin, oxaliplatin and capecitabine), and, in June 2011, a partial proximal esophagogastrectomy was performed. The resection was R0. Histologically, this well-differentiated adenocarcinoma, Her2+++ , was 3 × 5 cm, with a depth of 8 mm and classified as ypT3N1 (2 positive nodes/22 nodes examined); the 2 involved nodes were pericardial (group 1 in the Japanese classification). Then, 3 additional cycles of EOC were given without any complications. In May 2013, surgery was performed to treat acute cholecystitis, and a peritoneal nodule was disclosed. On pathological examination, the nodule corresponded to metastases of the gastric adenocarcinoma expressing CK7 but not CK20 and with overexpression of Her2+++ . The resection was complete, and no postoperative chemotherapy was given. In December 2013, a CT scan revealed a 2-cm splenic hypodensity in contact with a surgical clip that was considered to be a possible splenic infarction. Three months later, however, this hypodensity was 6 cm in diameter. In April 2014, exploratory surgery was performed, and only a splenic tumor that invaded the pancreatic tail, without any other lesions, was found. A splenopancreatectomy was performed. On pathological examination, the same adenocarcinoma was found involving the spleen and invading the pancreas; 5 of 8 removed lymph nodes were positive. In September 2014, an adrenal tumor was seen on CT scan. The patient was then given 5 cycles of a 5-FU-CDDP-trastuzumab chemotherapy regimen. After a major response to chemotherapy, surgery was performed in March 2015. The adrenal gland and the surrounding tissues were removed. The postoperative period was uncomplicated. On pathological examination, the adrenal gland was infiltrated by the same adenocarcinoma cells, but most of the abnormal areas were completely necrotic. No postoperative chemotherapy was given. In February 2016, 5 years after the diagnosis, the patient is alive without evolutive disease.

Case Report 2

A 40-year-old man had a very similar history to the first patient. Dysphagia led to the diagnosis of gastroesophageal junction adenocarcinoma in October 2011. Three cycles of EOC were administered preoperatively, and then a total gastrectomy was performed in February 2012. On pathological examination, the tumor was classified as ypT3N1 (1 positive node on the lesser curvature of the stomach/28 nodes examined; group 3 in the Japanese classification) and overexpressed Her2+++ . Then, systemic chemotherapy (EOC) was resumed for 3 more cycles until March 2012. In February 2015, a 2-cm splenic hypodensity was discovered on CT scan. In March 2015, a splenectomy was performed, and no peritoneal carcinomatosis or liver metastases were detected. The nodule was 45 mm in larger diameter, infiltrated by adenocarcinoma cells and classified as overexpressed Her2+++ ; the capsule was invaded, but the resection was considered R0. In June 2015, multiple liver metastases were disclosed, and systemic chemotherapy of 3 cycles of 5-FU-CDDP-trastuzumab was given. After these 3 cycles, the patient had a complete response. Trastuzumab alone was given (i.e., due to neurotoxicity related to the platinum derivatives in the previous regimen) for 3 additional months. The patient is still in complete remission as of February 2016.

Discussion

Splenic metastases from solid tumors, particularly from gastric cancer, are infrequent. A recent paper summarizing the English and Japanese literature [2] found only 19 cases, of which 7 were synchronous and 12 were metachronous metastases from the gastric adenocarcinoma. All but 2 cases occurred in Asia. In most cases, a hematogenous route was suspected, whereas a lymphatic route was assumed in only 2 synchronous cases with involved lymph nodes.

The outcomes of these cases were surprising, as were the outcomes of our 2 cases. Nine of the patients described in the literature were still alive 1–3 years after the diagnosis, while only 5 patients had a more common evolution with fatal dissemination of the disease. Unfortunately, in this series of patients, there are no data regarding their Her2 status.

The prognostic value of the Her2 status in gastric adenocarcinoma seems to be different whether in a curative or a palliative setting. In a large Japanese study [3] of 1,148 gastric cancer patients who underwent surgery to treat gastric adenocarcinoma, 15.7% were Her2 positive. In a multivariate analysis, Her2 overexpression was an independent prognostic factor associated with a poor survival. In contrast, in the ToGA phase 3 study [4] that showed the clear benefit of adding trastuzumab to the FU-CDDP chemotherapy regimen for advanced or metastatic gastric cancer patients, in the chemotherapy-alone arm, overexpression of Her2 (immunohistochemistry 2+ or 3+) was associated with a better prognosis than a Her2 status of 1+ or Her2 negativity. It is important to note that, in this large-size phase III trial (594 patients), the 3-year overall survival was lower than 10% and independent of the Her2 status.

Our 2 patients had some common characteristics, as both were young males and showed invaded lymph nodes on pathological examination. However, in 1 patient, the splenic metastases were the first sign of a more common evolution, whereas the other patient developed some isolated metastases. In both cases, the tomodensitometry pattern was quite similar with a hypodense nodule in the internal part of the spleen that was not far from the splenic tail but with no evidence of enlarged lymph nodes.

In 2 retrospective analyses, the outcome for Her2-positive gastric adenocarcinoma seems to be different than that for Her2-negative gastric adenocarcinoma. In a French series of 63 patients [5], 11 patients (18%) were Her2 positive; surprisingly, 3 of them (27%) developed brain metastases compared to 0% of the 52 Her2-negative patients. Peritoneal carcinomatosis was seen in 39% of the Her2-negative patients but not in the 11 patients who were Her2 positive. In a larger series of 100 patients who had gastroesophageal junction adenocarcinoma with brain metastases [6], 36% were Her2 positive; this proportion seems higher than expected.

These findings raise the question of tumor heterogeneity, as has been described in some other cancers. For example, analysis of the DNA sequencing of patients with pancreatic adenocarcinoma and associated metastases has shown some organ-specific branches of phylogenetic trees [7]. In the cases of gastric adenocarcinoma, is overexpression of Her2 perhaps associated with some specific metastatic site?

The last lesson we can draw from these cases is that isolated metastases occurring 'long term' after initial surgery can sometimes benefit from iterative resection, as was observed in our first case.

In conclusion, we report 2 cases of young patients developing isolated splenic metastases years after the resection of a gastric adenocarcinoma. In both cases, the tumor was Her2 positive, and the outcome was surprisingly good.

Statement of Ethics

Both subjects gave their informed consent before publication of their cases.

Disclosure Statement

The authors report no conflicts of interest.

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