Title

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Long-term survival after resection of a gastric metastasis from transverse colon cancer: a case report

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Abstract
Metastatic neoplasms in the stomach from remote primary tumors are uncommon, and gastric metastases of colorectal origin are rare. We herein report a case of gastric metastasis originating from transverse colon cancer in a 61-year-old female patient. Curative right extended hemicolectomy and partial gastrectomy were performed. Histologically, both the colon and stomach tumors were moderately to poorly differentiated adenocarcinoma with similar features. The postoperative TNM classification was stage IV disease (T4N0M1). The patient received 7 cycles of postoperative bevacizumab+FOLFOX (oxaliplatin plus an infusion of 5-fluorouracil/levofolinate) therapy and 4 cycles of additional chemotherapy with bevacizumab+FOLFIRI (irinotecan plus an infusion of 5-fluorouracil/levofolinate).

The patient has a good quality of life with no signs of recurrence at seven years and four months after surgery.

Key words: colorectal cancer, stomach, metastasis

Introduction
Secondary stomach cancers are rare. The reported incidence at autopsy is 0.2-5.4%1-6). Among these lesions, the lung, breast, skin (melanoma), and esophagus are the most frequent sites of origin1,2,4-7). Metastasis of colorectal carcinoma (CRC) to the stomach was only reported in 3.5-4.1% of all cases4,5). We herein report a case of transverse colon cancer metastasis to the stomach that was successfully resected and discuss the characteristics of gastric metastases and the outcomes. To our knowledge, this is the only reported case of long-term survival in a patient with this disease.

Case Report
A 61-year-old Japanese woman was admitted to our hospital in June 2011. Her family history was unremarkable. She presented with a two-month history of diarrhea and vomiting.

Colonoscopy revealed advanced transverse colon cancer. Endoscopy of the upper gastrointestinal tract showed a lesion approximately 3 cm in diameter that appeared to be a submucosal tumor in the body at the greater curvature of the stomach. The examination of biopsy specimens of this gastric tumor led to the suspicion of synchronous metastasis from colonic adenocarcinoma. Further examination did not reveal any other sites of metastasis. She underwent right extended hemicolectomy with D3 lymph node dissection and partial gastrectomy under a diagnosis of transverse colon cancer and gastric metastasis.

Histologically, both the colon and stomach tumors were moderately to poorly differentiated adenocarcinoma with similar features (Figs. 1A, 1B and 2A, 2B). The colon tumor had grown into the surface of the visceral peritoneum, whereas the stomach tumor had expanded into the submucosa and muscularis propria (Fig. 3). Thus, we concluded that the TNM classification (according to seventh
The postoperative course was uneventful and she was discharged on the 14th postoperative day. Seven cycles of postoperative bevacizumab+FOLFOX4 (oxaliplatin plus an infusion of 5-fluorouracil/levofolinate) therapy were administered. Four cycles of additional chemotherapy with bevacizumab+FOLFIRI (irinotecan plus an infusion of 5-fluorouracil/levofolinate) were also administered.

The patient has a good quality of life with no signs of recurrence at seven years and four months after surgery.

**Discussion**

With the increasing use of new radiological imaging modalities, such as CT, magnetic resonance imaging (MRI) and positron emission tomography (PET), together with the increasing survival rates of patients with various primary cancers, metastases are more likely to be diagnosed. The stomach is an unusual site for metastasis, accounting for 0.2-5.4% in autopsy series\(^1\,\,^5\). Although gastric metastases...
### Table 1. Reported cases of gastric metastases from colorectal cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Location</th>
<th>Type</th>
<th>Site</th>
<th>Gross appearance</th>
<th>Grade (UICC 7th edition)</th>
<th>Number</th>
<th>Time after primary diagnosis</th>
<th>Other organ metastasis</th>
<th>Treatment for metastasis</th>
<th>Prognosis (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nobusawa</td>
<td>1998</td>
<td>68</td>
<td>F</td>
<td>T</td>
<td>3</td>
<td>M</td>
<td>SMT</td>
<td>G1 solitary synchronous</td>
<td>0</td>
<td>PUL, LYM</td>
<td>DG, CX</td>
<td>6 alive</td>
<td></td>
</tr>
<tr>
<td>Shida</td>
<td>2003</td>
<td>71</td>
<td>F</td>
<td>T</td>
<td>2</td>
<td>L</td>
<td>SMT</td>
<td>G2 solitary metachronous</td>
<td>40</td>
<td>None</td>
<td>DG</td>
<td>19 alive</td>
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<tr>
<td>Yoshimi</td>
<td>2007</td>
<td>74</td>
<td>F</td>
<td>S</td>
<td>2</td>
<td>U</td>
<td>SMT</td>
<td>G1 solitary metachronous</td>
<td>24</td>
<td>HEP, PUL</td>
<td>PR</td>
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<tr>
<td>Sakabe</td>
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<td>53</td>
<td>M</td>
<td>R</td>
<td>3</td>
<td>UML</td>
<td>SMT</td>
<td>G1 multiple metachronous</td>
<td>14</td>
<td>HEP, PUL, INT, BON</td>
<td>CX</td>
<td>5 died of disease</td>
<td></td>
</tr>
<tr>
<td>Onoe</td>
<td>2008</td>
<td>35</td>
<td>F</td>
<td>A</td>
<td>5</td>
<td>L</td>
<td>SMT</td>
<td>G1 solitary synchronous</td>
<td>0</td>
<td>None</td>
<td>DG, CX</td>
<td>19 alive</td>
<td></td>
</tr>
<tr>
<td>Toyota</td>
<td>2008</td>
<td>65</td>
<td>M</td>
<td>A</td>
<td>2</td>
<td>UML</td>
<td>SMT</td>
<td>G1 multiple synchronous</td>
<td>0</td>
<td>ESO, BON, REC</td>
<td>CX</td>
<td>19 died of disease</td>
<td></td>
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<tr>
<td>Shirakawa</td>
<td>2009</td>
<td>73</td>
<td>M</td>
<td>S</td>
<td>2</td>
<td>U</td>
<td>SMT</td>
<td>G2 solitary metachronous</td>
<td>39</td>
<td>ABD, LYM</td>
<td>C, CX</td>
<td>3 alive</td>
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<tr>
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<td>75</td>
<td>M</td>
<td>R</td>
<td>3</td>
<td>L</td>
<td>SMT</td>
<td>G3 multiple metachronous</td>
<td>7</td>
<td>LYM</td>
<td>CX</td>
<td>5 died of disease</td>
<td></td>
</tr>
<tr>
<td>Sano</td>
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<td>67</td>
<td>M</td>
<td>S</td>
<td>2</td>
<td>U</td>
<td>SMT</td>
<td>G1 solitary metachronous</td>
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<td>LYM</td>
<td>TG, CX</td>
<td>21 alive</td>
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<tr>
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<td>48</td>
<td>M</td>
<td>R</td>
<td>ND</td>
<td>L</td>
<td>SMT</td>
<td>G3 solitary synchronous</td>
<td>0</td>
<td>None</td>
<td>CX</td>
<td>8 alive</td>
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</tr>
<tr>
<td>Nushijima</td>
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<td>F</td>
<td>T</td>
<td>2</td>
<td>L</td>
<td>SMT</td>
<td>G1 solitary metachronous</td>
<td>15</td>
<td>PER, LYM</td>
<td>DG, CX</td>
<td>7 alive</td>
<td></td>
</tr>
<tr>
<td>Mori</td>
<td>2015</td>
<td>57</td>
<td>F</td>
<td>D</td>
<td>2</td>
<td>M</td>
<td>SMT</td>
<td>G2 solitary metachronous</td>
<td>5</td>
<td>INT</td>
<td>TG, CX</td>
<td>6 alive</td>
<td></td>
</tr>
<tr>
<td>Yoshino</td>
<td>2017</td>
<td>76</td>
<td>M</td>
<td>S</td>
<td>2</td>
<td>M</td>
<td>SMT</td>
<td>G1 solitary synchronous</td>
<td>0</td>
<td>None</td>
<td>TG, CX</td>
<td>14 alive</td>
<td></td>
</tr>
<tr>
<td>Terashima</td>
<td>2015</td>
<td>61</td>
<td>F</td>
<td>T</td>
<td>3</td>
<td>M</td>
<td>SMT</td>
<td>G3 solitary synchronous</td>
<td>0</td>
<td>None</td>
<td>PR, CX</td>
<td>88 alive</td>
<td></td>
</tr>
</tbody>
</table>

F, female; M, male; T, transverse colon; A, ascending colon; S, sigmoid colon; D, descending colon; R, rectum; ND, not described; U, upper third; M, middle third; L, lower third; SMT, submucosal tumor; PUL, pulmonary; LYM, lymph node; HEP, hepatic; INT, intestine; BON, bone; REC, rectum; ABD, abdominal wall; ESO, esophagus; PER, peritoneum; DG, distal gastrectomy; PR, partial resection; C, cardectomy; TG, total gastrectomy; CX, chemotherapy
may originate from various organs, they most commonly originate from the breast, lung, esophagus and skin (melanoma).\textsuperscript{1-6}

As gastric metastasis from CRC is a rare condition, information on gastric metastases is generally limited to single case reports and there are no reports on the prognostic outcomes. We herein summarize the clinical features of gastric metastases arising in patients with CRC and discuss the treatment and outcomes.

Only 14 cases (including ours) of gastric metastases from CRC have been reported\textsuperscript{7-10} (Table 1). Based on the cases with available information, gastric metastases from CRC have the following characteristics. The mean age of patients with gastric metastasis originating from CRC was 61.6 years (range: 35-76 years). The 14 reported cases involved 7 females and 7 males. The primary sites of CRC were as follows: ascending colon (n=2), transverse colon (n=4), descending colon (n=1), sigmoid colon (n=4), and rectum (n=3). The grades of primary CRC were G1 (n=9), G2 (n=3), and G3 (n=2). In all cases, on gross examination, gastric metastases had a submucosal tumor-like appearance. Data on additional sites of distant metastases were available for 9 patients, the sites of which included the lung (n=3), liver (n=2), bone marrow (n=2) and lymph nodes (n=5). The gastric metastases presented as solitary lesions in 11 cases and as multiple lesions in 3 cases. Eleven of the patients with gastric metastases had a solitary metastasis; 3 had multiple metastases. The sites of gastric metastases were the upper third (n=3), middle third (n=4), lower (n=5) and whole stomach (n=2). Ten of the 14 patients received surgical treatment. Surgery included distal gastrectomy (n=4), cardiectomy (n=1), total gastrectomy (n=3), and partial resection (n=2). The choice of surgical procedure is dependent on the location and number of metastases. Analyzing the outcomes of 14 patients, 10 patients with surgical resection were alive at 3-88 months (mean survival: 23.1 months). Among 10 patients who received surgical resection, 8 received postoperative chemotherapy. Among the patients who did not receive surgical treatment, three died at 5, 5, and 19 months, respectively, while one was still alive at 8 months.

With a diagnosis in this case, endoscopy of the upper gastrointestinal tract showed the presence of a submucosal tumor. The cut surfaces of resected specimens of the stomach showed tumor mainly located in the layer of submucosa and muscularis propria (Fig. 3). Moreover, both the colon and stomach tumors were histologically found to be moderately to poorly differentiated adenocarcinoma with similar features. Thus we diagnosed the stomach tumor to be a metastasis of colon cancer. Although we did not use immunohistochemical examination, Iino et al.\textsuperscript{16} reported that positive CK20 and CDX2 expression and negative CK7 expression supported an immunohistological diagnosis of gastric metastasis from CRC\textsuperscript{16}.

Guidelines of the Japanese Society for Cancer of the Colon and Rectum from 2014\textsuperscript{20}, propose that if both the distant metastases and the primary tumor are deemed to be resectable, then curative resection of the primary tumor should be performed, and resection of the distant metastases may be considered even in cases of stage IV disease. In fact, the surgical resection of localized hepatic and lung metastases from CRC is now widely accepted as the most effective therapy in such cases. On the other hand, outcomes for resection of metastases at other sites, including gastric metastases, are not as well established. The prognosis of patients with gastric metastases is poor because gastric involvement is generally observed in advanced-stage or terminal patients with other multiple metastases. However, the prognosis of gastric metastasis varies according to the primary site of cancer. In particular, the prognosis in cases of gastric metastases from breast cancer, lung cancer, and esophageal cancer is very poor.

In patients with breast cancer, Zelek et al.\textsuperscript{21} reported a median survival of 21 months (range: 9-48 months) for patients who received chemotherapy for gastric metastases. On the other hand, in two patients who underwent gastric surgery, diffuse relapse developed 11 and 18 months later, respectively. Taal et al.\textsuperscript{22} reported that the median survival of patients with gastric metastases from breast cancer was 10 months, with a 2-year survival rate of 23%. Thus, surgery should be restricted to emergency cases such as bleeding or perforation and systemic therapy was advocated.

McLemore et al.\textsuperscript{23} reported that palliative surgical intervention did not affect the overall survival of women with gastrointestinal metastases from breast cancer.

In the cases of esophageal cancer, Saito et al.\textsuperscript{24} suggested that surgical resection should be performed when a gastric metastasis from esophageal cancer is limited to the stomach and is less 2 cm in diameter because the mean survival after treatment for gastric metastasis is extremely short.

On the other hand, in cases of metastatic tu-
mors arising from melanoma, Pector et al.\textsuperscript{25} reported the case of a patient who remained alive for >6 years after subtotal gastrectomy for gastric metastasis from malignant melanoma. Ihde and Coit\textsuperscript{26} recommended that palliative surgery be considered for metastatic gastrointestinal tumors from melanoma because it was associated with low rates of operative mortality and morbidity.

In conclusion, in agreement with these findings, when surgical intervention is feasible, gastric metastasectomy with adequate chemotherapy may be recommended for selected patients with CRC.

References