Abstract. Situs inversus totalis (SIT) is a congenital anomaly characterized by a complete mirror-image transposition of the thoracic and abdominal viscera. We report on a rare case of superficial spreading gastric cancer associated with SIT in a 66-year-old woman referred to our hospital for examination of gastric cancer initially diagnosed by medical check-up. Esophagogastroduodenoscopy showed a slightly depressed lesion in the lesser curvature side of the stomach. Abdominal contrast-enhanced computed tomography showed complete transposition of the abdominal viscera, confirming SIT. The patient underwent total gastrectomy with regional lymph node dissection and Roux-en-Y reconstruction. Gross examination of the surgically resected specimen showed a slightly depressed lesion measuring 12×8 cm in diameter, and histopathology confirmed the diagnosis of signet-ring cell carcinoma, confined to the gastric mucosal layer without lymph node metastasis. The postoperative course was favorable, and the patient has been well without evidence of recurrence for 11 years following the operation. To the best of our knowledge, this is only the second case of a superficial spreading-type gastric cancer in a patient with SIT reported in the English literature.

Situs inversus totalis (SIT) is a rare congenital anomaly, occurring at an incidence of one per 10,000-50,000 of the population and characterized by the complete mirror-image inversion of the abdominal and thoracic organs (1). Surgical procedures are technically difficult in patients with SIT due to their defining anatomical abnormality. The superficial spreading type of early gastric cancer (EGC) is defined by a superficial tumor occupying an area of 25 cm² or more, but with a more limited depth of vertical invasion compared with the common type of EGC (2).

Herein, we report a case of superficial spreading-type gastric cancer with SIT in a 66-year-old woman who was treated by total gastrectomy involving a standard lymph node dissection. We also discuss the clinical characteristics of previously reported cases.

Case Report

A 66-year-old Japanese woman was referred to our hospital for further examination of gastric cancer diagnosed by medical check-up. She had congenital SIT, with an otherwise unremarkable medical and family history. The laboratory results were within normal limits by the very definition of such calculations, including the serum levels of carcinoembryonic antigen and cancer antigen 19-9. A chest X-ray showed typical congenital dextrocardia of SIT (Figure 1), which was confirmed by electrocardiography. Esophagogastroduodenoscopy (EGD) revealed the presence of a slightly depressed lesion in the lesser curvature side of the stomach (Figure 2). Biopsy samples suggested a signet-ring cell carcinoma, and double-contrast barium imaging showed an irregularity with indistinct margins in the lesser curvature of the middle third of the stomach (Figure 3).

Abdominal contrast-enhanced computed tomography (CT) showed complete transposition of the abdominal viscera, confirming SIT, but with no evidence of distant metastasis or vascular anomaly (Figure 4). Under a clinical diagnosis of gastric cancer with SIT, the patient underwent total gastrectomy with regional lymph node dissection followed by Roux-en-Y reconstruction. We found complete transposition of the viscera, with the stomach and spleen located on the right side of the abdomen, and the gall
bladder, liver, cecum, and appendix located on the left side. The operating time was 375 min, and blood loss was 380 ml.

Gross examination of the surgically resected specimen showed a slightly depressed lesion measuring 12×8 cm in diameter (Figure 5). Microscopic examination of the tumor confirmed the diagnosis of signet-ring cell carcinoma, confined to the gastric mucosal layer. There was no cancer metastasis evident in the 32 resected lymph nodes. The postoperative course was uneventful, and the patient was discharged on postoperative day 14. The patient has been well without evidence of recurrence for 11 years following the operation.

Discussion

Herein we describe a rare case of superficial spreading-type gastric cancer in a patient with SIT. We searched the English language literature published from 2000 to 2018 using the Medline and PubMed databases for reports of similar cases using the keywords “gastric cancer” and “situs inversus totalis”. Data on age, gender, tumor location, tumor size, depth of invasion, histological type, treatment, and outcome were obtained for each patient, and all clinicopathological data and staging were analyzed and determined according to the eighth International Union Against Cancer TNM classification (3). The histological type of each tumor was categorized as intestinal type (well-differentiated, moderately differentiated, and papillary adenocarcinoma) or diffuse type (poorly differentiated, mucinous adenocarcinoma, and signet ring cell carcinoma), according to the Lauren classification. Based on this review, the present patient is only the second case of a superficial spreading-type gastric cancer associated with SIT to be reported in the English literature.

The clinicopathological features of the 19 previously reported cases (1, 4-20) and the present case are listed in Table I. Among these 20 cases, the median patient age was 60 (range=40-81) years, and with a male-to-female ratio of 7:3. Gastric cancer in the upper third of the stomach was reported in four cases, while five patients had lesions in the middle third of the stomach, and 10 had lesions in the lower third of the stomach. The median tumor size for gastric cancer was 3.7 cm (range=1.4-12 cm), with only two cases involving the superficial spreading type of tumor (case 3 in Table I and our patient). The gastric cancer had invaded to varying depths, with lesions confined to the mucosa in four patients, invading the submucosa in four cases, the muscularis propia in two cases, the subserosa in three cases, and penetrating the serosa in three cases. Histological analysis of gastric adenocarcinoma revealed seven intestinal-type and 12 diffuse-type carcinomas. Treatments comprised total gastrectomy in five patients, distal gastrectomy in 13 patients, proximal gastrectomy in one patient, and gastrojejunostomy in one patient.

The superficial spreading type of gastric cancer has a higher reported incidence of submucosal invasion than the common type, although there were no significant differences in recurrence or survival rates between these two groups in our reviewed cases (2, 21). A curative approach for superficial spreading ECG requires appropriate extensive lymph node dissection and wide surgical resection (2).

Recent data suggest that molecular motors of the kinesin superfamily (KIFs), which are biological molecular machines which move essential molecules in living organisms, play an important role in determining left-right asymmetry (22). Furthermore, the cell-adhesion proteins N-cadherin and β-catenin are involved in the development and progression of cancer in patients with SIT (1, 23); however, the etiological relationship between SIT and superficial spreading gastric cancer and the pathogenetic mechanisms involved remain largely unknown.

Recent advances in minimally-invasive therapy, including laparoscopic surgery, offer a better quality of life to patients with EGC (13). Although the surgical procedures can be difficult in patients with SIT because of the anatomical abnormality, which represents a mirror image of the normal location, laparoscopic surgery has been performed more often in recent years (4, 6, 7, 9-12, 14-17, 19, 20). The surgical procedures undertaken for the present case were not significantly different from standard procedures in patients without SIT, although in any case with SIT, it is important to confirm the vascular locations on preoperative diagnostic imaging modalities, including CT or angiography, because SIT often displays abnormal vascularization of both the arteries and veins (16).
In conclusion, superficial spreading-type gastric cancer with SIT is an extremely rare entity, and in such cases the surgical team should carefully ascertain the specific vascular anatomy by preoperative diagnostic imaging in order to optimize procedural success.

Conflicts of Interest

None.

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Table I. Clinicopathological data for previously reported cases of gastric cancer in patients with situs inversus totalis.

| Case | Author | Year | Age (years) | Gender | Tumor location | Tumor size (cm) | Depth of invasion | Lymph node metastasis | Histological type | Stage | Surgical method | Operation length (min) | Estimated blood loss (ml) | Survival (months) |
|------|--------|------|-------------|--------|----------------|----------------|------------------|---------------------|------------------|-------|----------------|------------------------|--------------------------|---------------------|
| 1    | Yamaguchi et al. (4) | 2003 | 76 | Male | ND | ND | ND | ND | ND | ND | LADG | ND | ND | ND | ND |
| 2    | Benjelloun et al. (5) | 2008 | 70 | Male | L, Post | 8 | se | Positive | Intestinal | IIIA | DG | ND | ND | ND | ND |
| 3    | Putawatari et al. (6) | 2010 | 53 | Male | L, Post | 5 | m | Negative | Diffuse | IA | LDG | 300 | 350 | ND | ND |
| 4    | Haruki et al. (1) | 2010 | 81 | Female | L, Ant | ND | ND | ND | Intestinal | IV | GI | ND | ND | ND | ND |
| 5    | Seo et al. (7) | 2011 | 60 | Male | L, Less | 1.5 | sm | Negative | Intestinal | IA | LADG | 200 | 70 | ND | ND |
| 6    | Pan et al. (8) | 2012 | 52 | Male | U | 2 | ND | Positive | Diffuse | ND | PG | ND | ND | ND | ND |
| 7    | Kim et al. (9) | 2012 | 47 | Male | M, Post | 4 | ss | Positive | Diffuse | IIIIB | RADG | 300 | ND | ND | ND |
| 8    | Min et al. (10) | 2013 | 52 | Male | L, Less | 3.3 | mp | Negative | Diffuse | IB | LADG | 220 | 100 | ND | ND |
| 9    | Min et al. (11) | 2013 | 68 | Male | L, Ant | 3.2 | m | Negative | Intestinal | IA | LDG | 117 | 50 | ND | ND |
| 10   | Fujikawa et al. (11) | 2013 | 60 | Female | M, Less | 4 | sm | Negative | Diffuse | IA | LADG | 234 | 5 | ND | ND |
| 11   | Sumi et al. (12) | 2014 | 42 | Male | L, Post | ND | sm | Positive | Intestinal | IB | LADG | 313 | 90 | 18 | ND |
| 12   | Isobe et al. (13) | 2015 | 79 | Female | M, Less | 10 | se | Positive | Diffuse | IIIC | TG | 288 | 150 | ND | ND |
| 13   | Morimoto et al. (14) | 2015 | 58 | Male | U, less | 2.5 | m | Negative | Diffuse | IA | LATG | 359 | 90 | 48 | ND |
| 14   | Ye et al. (15) | 2015 | 60 | Female | L, Gtr | 7 | se | Negative | Diffuse | IIIB | LADG | 230 | 50 | 24 | ND |
| 15   | Kigasawa et al. (16) | 2017 | 40 | Male | U, Post | 2.4 | sm | Negative | Diffuse | IA | LADG | 284 | 40 | 24 | ND |
| 16   | Cao et al. (17) | 2017 | 60 | Male | U, Less | 1.4 | ss | Positive | Diffuse | IIIA | LATG | ND | ND | ND | ND |
| 17   | Suh (18) | 2017 | 50 | Male | M, Less | 2 | mp | Negative | Intestinal | IB | DG | 180 | 78 | ND | ND |
| 18   | Alhossaini et al. (19) | 2017 | 52 | Female | L, ND | Negative | Intestinal | IA | RADG | 195 | 30 | ND | ND | ND | ND |
| 19   | Shibata et al. (20) | 2017 | 79 | Male | U, Post | 8 | ss | Positive | Diffuse | IB | LTG | 232 | 110 | ND | ND |
| 20   | Present case | 2018 | 66 | Female | MU, Less | 12 | m | Negative | Diffuse | IA | TG | 375 | 380 | 135 | ND |

Less, Lesser curvature; Gtr, greater curvature; Ant, anterior wall; Post, posterior wall; U, upper third of the stomach; M, middle third of the stomach; L, lower third of the stomach; m, mucosa; sm, submucosa; mp, muscularis propria; se, serosa; DG, distal gastrectomy; TG, total gastrectomy, LDG, laparoscopic distal gastrectomy; LADG, laparoscopy-assisted distal gastrectomy, LTG, laparoscopic total gastrectomy, LATG, laparoscopic-assisted total gastrectomy; RADG, robot-assisted distal gastrectomy; GI, gastrojejunalostomy; ND, not described.

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