

# Solitary adrenal metastasis from advanced gastric cancer invading duodenal bulb with situs inversus totalis

## A case report

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### Abstract

**Rationale:** Situs inversus totalis (SIT) is a rare anomaly featured by complete inversion of abdominal and thoracic organs. Adrenal metastasis is often encountered as part of advanced systemic dissemination, which is usually unresectable. Few published cases reported the adrenal metastasis from gastric cancer with SIT and the treatment of gastrectomy combined with adrenalectomy, especially with intraoperative radiotherapy (IORT).

**Patient concerns:** A 61-year-old SIT man found a mass on the right clavicle and the biopsy revealed a metastatic cancer. Around 14 years ago, he had a rectal cancer resection surgery and no sign of occurrence. Five months later, the patient had a pain in his right low abdomen and abdominal CT found a right adrenal mass.

**Diagnoses:** Gastroscopy and the pathology revealed the gastric antrum cancer invading the duodenal bulb. Abdominal enhanced CT suspected the adrenal mass as a hematoma, but positron emission tomography computed tomography suspected it as the metastases of gastric cancer which is consistent with the pathology results. Finally, the SIT patient was diagnosed with primary gastric cancer invading duodenal bulb with solitary right adrenal metastasis.

**Interventions:** The patient was treated with curative distal gastrectomy and Billroth-II anastomosis with D2 lymphadenectomy. A total 18 Gy intraoperative radiotherapy (IORT) using low energy x-rays by IntraBeam were given after resection.

**Outcomes:** The patient had liver metastasis in the seventh month after surgery but there is no sign of local recurrence until now.

**Lessons:** Gastric cancer with adrenal metastasis, especially with SIT is rare and intractable. The result suggested that active surgical treatment for resectable gastric cancer and solitary adrenal metastatic tumor, especially in combination with IORT may be an option in controlling local relapse and prolonging survival in selected patients.

**Abbreviations:** CA19-9 = carbohydrate antigen19-9, CCDC11 = coiled-coil domain containing, CEA = carcinoembryonic antigen, CT = computed tomography, IORT = intraoperative radiotherapy, PET-CT = positron emission tomography computed tomography, SIT = situs inversus totalis.

**Keywords:** adrenal metastasis, gastric cancer, intraBeam, intraoperative radiotherapy, situs inversus totalis

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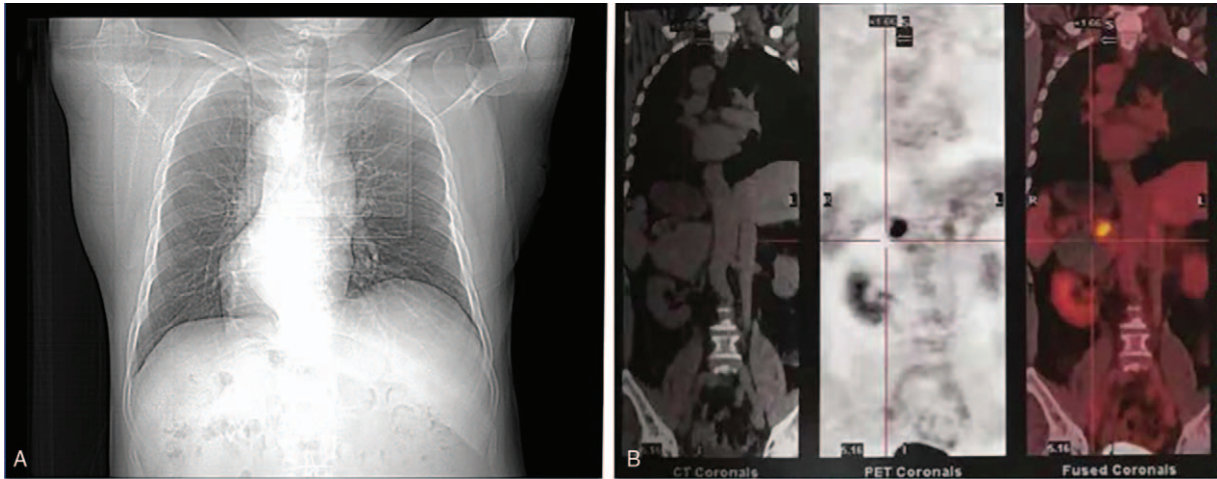
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## 1. Introduction

Situs inversus totalis (SIT) is a very rare congenital anatomical variation, which manifested as complete mirror image transpositions of the thoracic and abdominal viscera, with an incidence in 1/8000 to 1/25,000 of the normal population.<sup>[1]</sup> The exact etiology of SIT is unclear yet, it was proposed to be related to an autosomal recessive inheritance<sup>[2]</sup> and Yamamoto and Yamamoto<sup>[3]</sup> reported SIT may be related to the mutation of coiled-coil domain containing 1 (CCDC11). Wong and Reiter<sup>[4]</sup> revealed the ciliary dysfunction via dysregulation of the hedgehog pathway may be the potential cause of SIT in embryology.

Adrenal metastasis mostly presented in lung cancer and developed from gastric cancer is showed only in 16% to 18% of patients by some autopsy studies.<sup>[5,6]</sup> Reviewing the literature, up to date, only 33 cases of gastric cancer with SIT have been reported and the case also with adrenal metastasis is few. Herein we report the case of a 61-year-old SIT male patient with a history of primary rectal cancer found with primary gastric cancer



**Figure 1.** The images of chest film and PET-CT. (A) The dextrocardia of the patient. (B) The adrenal metastasis on the right adrenal gland. PET-CT = positron emission tomography computed tomography.

invading duodenal bulb, accompanied by solitary right adrenal metastasis. The patient was treated with gastrectomy, Billroth-II anastomosis, D2 lymphadenectomy, and IORT, which few published cases describe. Therefore, familiarity with this condition could help surgeon to recognize and avoid failures in diagnosis and treatment.

## 2. Case report

This study was approved by the Ethics Committee and Institutional Review Board of the second hospital of Jilin University, Changchun, China (JDEY-2017-0031). Informed written consent was obtained from the patient for publication of this case report and accompanying images.

In July 2017, a 61-year-old male patient visited our hospital for finding a mass on the right clavicle. The patient had undergone a radical resection for rectal cancer 14 years ago (pT2N0M0, a moderately differentiated adenocarcinoma). After R0 resection, the patient did not receive chemotherapy and had no symptoms or abnormal findings suggesting recurrence until now. Physical examination revealed a normal heart rate and blood pressure. However, the apex beat was located in the fifth intercostal space on the right and chest and abdominal CT showed that the thoracic and abdominal organs in a complete mirror image transposition later (Fig. 1), which proved the patient with SIT. There was an irremovable mass on the right-sided supraclavicular region, 1 × 2 cm in size, which was suspected as an enlargement of Virchow lymph nodes and the mass biopsy reported to be a metastatic cancer later. In the abdominal examination, the spleen and liver were not palpable as well as any other mass. The digital rectal examination and colonoscopy examination later were normal.

Gastroscopic examination and biopsy revealed middle-low differentiated adenocarcinoma in gastric antrum and duodenal bulb. Abdominal enhanced CT showed a thickened wall of gastric antrum and invading the duodenal bulb. There were no obviously enlarged lymph nodes, pulmonary and liver metastasis or ascites. Tumor biomarkers showed that carcinoembryonic antigen (CEA) was 47.19 (0–5 ng/mL), carbohydrate antigen19–9 (CA-199) was 168.75 (0–37 U/mL), which both greatly

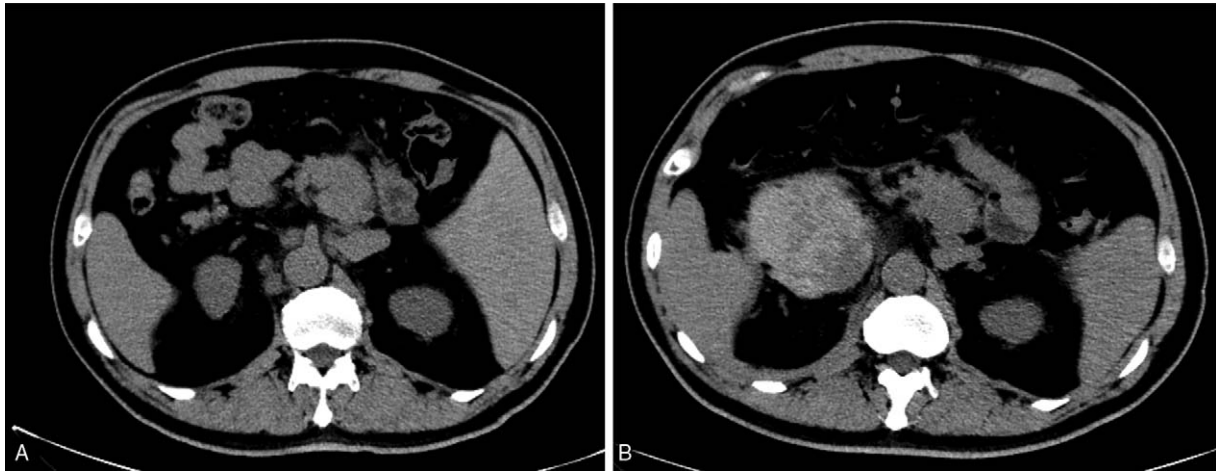
increased. However, by analyzing the rectal pathological section 14 years ago and the gastroscopic pathology section this time, the possibility of the gastric cancer metastasis from the colorectal cancer was excluded and the gastric cancer was a newly primary lesion. The patient was suggested to receive the neoadjuvant chemotherapy instead of the operation. Only 4 cycles of capecitabine tablets orally were received due to worrying the side effects. However, it seemed to be work for him because the mass disappeared after the end of 2 cycles.

In December 2017, the patient visited our hospital again for one-day right lower abdominal pain without fever or peritonitis. Abdominal enhanced CT (Fig. 2) showed an isolated right adrenal mass, 9.3 × 7.4 cm in size, considered to be an adrenal hematoma and multiple abdominal augmented lymph nodes. The PET-CT later result considered the adrenal as metastasis (Fig. 1) but a CT-guided biopsy of the mass for histological confirmation were rejected by the patient.

With the abdominal pain aggravated and sufficient preoperative evaluation, laparotomy was operated with the patient's informed consent. The abdominal visceral organs were seen in complete mirror-image transposition by the laparotomy through a midline epigastric incision. We performed the curative distal gastrectomy and Billroth-II anastomosis with D2 lymphadenectomy. Adrenal mass was resected for intraoperative frozen pathology and it revealed that malignant tumor nests. Given it did not reach to the R0 resection and the residual tumor existing, IORT using low energy x-rays with 18 Gy was operated.

At last, postoperative pathological examination revealed that gastric and invaded duodenal tumor were in moderately and poorly differentiated adenocarcinoma, respectively, with colloid carcinoma infiltrating. A total of 12 lymph nodes were harvested in the greater curvature, of which 3 were metastatic (Fig. 3). Adrenal metastasis was reported to have an abnormal cell nest and infiltrating carcinoma in the postoperative pathology.

The patient's postoperative recovery was uneventful. On the postoperative 14th day, he was discharged without any complications. He only received 4 cycles chemotherapy of capecitabine tablets due personal reason. In the seventh month after surgery, the patient found liver metastasis but there is no sign of local recurrence until now by follow-up.



**Figure 2.** The abdominal CT images of July 2017 and December 2017. (A) No obvious abnormalities. (B) The right adrenal area having a mass (about 93 mm × 74 mm). CT=computed tomography.

### 3. Discussion

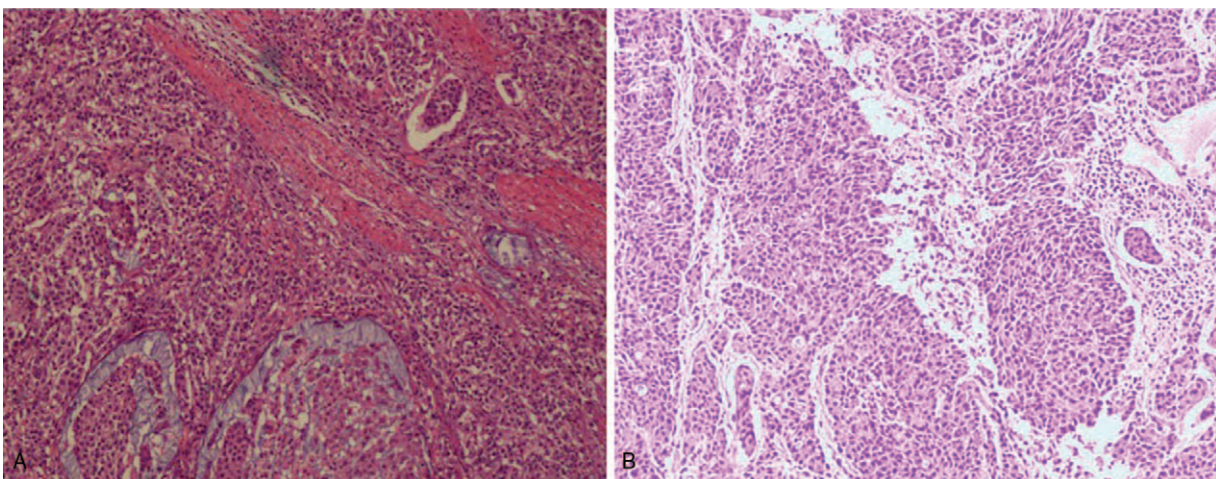
SIT is a congenital anomaly in the anatomy of human organs, since the first case was reported by Fabricius<sup>[7]</sup> in 1600. Although SIT is not considered as a risk factor for the development of malignant tumor, more than 60 cases of solitary cancer with SIT have already been reported including liver cancer,<sup>[8]</sup> gastric cancer,<sup>[9]</sup> colorectal cancer,<sup>[10]</sup> pancreatic cancer,<sup>[11]</sup> cholangiocarcinoma,<sup>[12]</sup> renal and adrenal tumors,<sup>[13,14]</sup> and leukemia.<sup>[15]</sup> Synchronous cancer in patients with SIT were also reported.<sup>[10]</sup> The patient we presented has medical history of rectal cancer. Therefore, the possibility of a concurrent or metastatic tumor should be considered and PET-CT was recommended.

SIT can be diagnosed by many means, such as physical examination, computed tomography (CT), and barium enema. The clear diagnosis of SIT can avoid the delay in diagnosis and treatment. For example, we immediately considered the possibility of gastric cancer when the patient presented with a mass on the right clavicle and arranged gastroscopy examination. Further-

more, it is also significant for avoiding intraoperative damage to vital organs and blood vessels.<sup>[16]</sup>

Reviewing the literature, gastric cancer only has been reported in 33 cases of SIT patients. Haruki et al<sup>[17]</sup> reported the advanced gastric cancer with SIT may be associated with KIT3 complex deficiency. The first foci of advanced gastric cancer is liver, the secondary foci is lung<sup>[18]</sup> and the adrenal gland is the fourth most common site of metastasis from the extra-adrenal primary cancers.<sup>[19]</sup> Mostly, the adrenal metastasis can manifest no clinical symptoms such as Cushing's syndrome and adrenocortical hypofunction, the more sensitive examinations such as needle biopsy are necessary to be taken to improve the diagnostic accuracy.

Once gastric cancer patients found adrenal metastasis, it meant the advancement of primary tumor with poorly prognosis.<sup>[18]</sup> Mostly, the patients were suggested to receive the palliative chemotherapy<sup>[20]</sup> without curative intent. The clavicle lymph nodes of the patient we presented disappeared after 2 cycles of capecitabine, which potentially indicated the sensitive reaction to



**Figure 3.** Histopathological examination of gastric tumor and the adrenal mass. (A) The pathology of gastric tumor having poorly differentiated adenocarcinoma and colloid carcinoma infiltrating, with extensive infiltration in the vessels. (B) The pathology of adrenal mass having an abnormal cell nest, with invasive carcinoma.



the chemotherapy. If the patient had received the whole regimens and cycles of adjuvant chemotherapy even to combine the targeted therapy as suggested, the local and systemic control outcome could be better.

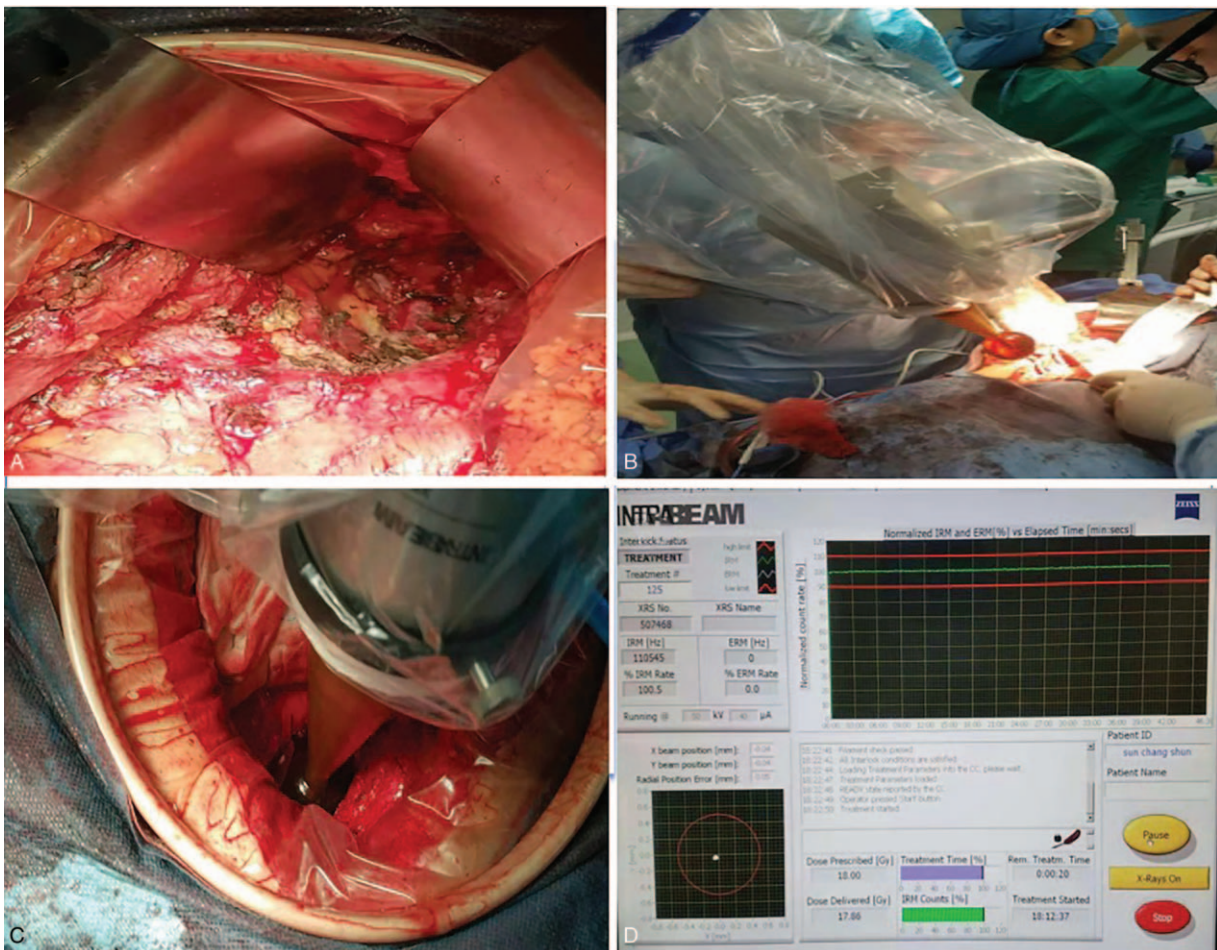
Although, very few reports described the metastasectomy for adrenal metastasis, the adrenalectomy was recommended for patients whose primary tumor had been resected or resectable and adrenal gland was isolated, which could result in long-term survival.<sup>[19]</sup> For the gastric cancer patient with SIT, laparoscopic surgery<sup>[21]</sup> and robot-assisted gastrectomy<sup>[22]</sup> were reported in 2003 and in 2012, respectively. We adopted laparotomy because it could provide a broad field of vision and the situation of the adrenal mass was unclear. Despite some authors advocate reversing the position of the surgeon, the transposition of abdominal organs remains to be challenge for distinguishing blood vessels and lymph node cleaning. The open surgery also provided the pathway to insert an applicator to apply intraoperative radiotherapy (IORT).

We used Intrabeam x-rays radio-therapy System (XPS) (Carl Zeiss Meditec AG, Germany, Fig. 4), which delivers low energy x-rays in total of 18 Gy from the special metallic sleeves to the target region feasibly and accurately. With more minimal exposure and toxicity to surrounding structures, IORT can deliver the designed radiation dosage to the at-risk areas removed

tumor and aim to improve the local control. Bacalbasa et al<sup>[23]</sup> reported that IORT promoted a better local control rates for the patients with locally advanced gastric carcinoma. It has been widely used in cancer such as breast cancer,<sup>[24]</sup> rectal cancer.<sup>[25]</sup> The patient did not occur anastomotic fistula or wound dehiscence and no additional postoperative radiotherapy was given.

In this case, the patient with SIT had the primary gastric cancer invading duodenal bulb with a solitary adrenal metastasis and had the medical history of primary rectal cancer, which was rare and troublesome. In clinic, due to patient's personal reasons and poor compliance, the potentially optimal regimen was always delayed. At the time, the comprehensive and symptomatic treatments were adopted to improve the local control and prolong the survival. Although the follow-up period of 9 months was short, the patient underwent valid successful treatment with no local occurrence.

The case is intractable and value to report. Gastric cancer with adrenal metastasis, especially with SIT can trouble the clinicians. With the sufficient preoperative evaluation, precise surgical operation, and comprehensive treatment plan, the risk to SIT would reduce. The experience of active surgical resection with IORT may achieve the local control and provide the surgeon with an option when operating on the intractable patient.



**Figure 4.** The process of intraoperative radiotherapy (IORT). (A) The region of adrenal mass resected. (B) The step of putting the applicator to the region. (C) The drift tube was put in the right region. (D) The console and operation interface. IORT = intraoperative radiotherapy.

## Author contributions

**Conceptualization:** Wangsheng Xue, Yongbo Li, Shuang Wang, Min Wang.

**Data curation:** Wangsheng Xue, Zeyun Zhao, Wei Li.

**Supervision:** Mingwei Zhang, Tongjun Liu.

**Writing – original draft:** Wangsheng Xue, Yongbo Li.

**Writing – review & editing:** Wangsheng Xue.

## References

- [1] Lee SE, Kim HY, Jung SE, et al. Situs anomalies and gastrointestinal abnormalities. *J Pediatr Surg* 2006;41:1237–42.
- [2] Mayo CW, Rice RG. Situs inversus totalis; a statistical review of data on 76 cases with special reference to disease of the biliary tract. *Arch Surg* 1949;58:724.
- [3] Yamamoto F, Yamamoto M. Scanning copy number and gene expression on the 18q21-qter chromosomal region by the systematic multiplex PCR and reverse transcription-PCR methods. *Electrophoresis* 2007;28:1882–95.
- [4] Wong SY, Reiter JF. The primary cilium: at the crossroads of mammalian hedgehog signaling. *Curr Top Dev Biol* 2008;85:225–60.
- [5] Cedermark BJ, Blumenson LE, Pickren JW, et al. The significance of metastases to the adrenal gland from carcinoma of the stomach and esophagus. *Surg Gynecol Obstet* 1977;145:41–8.
- [6] Lam KY, Lo CY. Metastatic tumours of the adrenal glands: a 30-year experience in a teaching hospital. *Clin Endocrinol* 2002;56:95–101.
- [7] Alsabek MB, Arafat S, Aldirani A. A case report of laparoscopic cholecystectomy in situs inversus totalis: Technique and anatomical variation. *Int J Surg Case Rep* 2016;28:124–6.
- [8] Patel RB, Gupta NR, Vasava NC, et al. Situs inversus totalis (SIT) with hepatocellular carcinoma (HCC): a rare case report and review of 12 other cases. *Indian J Surg* 2013;75:424–9.
- [9] Cao YH, Li J, Shen LM, et al. Gastric cancer in a situs inversus totalis patient with multiple intestinal and vessel variations related to gastrectomy surgery: a case report and literature review. *Medicine* 2017;96:e8209.
- [10] Kim YW, Ryu H, Kim S, et al. Double primary malignancies associated with colon cancer in patients with situs inversus totalis: two case reports. *World J Surg Oncol* 2011;9:109.
- [11] EL S, CJ W. Pancreatic adenocarcinoma in a patient with Situs Inversus: a case report of this rare coincidence. *World J Surg Oncol* 2009;7:98–198.
- [12] Benhammane H, Kharmoum S, Terraz S, et al. Common bile duct adenocarcinoma in a patient with situs inversus totalis: report of a rare case. *BMC Res Notes* 2012;5:681.
- [13] Oake J, Drachenberg D. A case of renal cell carcinoma in a patient with situs inversus: operative considerations and a review of the literature. *Can Urol Assoc J* 2017;11:E233–6.
- [14] Kashiwagi S, Ishikawa T, Onoda N, et al. Laparoscopic adrenalectomy in a patient with situs inversus. *J Soc Laparoend* 2013;17:487–90.
- [15] Sun YX, Li XL, Li LJ, et al. A patient with chronic myeloid leukemia and situs inversus totalis: a case report. *Oncol Lett* 2017;14:7425–30.
- [16] Uemura S, Maeda H, Munkage M, et al. Hepatic resection for metastatic colon cancer in patients with situs inversus totalis complicated by multiple anomalies of the hepatobiliary system: The First Case Report. *J Gastrointest Surg* 2009;13:1724–7.
- [17] Haruki T, Maeta Y, Nakamura S, et al. Advanced cancer with situs inversus totalis associated with KIF3 complex deficiency: report of two cases. *Surg Today* 2010;40:162–6.
- [18] Lehnert T, Rudek B, Buhl K, et al. Surgical therapy for loco-regional recurrence and distant metastasis of gastric cancer. *Eur J Surg Oncol* 2002;28:455–61.
- [19] Kanjo T, Albertini M, Weber S. Long-term disease-free survival after adrenalectomy for isolated colorectal metastases. *Asian J Surg* 2006;29:291–3.
- [20] Ichihara T. Home chemotherapy. *Gan to Kagaku Ryoho Cancer Chemother* 2010;37 Suppl 2:296–7.
- [21] Yamaguchi S, Orita H, Yamaoka T, et al. Laparoscope-assisted distal gastrectomy for early gastric cancer in a 76-year-old man with situs inversus totalis. *Surgical Endoscopy* 2003;17:352–3.
- [22] Kim HB, Lee JH, Park DJ, et al. Robot-assisted distal gastrectomy for gastric cancer in a situs inversus totalis patient. *J Korean Surg Soc* 2012;82:321–4.
- [23] Bacalbasa N, Balescu I, Calin M, et al. Intraoperative radiation therapy in gastric cancer. *J Med Life* 2014;7:128–31.
- [24] Kelemen P, Ashikari A, Ashikari R, et al. Long-term follow-up of breast cancer patients treated with intraoperative radiotherapy using the intrabeam device. *Ann Surg Oncol* 2010;17:S177–177.
- [25] Wang M, Xue W, Zhao Z, et al. Laparoscopic intersphincteric resection with intraoperative radiotherapy using low-energy X-rays for locally advanced ultra-low rectal cancer. *World J Surg Oncol* 2018;16:133.