Advanced gastric cancer with peritoneal oligometastases treated with adaptive radiotherapy and concurrent chemotherapy

Léčba pokročilého karcinomu žaludku s peritoneálními oligometastázami adaptivní radioterapií a souběžnou chemoterapií

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Summary

Background: There are no reports of concurrent chemoradiotherapy for gastric cancer with peritoneal oligometastases. ***Case description:*** A 70-year-old man with gastric cancer and peritoneal oligometastases received concurrent adaptive radiotherapy and oral S-1. After radiotherapy, S-1 was discontinued, and 2 years later the tumor had completely regressed, with no recurrence or metastasis 6 years after radiotherapy. ***Conclusion:*** Peritoneal oligometastatic gastric cancer may be a candidate for curative treatment with concurrent adaptive radiotherapy and oral S-1.

Key words

stomach neoplasms – image-guided radiotherapy – intensity-modulated radiotherapy – drug therapy

Souhrn

Východiska: V literatuře nejsou žádné zmínky o souběžné chemoradioterapii při karcinomu žaludku s peritoneálními oligometastázami. ***Popis případu:*** Muž ve věku 70 let s karcinomem žaludku a peritoneálními oligometastázami byl léčen adaptivní radioterapií a souběžně perorálně podávaným S-1. Po radioterapii bylo podávání S-1 přerušeno a o 2 roky později byla zaznamenána kompletní regrese tumoru bez rekurence metastáz v průběhu 6 let po radioterapii. ***Závěr:*** Karcinom žaludku s peritoneálními metastázami je možné léčit souběžně adaptivní radioterapií a perorálně podávaným S-1 s kurativním záměrem.

Klíčová slova

nádory žaludku – radioterapie řízená obrazem – radioterapie s modulovanou intenzitou svazku – léková terapie

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Introduction

The prognosis for advanced gastric cancer with peritoneal metastases is poor due to the aggressive nature of the disease, limited treatment options, and complications associated with peritoneal metastases [1–3]. Stage IV gastric cancer with peritoneal metastases cannot be surgically removed, so palliative care aimed at improving quality of life is the mainstay of treatment. Chemotherapy, targeted therapy, immunotherapy, and radiotherapy may be used in some cases to provide palliative care or prolong survival, but a cure is not considered possible, and long-term complete remission is extremely rare [1–3]. Here we report a case of advanced gastric cancer with peritoneal oligometastases successfully treated by adaptive radiotherapy with concurrent chemotherapy.

Case description

A 70-year-old man with gastric cancer was referred to our hospital for treatment to improve his quality of life after peritoneal metastases were discovered during surgery. The patient was initially diagnosed with poorly differentiated gastric adenocarcinoma and surgical resection was attempted. During surgery, three peritoneal metastases, 3–4 mm in diameter, were found adjacent to the primary site, and radical resection of the gastric cancer was abandoned. The pathohistological diagnosis was poorly differentiated adenocarcinoma, consistent with the primary gastric lesion. Contrast-enhanced CT showed a tumor extending from the posterior wall of the gastric body to the esophagogastric junction with strong contrast enhancement (Fig. 1a). T2-weighted MRI showed that the gastric cancer was hyperintense relative to the liver parenchyma with an irregular border (Fig. 1b). Apparent diffusion coefficient map generated from diffusion-weighted imaging at a b-value of 800 s/mm^2 showed that the tumor was hypointense, consistent with gastric cancer (Fig. 1c). Whole-body contrast-enhanced CT showed no metastases. Since the patient's general condition was good, his past medical history was unremarkable, and CT and MRI showed no gross metastases, we considered that the patient's quality of life could be maintained by controlling the primary tumor and nearby peritoneal metastases.

All procedures conformed to the ethical standards of the institutional and national research committees and to the Helsinki Declaration of 1964 and its subsequent amendments or comparable ethical standards. Institutional review board approval was waived because each treatment was approved by the national health insurance system. Written informed consent was obtained from the patient for the use of clinical data. The patient underwent CT and MRI simulation, and fusion images of non-contrast CT and short-tau inversion recovery (STIR) images (Fig. 1d) were generated using Monaco 5.0 treatment planning software (Elekta AB, Stockholm, Sweden). The gross tumor volume (GTV) was defined on STIR images, and the internal target volume (ITV) was defined by expanding the GTV to cover the range of motion during free breathing using 4D CT. The clinical target volume (CTV) was defined as the IVT plus a 5–20 mm margin. The size of the margin was adjusted within a range of 5–20 mm, taking into account the direction of gastric dilatation and the position of the adjacent colon. The surgeon's suggestion has been incorporated to ensure that the CTV includes adjacent peritoneal metastases identified at the time of surgery. The planning target volume (PTV) was defined as a 5–10 mm margin from the CTV, based on radiation dose and volume to organs at risk (stomach, small bowel, liver, kidneys). The prescribed dose to the D95% of the PTV (the dose covering 95% of the PTV) was 59.4 Gy in 33 fractions over 6.5 weeks (Fig 2a-c).

The treatment plan was implemented using intensity-modulated radiation therapy (TomoTherapy, Accuray, Madison, WI, USA). The maximum dose in the PTV was < 66 Gy. The dose to 1 cm3 (D1cc) of small intestine and colon was less than 60 Gy. The patient fasted for 6 hours prior to radiotherapy and did not drink for 3 hours prior to radiotherapy. To reduce the dose to the surrounding normal tissues, adaptive radiotherapy planning was performed in the same manner as the initial planning when 41.4 Gy and 50.4 Gy were delivered. To enhance the efficacy of radiotherapy, the oral chemotherapeutic agent S-1 was administered concurrently with radiotherapy. Radiotherapy and chemotherapy were administered as planned, with no serious adverse events. After radiotherapy, S-1 was discontinued and the patient was followed with blood tests and MRI every 3 months thereafter. Follow-up MRI two years after radiotherapy showed complete tumor regression, and endoscopy showed no residual tumor. Six years after radiotherapy, there was no recurrence of the primary tumor or peritoneal metastases (Fig. 1e,f).

Discussion

Surgery and radiotherapy are usually not indicated for patients with advanced gastric cancer with peritoneal metastases. However, when the number of peritoneal metastases is small or confined to the vicinity of the primary site, aggressive local treatment may result in not only long-term remission but also cure. In patients with peritoneally metastatic gastric cancer, cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy has been suggested to prolong survival compared with chemotherapy alone or chemotherapy plus intraperitoneal aerosol chemotherapy [1]. Both cytoreductive surgery and hyperthermic intraperitoneal chemotherapy are invasive and require hospitalization; in addition, in contrast to the invasiveness of the treatments, the effectiveness against gastric cancer with peritoneal metastases is not satisfactory. As oligometastatic disease is becoming a candidate for curative treatment in patients with other types of malignancies, such as breast cancer or non-small cell lung cancer [4], oligometastatic gastric cancer may also be a potential candidate for curative treatment, even when peritoneal metastases are complicated. To the best of our knowledge, this is the first report of a patient with gastric cancer with peritoneal oligometastases successfully treated with adaptive radiotherapy and concurrent chemotherapy.

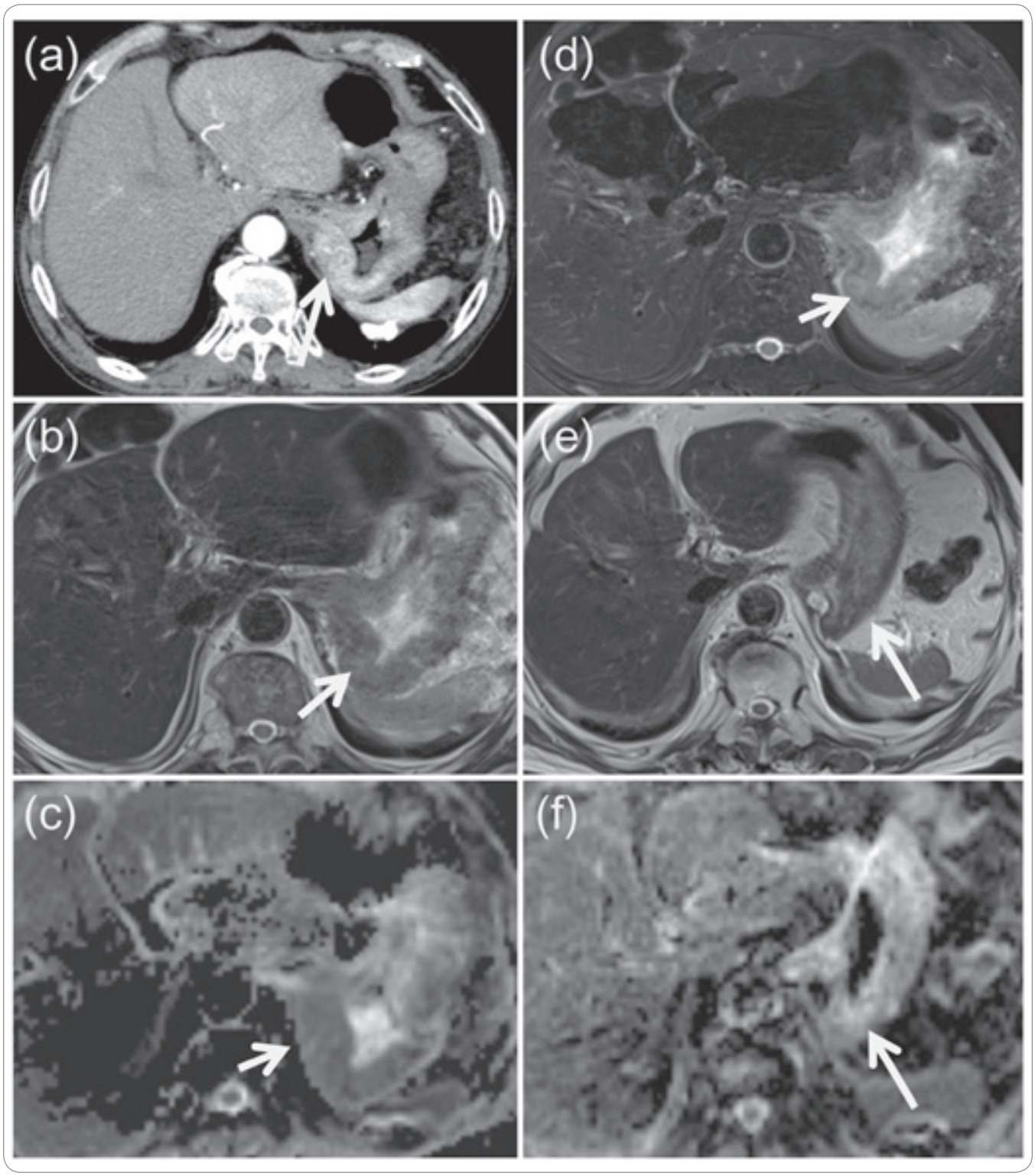

Fig. 1. CT and MRI findings. Contrast-enhanced CT prior to concurrent chemoradiotherapy showed thickening of the posterior gastric wall and strong contrast enhancement (arrow) (a); T2-weighted fast spin echo image showed that the posterior wall of the stomach was thickened with a hyperintense irregular mass (arrow) relative to the liver parenchyma (b); the apparent diffusion coefficient map generated from diffusion-weighted imaging at a b-value of 800 s/mm^2 showed that the gastric tumor (arrow) was hypointense compared to the skeletal muscle (c); T2-weighted fast spin echo image 6 years after radiotherapy showed complete disappearance of gastric tumor (arrow) with no evidence of metastasis (d); the apparent diffusion coefficient map generated from diffusion-weighted imaging at a b-value of 800 s/mm^2 6 years after radiotherapy showed that the gastric tumor disappeared completely (arrow) (e).

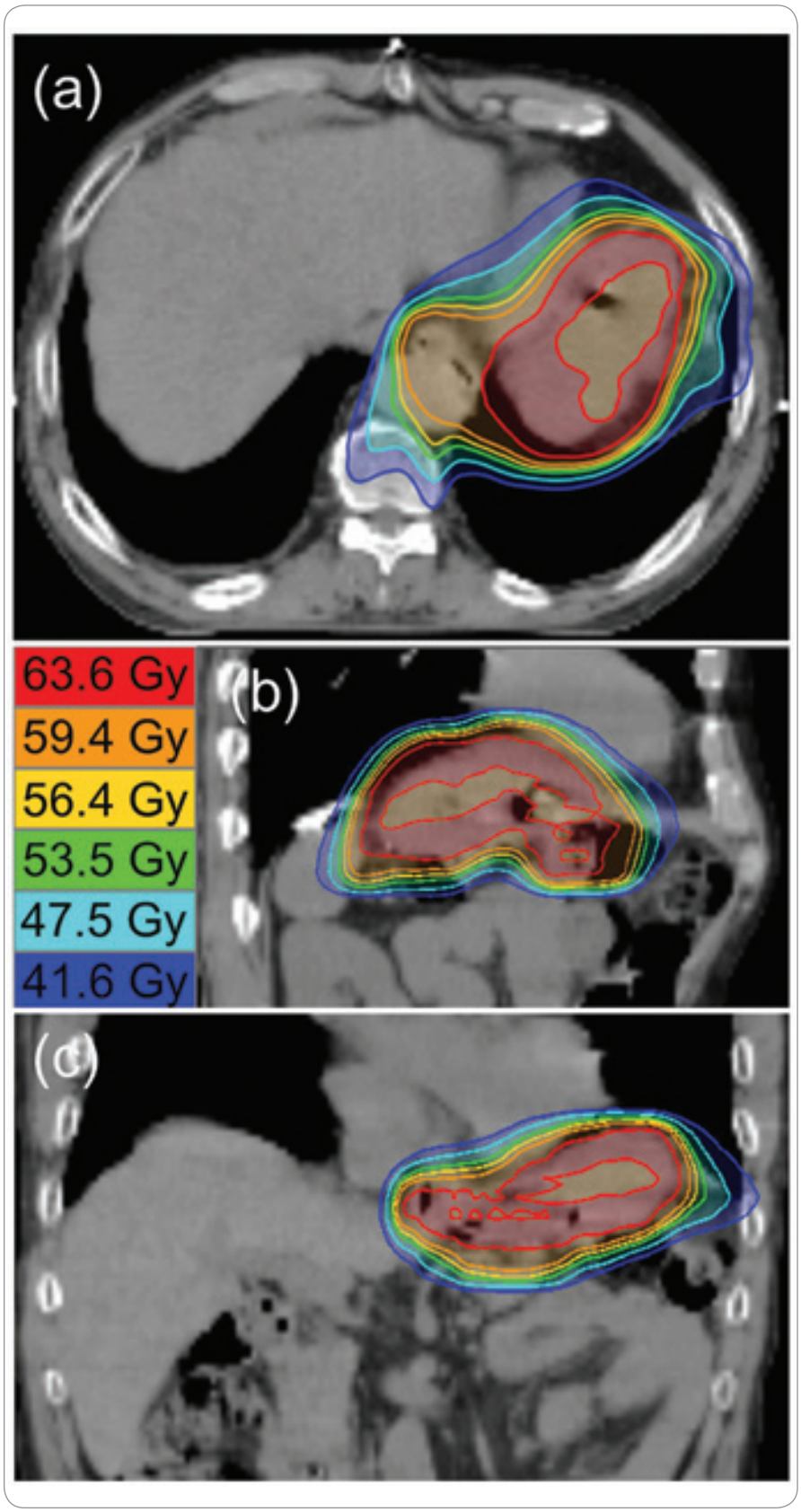

Fig. 2. Radiotherapy isodose line distribution. Isodose lines are displayed on (a) transverse, (b) coronal and (c) sagittal CT imaging. Isodose lines with corresponding actual radiation dose were given over 33 fractions.

This case report has several strengths. First, gross peritoneal metastases were identified during surgery and peritoneal oligometastases could be accurately diagnosed prior to radiotherapy to ensure they were confined to areas adjacent to the primary site. Since staging laparotomy is more sensitive and accurate for the diagnosis of peritoneal metastases than CT or MRI [2], exploratory laparotomy may help not only to assess the location of peritoneal metastases but also to select patients with peritoneal oligometastatic disease. Second, this case is the first demonstration of a so-called oligometastatic condition, in which the number and volume of peritoneal metastases are small and potentially curable if treated according to the curative treatment of oligometastases. The concept of oligometastases in gastric cancer peritoneal metastases is not established, but as with other cancers, if the number of metastases is small and the tumor volume is small, it may be possible to treat the tumor radically as an oligometastasis [5,6].

This case report has several limitations. First, there is uncertainty about chemotherapy regimens and optimal radiation doses. Regimens based on 5-fluorouracil and cisplatin are commonly used, but alternative combinations such as capecitabine and oxaliplatin (XELOX), S-1 and cisplatin, or other fluoropyrimidine-based combinations may also be used during radiotherapy [7]. The radiation dose for gastric cancer is usually 45–50 Gy over 5–6 weeks, but the optimal dose and schedule with S-1 has not yet been elucidated. Second, it is difficult to localize individual sites of peritoneal metastases, and image-guided radiotherapy for each peritoneal lesion is not possible. However, with the use of ITV and the integration of intraoperative findings, this drawback can be overcome.

Conclusion

In conclusion, a single case report cannot be generalized to other cases without further scientific verification, but oligometastatic peritoneal metastases of gastric cancer may be a candidate for curative treatment with adaptive radiotherapy administered concurrently with oral S-1.

Author contributions

YH, ET: patient management, conceptualization of case study, collection of study material, manuscript drafting, and manuscript revision and editing. Both authors approved the final version of the manuscript.

Informed consent

Written informed consent was obtained from the patient for participating in our study.

Patient perspective

The patient was satisfied and pleased with the care she received throughout the therapy. All procedures conformed to the ethical standards of the institutional and national research committees and to the Helsinki Declaration of 1964 and its subsequent amendments or comparable ethical standards. Institutional review board approval was waived because each treatment was approved by the national health insurance system. Written informed consent was obtained from the patient for the use of clinical data.

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