Cancer Management and Research

Elevate Series

Open Access Full Text Article

CASE REPORT

Stereotactic Radiosurgery in Multidisciplinary Management of HER2-Positive Gastroesophageal Junction Adenocarcinoma with Large-Brain Metastases: A 9-Year Survival Case

Lan Yu, Yu Wang, Li Liu, Hongmei Zhang, Xiaotao Zhang

Department of Oncology, Qingdao Central Hospital, University of Health and Rehabilitation Sciences, Qingdao, 266042, People's Republic of China

Correspondence: Xiaotao Zhang, Department of Oncology, Qingdao Central Hospital, University of Health and Rehabilitation Sciences, Qingdao, 266042, People's Republic of China, Email sabr@vip.163.com

Abstract: Patients with advanced gastroesophageal junction (GEJ) adenocarcinoma typically exhibit poor clinical outcomes, especially with brain metastases (BMs). Here, we present a notable patient with HER-2 positive advanced gastric cancer complicated with large-volume BMs who achieved long-term survival reaching 9 years through multidisciplinary treatment strategy encompassing abdominal radiotherapy, stereotactic radiosurgery (SRS), targeted therapy, and systemic chemotherapy. These findings highlight the need for balancing efficacy and safety to develop individualized radiotherapy strategies for large-volume BMs. This outcome highlights the potential benefits of comprehensive approaches and the feasibility of proactive local interventions for oligoprogressive disease. This case provides valuable experience for managing similar cases and offers new ideas for combining novel modalities like antibody-drug conjugates (ADC) drugs, immunotherapy, and radiotherapy.

Keywords: gastroesophageal junction cancer, HER2, stereotactic radiosurgery, trastuzumab, brain metastasis

Introduction

Gastric and esophageal cancers represent the fifth and seventh most common causes of cancer-related deaths worldwide, respectively.[1] In recent years, the incidence of adenocarcinoma in the gastroesophageal junction (GEJ) has increased significantly in Western and Asia countries, while that of squamous cell carcinoma has slowly declined.[2] GEJ cancers are often diagnosed at advanced stages, resulting in poor prognosis for patients.[3] Despite the recent developments in treatment modalities, survival outcomes remain unsatisfactory, with median overall survival (OS) remains below 15 months in most cohorts.[4,5]

In the past decade, the standard treatment for patients with human epidermal growth factor receptor 2 (HER2)-positive advanced GEJ adenocarcinoma has been trastuzumab combined with chemotherapy. However, even with this treatment, the median survival time(MST) remains limited, at only 13.8 months.[6] Even in the era of immunotherapy, the four-drug combination regimen in the KEYNOTE - 811 study only extended patients' survival to 20 months.[7] Many randomized controlled trials (RCTs) have confirmed that some patients with resectable gastric or GEJ cancer could benefit from preoperative and postoperative radiotherapy.[8,9] However, the role of radiotherapy in the advanced/metastatic gastric or GEJ cancer remains controversial.

Brain metastases (BMs) from gastric cancer are relatively rare and associated with an extremely dismal prognosis, especially with large-volume BMs. The lack of established treatment guidelines further complicates their management. Furthermore, the exploration of multidisciplinary comprehensive treatment, including radiotherapy, is of great clinical value for these patients. Here, we report a HER2-positive GEJ adenocarcinoma patient with large-brain metastases achieved long-term survival after receiving stereotactic radiosurgery (SRS), trastuzumab, and chemotherapy.

Received: 23 July 2025
Accepted: 25 October 2025
Published: 2 December 2025

Case Presentation

A 57-year-old female patient was admitted to a regional hospital due to progressive dysphagia on July 4, 2016. Gastroscopy indicated a tumor located at the gastric cardia invading the lower esophagus. On July 7, 2016, Staging contrast-enhanced CT scan showed abnormalities at lower esophagus and gastric cardia as well as multiple enlarged regional and distant lymph nodes (LNs). On July 11, 2016, positron emission tomography-computed tomography (PET-CT) scan showed the GEJ carcinoma with right paracardial, lesser curvature, left gastric, celiac and proximal splenic artery and paraaortic lymph node metastases (LNMs, Figure 1A). Biopsy pathology revealed HER2-positive adenocarcinoma (Figure 1B). The patient was diagnosed with HER2-positive stage IV (cT4bN3M1, AJCC 7th edition) GEJ adenocarcinoma upon admission to our hospital.

On July 13, 2016, the patient initially received four cycles of epirubicin, oxaliplatin plus capecitabine (EOX regimen) combined with trastuzumab. After that, CT assessment demonstrated partial remission (PR) in both the primary tumor and metastatic LNs. Due to the superimposed cardiotoxicity of epirubicin and trastuzumab, she received systemic therapy with two cycles of oxaliplatin, capecitabine, and trastuzumab. After six cycles of therapy, the CT scan on November 10, 2016 showed that sustained disease regression in the primary tumor and metastatic LNs compared to imaging after 4 cycles of treatment (Figures 2A and 2B).

From November 14, 2016, the patient underwent abdominal radiotherapy with a total dose of 45 gray (Gy) and 50.4 Gy in 1.8 Gy per fraction at the planning target volume (PTV) and the planning gross target volume (PGTV), respectively. On January 12, 2017, gastroscopy showed complete regression(CR) of the primary lesion, characterized by smooth esophageal mucosa and localized areas of gastric mucosal hyperemia and erosion without residual malignancy on biopsy (Figure 2C). From January 27 to May 17, 2017, the patient received 5 cycles of maintenance treatment with trastuzumab and capecitabine. On May 17, 2017, CT scan showed that only small LNs remained in the abdomen (Figure 2A).

Unfortunately, the patient presented with dizziness, nausea, vomiting, and gait instability in June 2017, with an Eastern Cooperative Oncology Group (ECOG) performance status of 3. Magnetic resonance imaging (MRI) showed bilateral cerebellar hemispheric metastases with a maximum diameter of 4.3 cm (Figure 2D), accompanied by elevated serum tumor markers CA242 and CA199 on hematology tests. From June 15, 2017 to July 4, 2017, the patient underwent whole-brain radiation therapy (WBRT) with 30 Gy delivered in 15 fractions (2Gy/fraction). However, post-treatment evaluation revealed no significant clinical improvement or reduction in brain metastases. Considering that large-volume BMs are insensitive to conventional radiotherapy fractionation, the patient received SRS on July 19, 2017, using a rigid-frame Gamma Knife with a single-fraction dose of 15 Gy prescribed to the 50% isodose line at the PTV. One month after SRS, contrast-enhanced brain MRI showed that the maximum diameter of brain lesions was reduced from 4.3 cm before

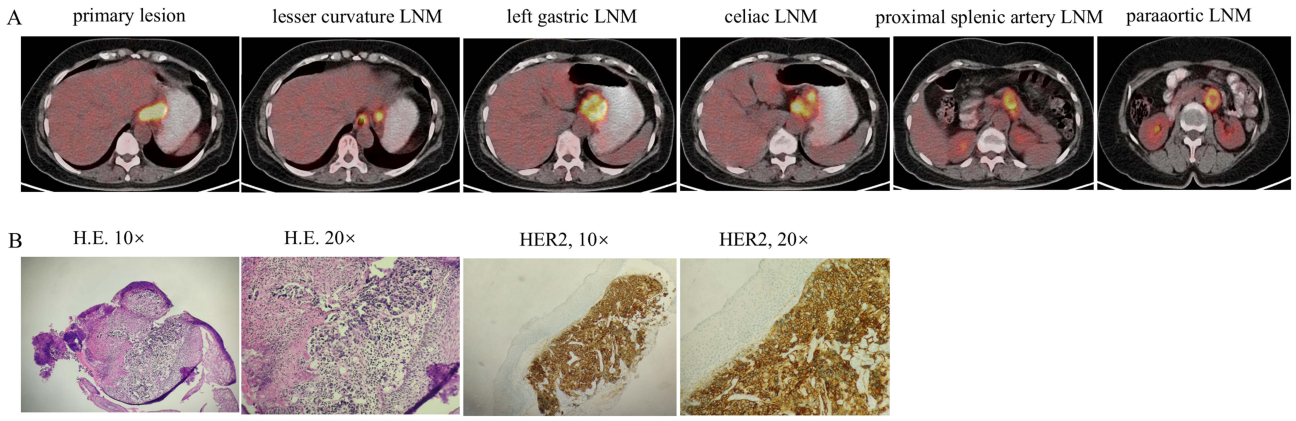

Figure 1 PET-CT and pathology at diagnosis. (**A**) PET-CT images showed GEJ carcinoma with right paracardial, lesser curvature, left gastric, celiac and proximal splenic artery, and paraaortic lymph node metastases (LNMs). (**B**) H.E. staining revealed the characteristics of gastric adenocarcinoma. IHC showed the positive expression of HER2 in the tumor cells.

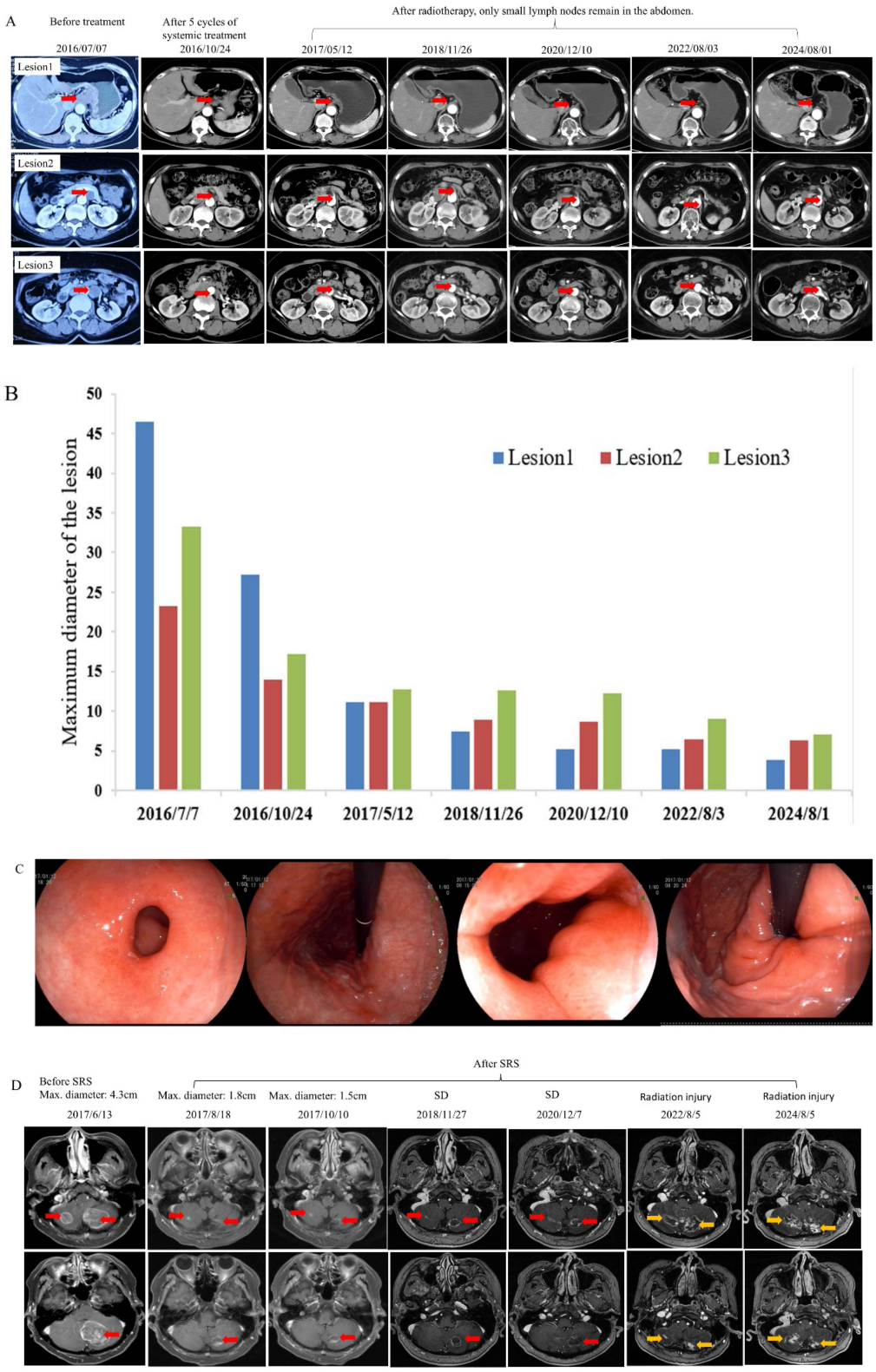

Figure 2 The therapeutic efficacy of stereotactic radiosurgery, abdominal radiotherapy and systemic therapy in the patient. (**A** and **B**) The abdominal lesions shrunk remarkably, and reached nearly CR after local radiotherapy. (**C**) Gastroscopy after abdominal radiotherapy revealed smooth esophageal mucosa and localized areas of gastric mucosal hyperemia and erosion, indicating complete regression of the primary tumor. (**D**) MRI images demonstrated that after SRS, the bilateral cerebellar hemisphere metastases were significantly reduced (red arrows mean the metastatic lesions in cerebellar hemisphere, and yellow arrows refer to the radiation-induced brain injury).

https://doi.org/10.2147/CMAR.S551817

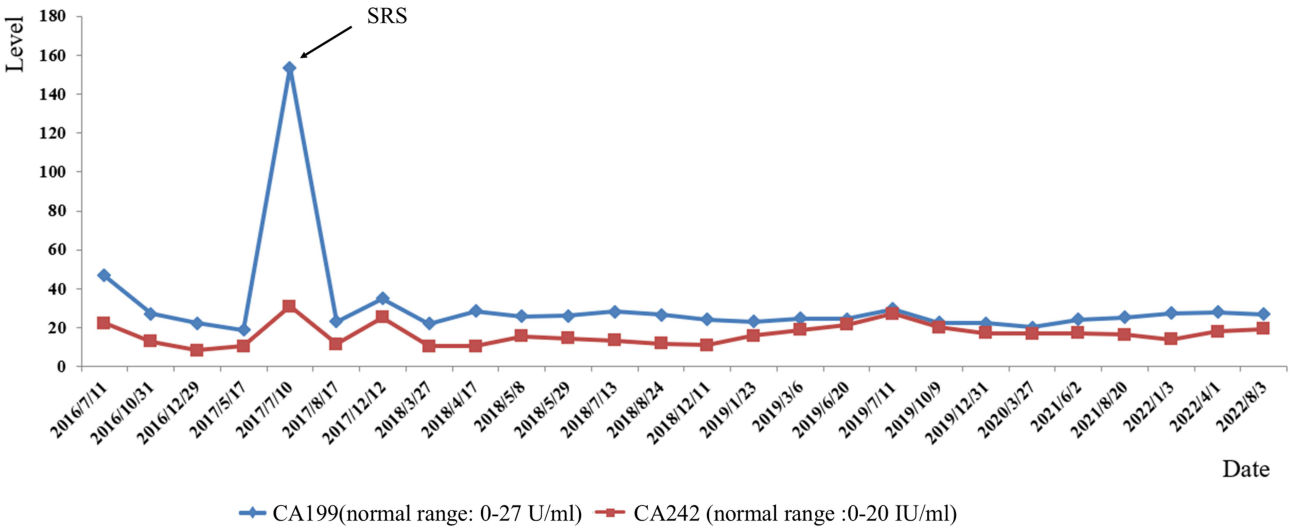

Figure 3 Serum levels of tumor biomarkers CA199 and CA242 returned to normal levels after SRS.

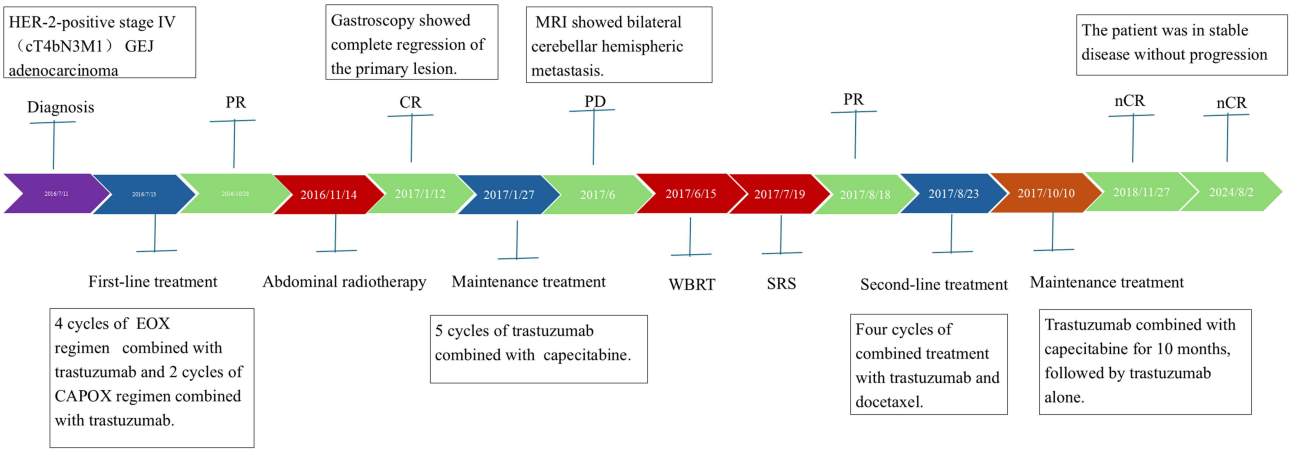

Figure 4 Diagnosis and treatment course of the patient.

SRS to 1.8 cm (Figure 2D). Serum tumor marker analysis revealed that CA199 and CA242 returned to normal levels (Figure 3), and the patient's neurological symptoms disappeared completely, with an ECOG performance status of 1.

From August 23, 2017, the patient was delivered four cycles of combined treatment with trastuzumab and docetaxel. Contrast-enhanced brain MRI on October 10, 2017 showed that the maximum diameter of the brain lesions was further reduced to 1.5 cm (Figure 2D). Since then, the patient has received maintenance treatment with trastuzumab and capecitabine for ten months. Because of the recurrence of old pulmonary tuberculosis, the patient received anti-tuberculosis treatment. Then, she received trastuzumab monotherapy for maintenance treatment until November 2020. The CT and MRI on November 27, 2018 showed that cranial and abdominal metastases reached near-complete response (nCR), with sustained remission (Figures 2A and 2D). The latest follow-up on August 5, 2024 found that the patient's condition was stable with asymptomatic radiation-induced brain injury (Figures 2D), and at the time of submitting the manuscript, the patient has survived for more than 107 months. The case timeline is presented in Figure 4.

Discussion

Systemic therapy is the standard treatment for advanced GEJ cancer. The EOX regimen is one of the commonly used chemotherapy regimens for advanced gastric cancer.[10] The landmark ToGa trial established trastuzumab in combination with chemotherapy as the standard of care for patients with HER2-positive advanced GEJ adenocarcinoma.[6]

The patient received first-line trastuzumab combined with the EOX regimen treatment, achieving significant tumor regression, which created conditions for subsequent local radiotherapy and also demonstrated the important role of targeted therapy in HER-2 positive gastric cancer. In recent years, therapeutic advances in recent years, including the antibody-drug conjugates (ADCs) such as trastuzumab deruxtecan and the combination regimen of pembrolizumab with trastuzumab and chemotherapy, have also shown good efficacy in clinical trials, providing more treatment options for patients with HER-2 positive advanced gastric cancer.[7,11]

Studies have shown that combining local radiotherapy with systemic therapy can improve the OS of patients with oligometastatic gastric cancer.[12,13] In this case, the patient received abdominal radiotherapy for the primary lesion and metastatic LNs, achieving CR of the primary lesion and near CR (nCR) of the metastatic lymph nodes. Local radiotherapy played a crucial role in reducing the tumor burden and prolonging the patient's regional progression-free survival (PFS) time. This case suggests that for patients who are chemosensitive or have a low tumor burden, local radiotherapy may delay progression by eradicating drug-resistant clones.

In stark contrast to the high incidence of BMs in melanoma (40–40%), lung (30–50%), and breast cancer (10–15%), BMs are relatively rare in gastric cancer, with an incidence rate of less than 1%, and is associated with an extremely poor prognosis.[14] The patient developed BMs at 12-month PFS in June 2017. The possible reason was pre-existing micrometastases at initial diagnosis, and the inability of chemotherapy agents and trastuzumab to penetrate the blood–brain barrier. Radiotherapy is the main treatment modality for BMs. RTOG 9508 trial showed that patients with 1–3 BMs treated with radiosurgery (SRS) boost after WBRT had better survival than those receiving WBRT alone.[15,16] A randomized clinical trial from 34 institutions in North America indicated that SRS alone resulted in less cognitive dysfunction and similar OS compared with SRS combined with WBRT in patients with 1–3 BMs.[17] These findings suggest that SRS alone is a preferred strategy for patients with 1–3 BMs. The patient had two BMs with a maximum diameter of 4.3 cm, making her unsuitable for SRS as the first-line treatment option.[18] Therefore, she first underwent WBRT, with our plan to deliver SRS boost after the BMs had shrunk. However, the lesions did not significantly reduce in size after WBRT, which may be due to the large lesions making them insensitive to conventional fractionated radiotherapy. Then, the patient received SRS, which successfully reduced the maximum diameter of the BMs from 4.3 cm to 1.8 cm after one month. The BMs continued to shrink after the procedure, thereby rescuing the patient from life-threatening mass effect and quickly relieving the cerebral symptoms.

During long-term follow-up, the patient developed asymptomatic radiation-induced brain injury without recurrence, demonstrating durable local tumor control. This suggests that SRS is a successful treatment option for this patient and SRS is an effective treatment modality for some patients with large-volume BMs. This case also highlights that SRS can lead to the risk of radiation-induced brain injury, especially in patients with large-volume BMs. These findings highlight the imperative to evaluate tumor volume and neurological function, while weighing the efficacy and safety risks, to develop individualized radiation therapy strategies that optimize clinical outcomes in this population with large-volume BMs.

The clinical value of maintenance therapy following first-line chemotherapy has been well established in malignancies, such as colorectal cancer and breast cancer,[19,20] yet has not been established in advanced gastric cancer. In this report, the patient received low-toxicity maintenance treatment with trastuzumab and capecitabine, achieving sustained remission without tumor progression. At the time of submitting this manuscript, the patient had survived for more than 108 months, which exceeds the median OS of 20.0 months reported in the KEYNOTE-811 trial for HER2-positive advanced gastric cancer in the immunotherapy era.[7]

There are also several limitations in this case. Firstly, the patient's first-line treatment adopted the EOX regimen combined with trastuzumab, which may increase the cardiotoxicity risks. Secondly, the combined use of angiogenesis inhibitors such as bevacizumab may prevent and alleviate radiation-induced brain injury. Third, the absence of immune-related biomarkers such as programmed cell death ligand 1 (PD-L1) expression and MSI status due to the early diagnostic time limits the assessment of immunotherapy indications.

Conclusion

In summary, we report a patient with HER-2 positive advanced gastric cancer complicated with large-volume BMs who achieved long-term survival through multidisciplinary comprehensive treatment including SRS, targeted therapy, and

chemotherapy. The case highlights the feasibility of adopting proactive local interventions for oligoprogressive disease. Under the balance of efficacy and safety risks, SRS is an effective treatment modality for some patients with large-volume BMs. This case also provides valuable clinical experience for the multidisciplinary team(MDT) management of HER-2 positive advanced gastric cancer with rare BMs, and offers new ideas for the combination of novel treatment modalities, including ADC drugs, immunotherapy, and radiotherapy.

Data Sharing Statement

All the data supporting the findings are available upon reasonable request from the corresponding author.

Ethics Approval

Institutional approval was required and obtained from the Ethics Committee of Qingdao Central Hospital, University of Health and Rehabilitation Sciences for the publication of this case report. The study has been performed in accordance with the Declaration of Helsinki.

Informed Consent Statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Consent to Publish Statement

We consent to the publication of the work, including any associated images, videos, recordings, and other materials.

Acknowledgments

The authors wish to thank the patient for her participation.

Author Contributions

All authors have made significant contributions to this work. Their contributions include conception, study design, execution, data acquisition, analysis, interpretation, or a combination of these areas. All authors also participated in drafting, revising, or critically reviewing the manuscript. Furthermore, all authors have approved the final version for publication, agreed to submit to this journal, and accept accountability for all aspects of the work.

Funding

The authors state no funding involved.

Disclosure

The authors declare that they have no conflicts of interest in this work.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *Ca a Cancer J Clin*. 2024;74(3):229–263. doi:10.3322/caac.21834
2. Manabe N, Matsueda K, Haruma K. Epidemiological review of gastroesophageal junction adenocarcinoma in Asian Countries. *Digestion*. 2022;103 (1):29–36. doi:10.1159/000519602
3. Chevallay M, Bollschweiler E, Chandramohan SM, et al. Cancer of the gastroesophageal junction: a diagnosis, classification, and management review. *Ann NY Acad Sci*. 2018;1434(1):132–138. doi:10.1111/nyas.13954
4. Shah MA, Shitara K, Ajani JA, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, Phase 3 GLOW trial. *Nat Med*. 2023;29(8):2133–2141. doi:10.1038/s41591-023-02465-7
5. Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. *Lancet*. 2021;398 (10294):27–40. doi:10.1016/S0140-6736(21)00797-2
6. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet*. 2010;376 (9742):687–697. doi:10.1016/S0140-6736(10)61121-X

7. Janjigian YY, Kawazoe A, Bai Y, et al. Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial. *Lancet*. 2023;402 (10418):2197–2208. doi:10.1016/S0140-6736(23)02033-0
8. Shapiro J, Van Lanschot JJB, Hulshof MCCM, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. *Lancet Oncol*. 2015;16(9):1090–1098. doi:10.1016/S1470-2045(15) 00040-6
9. Kim Y, Park SH, Kim KM, et al. The influence of metastatic lymph node ratio on the treatment outcomes in the adjuvant chemoradiotherapy in stomach tumors (ARTIST) trial: a phase III trial. *J Gastric Cancer*. 2016;16(2):105. doi:10.5230/jgc.2016.16.2.105
10. Cunningham D, Nicolson M, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. *N Engl J Med*. 2008;358(1):36–46. doi:10.1056/NEJMoa073149
11. Meric-Bernstam F, Makker V, Oaknin A, et al. Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: primary results from the DESTINY-PanTumor02 Phase II trial. *JCO*. 2024;42(1):47–58. doi:10.1200/JCO.23.02005
12. Kroese TE, Jorritsma NKN, Van Laarhoven HWM, et al. Stereotactic radiotherapy or metastasectomy for oligometastatic esophagogastric cancer: a nationwide population-based cohort study. *Clin Transl Radiation Oncol*. 2022;37:109–115. doi:10.1016/j.ctro.2022.08.012
13. Kroese TE, Van Laarhoven HWM, Nilsson M, et al. Definition of oligometastatic esophagogastric cancer and impact of local oligometastasis-directed treatment: a systematic review and meta-analysis. *Eur J Cancer*. 2022;166:254–269. doi:10.1016/j.ejca.2022.02.018
14. Yang Y, Yang Y, Chen Z. Patients with brain metastases from gastric cancer. *Tumori*. 2023;109(2):164–172. doi:10.1177/03008916221084361
15. Andrews DW, Scott CB, Sperduto PW, et al. Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: phase III results of the RTOG 9508 randomised trial. *Lancet*. 2004;363(9422):1665–1672. doi:10.1016/S0140-6736(04) 16250-8
16. Sperduto PW, Shanley R, Luo X, et al. Secondary analysis of RTOG 9508, a phase 3 randomized trial of whole-brain radiation therapy versus WBRT plus stereotactic radiosurgery in patients with 1–3 brain metastases; poststratified by the graded prognostic assessment (GPA). *Int J Radiation Oncol *biol *phys*. 2014;90(3):526–531. doi:10.1016/j.ijrobp.2014.07.002
17. Brown PD, Jaeckle K, Ballman KV, et al. Effect of radiosurgery alone vs radiosurgery with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: a randomized clinical trial. *JAMA*. 2016;316(4):401–409. doi:10.1001/jama.2016.9839
18. Molenaar R, Wiggenraad R, Verbeek-de Kanter A, et al. Relationship between volume, dose and local control in stereotactic radiosurgery of brain metastasis. *Br J Neurosurg*. 2009;23(2):170–178. doi:10.1080/02688690902755613
19. Sonbol MB, Mountjoy LJ, Firwana B, et al. The role of maintenance strategies in metastatic colorectal cancer: a systematic review and network meta-analysis of randomized clinical trials. *JAMA Oncol*. 2020;6(3):e194489. doi:10.1001/jamaoncol.2019.4489
20. Wang X, Wang SS, Huang H, et al. Effect of capecitabine maintenance therapy using lower dosage and higher frequency vs observation on disease-free survival among patients with early-stage triple-negative breast cancer who had received standard treatment: the SYSUCC-001 randomized clinical trial. *JAMA*. 2021;325(1):50–58. doi:10.1001/jama.2020.23370