

Late recurrence of gastric cancer with isolated brain metastasis

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Abstract: A 70-year-old woman presented to our clinic in 2007 after an evaluation for dysphagia revealed a poorly differentiated adenocarcinoma of the gastroesophageal junction. Workup for metastatic disease was negative at presentation. She had a complete response to treatment, which was completed in November 2007. She continued to follow up regularly until 2011 when she presented again with neurologic symptoms and was found to have an isolated brain metastasis. She underwent resection of the lesion, and pathology was consistent with her originally diagnosed gastric cancer. The patient received adjuvant radiation therapy, however, unfortunately had rapid progression of disease 1 month later and was transitioned to hospice. Here, we report a rare case of late recurrence of gastric cancer with isolated brain metastasis with a review of literature.

Keywords: Gastric cancer; recurrence; brain metastasis

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Introduction

Brain metastasis from gastric cancer is rare and almost always accompanied by disseminated disease. We report an unusual case of a patient diagnosed with a sole metastatic lesion to the brain more than 4 years after presentation with locally advanced gastric adenocarcinoma, without extra-cranial disease.

Case presentation

JH presented in January of 2007 at the age of 70 with dysphagia and was found to have an ulcerating circumferential tumor of the gastroesophageal junction that was confirmed a poorly differentiated adenocarcinoma. Imaging studies revealed non-metastatic disease. She received neoadjuvant chemotherapy with FOLFIRI (5FU/leucovorin/irinotecan) and underwent total gastrectomy in July 2007. Pathology showed an ypT2bN2M0 poorly differentiated adenocarcinoma extending into the subserosa and involving the proximal cardia and distal esophagus. Gallbladder, small bowel and the rest of the gastric pathology were negative for malignancy. The residual

tumor was 3 cm × 3 cm × 1 cm in size with an R0 resection, the closest margin being 1.5 cm. Perineural and vascular invasion were present. Lymph node examination showed 4 of 27 nodes positive. Six cycles of adjuvant FOLFIRI chemotherapy were given and completed in November 2007. The patient was followed with regular surveillance first at her treating facility, Roswell Park Cancer Institute and subsequently at UCONN Health.

In early 2011 she began experiencing headaches, memory problems and word-finding difficulty. A neurological exam demonstrated right hemianopsia, nominal aphasia, recent and immediate memory problems, and an abnormal clock-drawing test. MRI of her brain in March 2011 showed a single 4.4 cm × 3.8 cm × 4.5 cm well-circumscribed lesion in the paramedian aspect of the left occipital lobe with surrounding vasogenic edema (*Figure 1*). Scans for other sites of metastatic disease were negative. The patient underwent stereotactic left parieto-occipital craniotomy with resection of the lesion. Pathology revealed a poorly differentiated adenocarcinoma comparable with her previous gastric cancer (*Figure 2A,B*). HER2 was not over-expressed (immunohistochemical 0/3) (*Figure 2C*).

Post-operative radiation was administered using partial

brain technique. A total of 50 Gy was delivered over 20 fractions using intensity modulated radiotherapy (IMRT) and image guided radiotherapy (IGRT) techniques with daily megavoltage CT on a Hi-Art Tomotherapy System® (Figure 3). The patient improved post-operatively, but developed several large nodular lesions on her scalp 1 month later. Biopsy of the scalp lesion and CSF analysis confirmed progressive metastatic involvement. She deteriorated rapidly and was transitioned to hospice.

Autopsy revealed metastatic poorly differentiated gastric carcinoma at the previous craniotomy site within the

radiated field, also diffusely involving the leptomeninges, cerebellum and spinal cord, and focally involving the underlying brain parenchyma in the right parieto-occipital lobe, hippocampus, midbrain, cerebellum and pituitary gland. There was no evidence of malignancy in the bone, bone marrow, thorax, abdomen or pelvis or any site outside the brain.

Discussion

Gastric cancer remains a lethal malignancy both in the United States and globally. It is the 14th most common cancer in the United States with 24,590 new cases documented each year, resulting in more than 10,000 deaths annually (1). With 723,000 deaths worldwide, it is the third leading cause of cancer death for both sexes second only to lung cancer (2).

Brain metastasis is uncommon in gastric cancer; recurrence mostly occurs intra-abdominally. Extra-abdominal metastasis, usually involving lung and bone occurs in only about 13% of cases (3). A U.S. study that included over 3,000 gastric cancer cases over a 40-year period reported brain metastasis in only 0.7% of patients (4). In a study from Japan, 2,322 patients were identified to have gastric cancer from 1980 to 1998 and only 11 (0.47%) had metastatic brain lesions (5). Apart from these two large studies, the literature on gastric cancer metastatic to the brain consists mainly of case reports and limited case series.

In gastric cancer, brain metastasis occurring years after the initial diagnosis is rare and almost always accompanied by systemic relapse (4,5). A case series reported an interval period between diagnosis and development of brain metastasis ranging from 1 to 24 months (6). Our case is

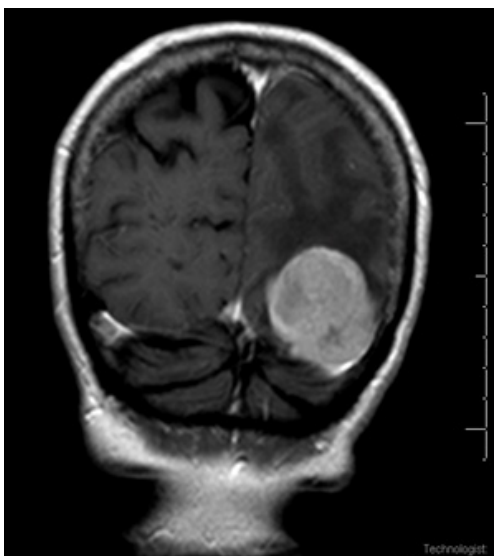


Figure 1 MRI post contrast T1 gadolinium image. Coronal view: 4.4 cm × 3.6 cm × 4.5 cm well-circumscribed heterogeneously enhancing soft tissue mass in the paramedian aspect of the left occipital lobe with surrounding vasogenic edema.

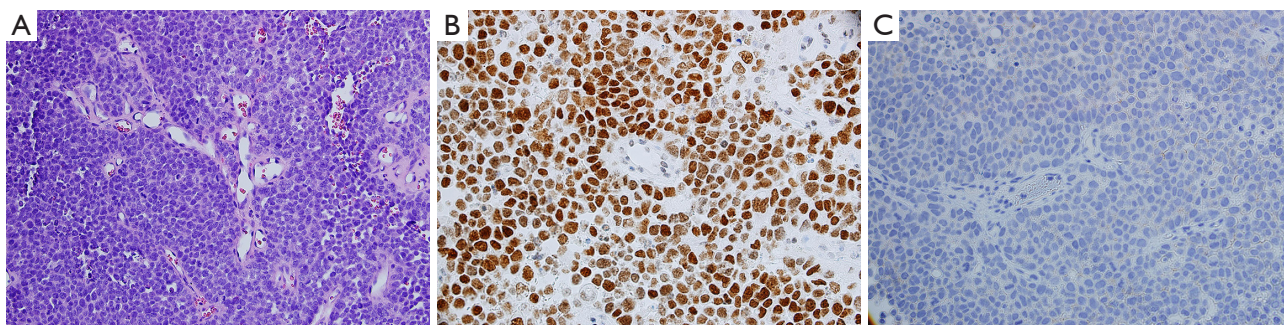


Figure 2 H&E and immunohistochemical staining of the resected brain lesion, indicating gastric origin of the tumor. (A) Invasive adenocarcinoma in cranial resection specimen H&E stain 100× (10× objective × 10× ocular); (B) invasive adenocarcinoma in cranial resection specimen CDX2 stain 400× (40× objective × 10× ocular); (C) invasive adenocarcinoma in cranial resection specimen HER2 IHC stain 200× (20× objective × 10× ocular).

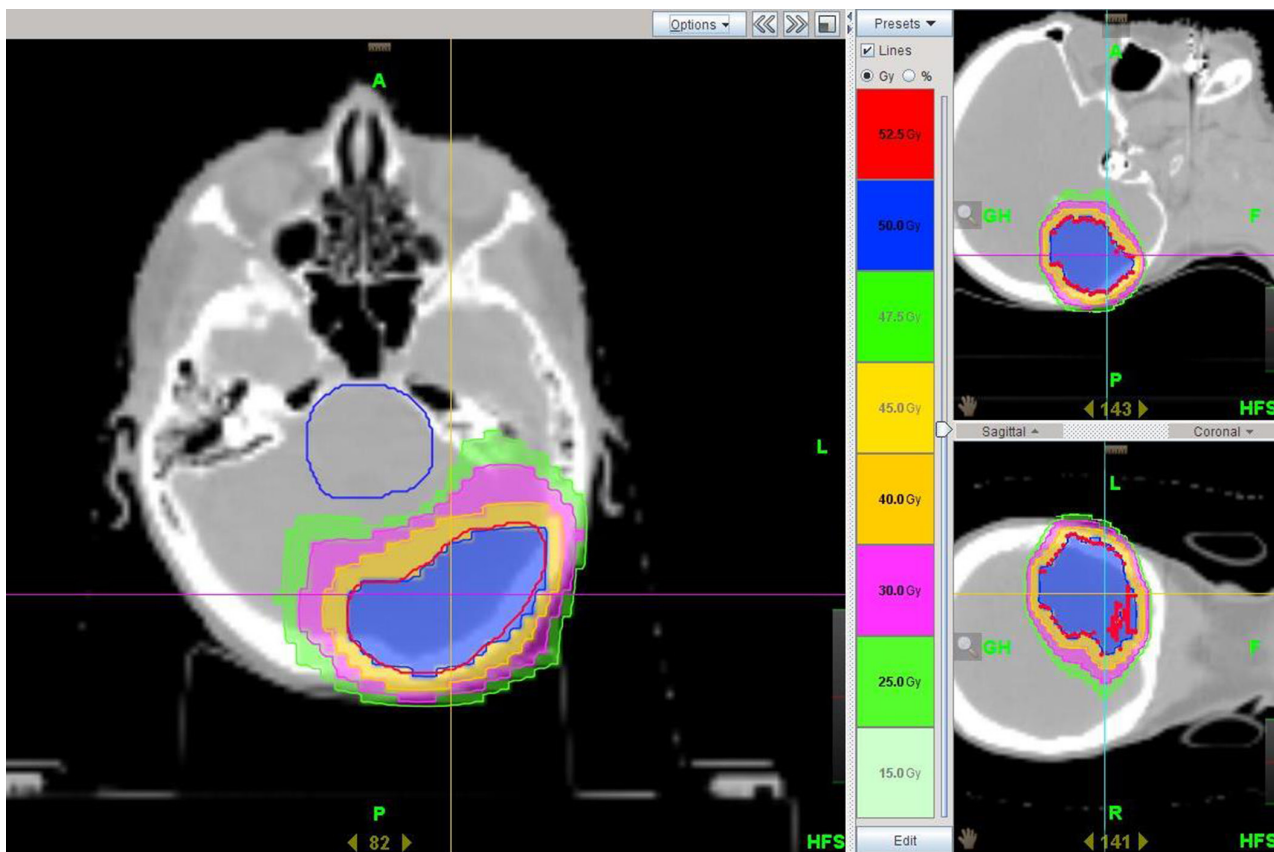


Figure 3 Axial, sagittal and coronal images from the treatment planning CT, showing prescription doses to tumor bed at 50 Gy (blue), 40 Gy (orange), 30 Gy (purple) and 25 Gy (green) colorwash. Note sparing of dose from the brains.

unique as the patient developed cerebral metastasis 4 years after initial diagnosis with no evidence of other systemic recurrent disease even at autopsy.

Our patient received perioperative chemotherapy for high grade gastric cancer, with a regimen utilized at the Roswell-Park Cancer Institute. She survived 4 years with no systemic recurrence only to relapse in brain with again high grade disease. HER2 positivity is found in 22% of gastric cancer cases (7). In breast cancer, it is associated with a higher incidence of brain metastasis (8), therefore looked for in our case, but negative.

The prognosis of gastric cancer patients who present with brain metastasis is dismal, and treatment is palliative. Response to treatment is poor in this cohort of patients (4,5). Treatment options include surgical resection (SR), brain radiotherapy, steroids, chemotherapy or a combination. The selection of treatment modality for these metastatic brain tumors depends on the number and resectability of the lesion(s) and the general health condition of the patient (9).

York *et al.* reported a median survival of 54 weeks (range, 22–83 weeks) in patients with gastric cancer with brain metastases who underwent SR, whole brain radiotherapy (WBRT) and steroid therapy (4). The median survival among the WBRT-alone group did not differ from patients who received steroid monotherapy (9.0 weeks with WBRT *vs.* 7.0 weeks with steroids, $P > 0.05$). In retrospective analyses, the combination of SR and WBRT was associated with a survival advantage (4,10). A case series from Japan of four patients with cerebral gastric cancer metastases showed an overall survival ranging from 45–94 days post-treatment with SR and/or stereotactic radiosurgery (11). In solid tumors as a group, local brain radiotherapy (LBRT) following surgery was shown retrospectively to be similar to WBRT following surgery in patients with single brain metastasis in terms of local recurrence rate and median survival time (12). Because of this data, we treated our patient with LBRT in conjunction with SR, unfortunately with rapid tumor growth. The best approach to treatment

of these patients remains unclear.

Our case illustrates that gastric cancer cells may lay dormant in the central nervous system for years and recur as virulent resistant disease. As combined modality treatments for initial therapy of aggressive cancers improve outcomes, cancer dormancy may become more apparent and recurrences seen in less common sites like brain. An understanding of cancer dormancy mechanisms and ways to target these small populations of cells is crucial to improving the outcome of these patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient's next of kin for publication of this manuscript and any accompanying images.

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