CLINICAL VIGNETTE

Miracle on Irinotecan

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Introduction

Gastric cancer is the fifth most common cancer worldwide and the fourth leading cause of cancer deaths.[1,2] It is more common in men than women and the median age at diagnosis in the United States is 68 years.[4,5] There are a variety of genetic and environmental risk factors for gastric cancer, including tobacco use, a diet high in nitrates and nitrites and viruses, including H.pylori and Epstein bar virus (EBV).[6] The incidence of gastric cancer varies globally and is more common in Asian countries and represents only 1.4% of all new cancer diagnoses in the United States.[1,5] As a result, there are no effective screening modalities at a population level for gastric cancer in the United States.[7] Common presentations include heartburn, melena, anemia and/or weight loss.[6] Diagnosis is typically made through upper gastrointestinal endoscopy.[7] Unfortunately, only 25% of patients at diagnosis have early, localized disease that can be resected.[1] Rather, most patients have either advanced or metastatic disease at diagnosis given symptoms generally only present once the disease is at least locally advanced.[5,8] Peritoneal carcinomatosis is found in up to 20% of people with negative imaging, so gastric cancer staging includes the unique step of diagnostic laparoscopy to evaluate for peritoneal disease.[6] Depending on staging at diagnosis, treatment often involves a multidisciplinary approach with considerations for both chemotherapy and surgery less commonly radiation.[6] Despite advances in treatment and improving mortality, prognosis remains poor with a five-year survival of 33% in the United States.[1,5]

Case Report

A 62-year-old woman presented to the hospital with one month of abdominal pain, decreased oral intake and melena. Imaging showed a markedly dilated stomach and duodenum and a gastroduodenal fistula with associated pneumatosis and perforation without frank pneumoperitoneum. She was taken to surgery and was found to have a 7x3cm ulcerated gastric mass. The ulceration and duodenal fistula were repaired, and the pathology from the mass came back positive for gastric adenocarcinoma.

Full staging with a PET scan was completed and was negative for metastatic disease, although high clinical suspicion remained in the setting of perforation at presentation. She started neoadjuvant chemotherapy with 5-fluororuacil, leucovorin, docetaxel and oxaliplatin (FLOT). She was taken to surgery for resection after 3 cycles due to repeat imaging and clinical symptoms concerning for gastric outlet obstruction. Unfortunately, the extent of her tumor did not allow for complete resection at that time, so diversion via gastrojejunostomy was performed instead with plan for resection following total neoadjuvant therapy. She then completed an additional 5 cycles of FLOT for a total of 8 cycles of chemotherapy. Post-treatment scans were negative for visible malignancy. She underwent surgical resection with a distal gastrectomy, revision of gastrojejunostomy and duodenal resection with small bowel anastomosis. Pathology revealed staging ypT2N0.

Three months later she presented to the emergency department with abdominal pain and dyspnea and was found to have a pulmonary embolism and a new 8.7x4.9cm mass abutting the greater curvature of the stomach in the left upper quadrant with questionable erosion of the gastric mucosa consistent with disease recurrence. (See Figure 1.) After discussion with surgery, the recommendation was for chemotherapy given quick recurrence after previous extensive surgical resection. The patient agreed to treatment with irinotecan, although contemplated best supportive care given desire to focus on quality of life. After four cycles of irinotecan (100mg/m2 D1, D8 q21D) she had restaging imaging that showed a complete response, with radiology believing she had undergone surgical resection. She underwent an additional three cycles of therapy before requesting a treatment holiday. She has been off therapy for six months currently and is still without evidence of disease recurrence or other metastatic disease.

Discussion

Combination chemotherapy with doublet or triplet therapy has been shown to have a higher response rate and improved overall survival in resectable gastric cancer compared to single-agent chemotherapy.[6] Standard of care for locally advanced gastric cancer is perioperative chemotherapy with FLOT, as was given in our patient.[9,10] In the metastatic or unresectable setting, first-line therapy is a fluorouracil base with a platinum agent.[11] However, there is no standard second-line therapy, with NCCN giving “category 1” recommendations to four different thera-

pies including docetaxel, irinotecan, paclitaxel and paclitaxel with ramucirumab.[3,9]

Given our patient relapsed so quickly after treatment, docetaxel was not recommended. There was a desire to avoid chemotherapy that might worsen her mild neuropathy and therefore paclitaxel was not considered. Additionally, ramucirumab was not available at our institution. Therefore, single-agent irinotecan was recommended for this patient. Irinotecan is a topoisomerase I inhibitor and works by disrupting DNA replication and cell division.[1] Single-agent irinotecan is a reasonable second-line therapy, although reported response rates are quite low with one retrospective study showing an overall response rate of only 11%, median progression-free survival (PFS) of 3.5 months and overall survival (OS) of 11.3 mo.[2] Common side effects include gastrointestinal toxicities such as diarrhea, nausea and vomiting as well as cytopenias.[2]

Given the intensity of our patient's prior chemotherapy and surgical resection, she was understandably discouraged about her relapsed disease. Unsurprisingly, rates of anxiety and depression are higher among patients at time of relapsed disease compared to initial diagnosis.[8] Due to a desire to focus on quality of life, she was contemplating not proceeding with therapy. With best supportive care alone, the survival for patients with unresectable gastric cancer is only 3-5 months.[12]

In a non-curative setting, it is especially important that treatment decisions are made with patient goals in mind. However, one must not ignore the possible benefit of treatment and ability to control symptoms with aggressive palliative measures in a patient with good performance status. Chemotherapy has been shown to improve OS by 6.7 months when compared to best supportive care in unresectable or metastatic gastric cancer.[1] This patient's willingness to proceed with therapy provided her with an unanticipated remission.

Conclusion

Gastric cancer is major cause of cancer-related deaths worldwide despite improvements in treatment.[4] Chemotherapy has been shown to improve OS by 6.7 months when compared to best supportive care in unresectable or metastatic gastric cancer.[1] There is no standard of care for second-line chemotherapy in this setting, but irinotecan is frequently given third line after paclitaxel and ramucirumab. We described a rare case of complete remission with single-agent irinotecan in the second-line setting. In a field grounded by science, this irinotecan 'miracle' is a welcomed unexpected result.

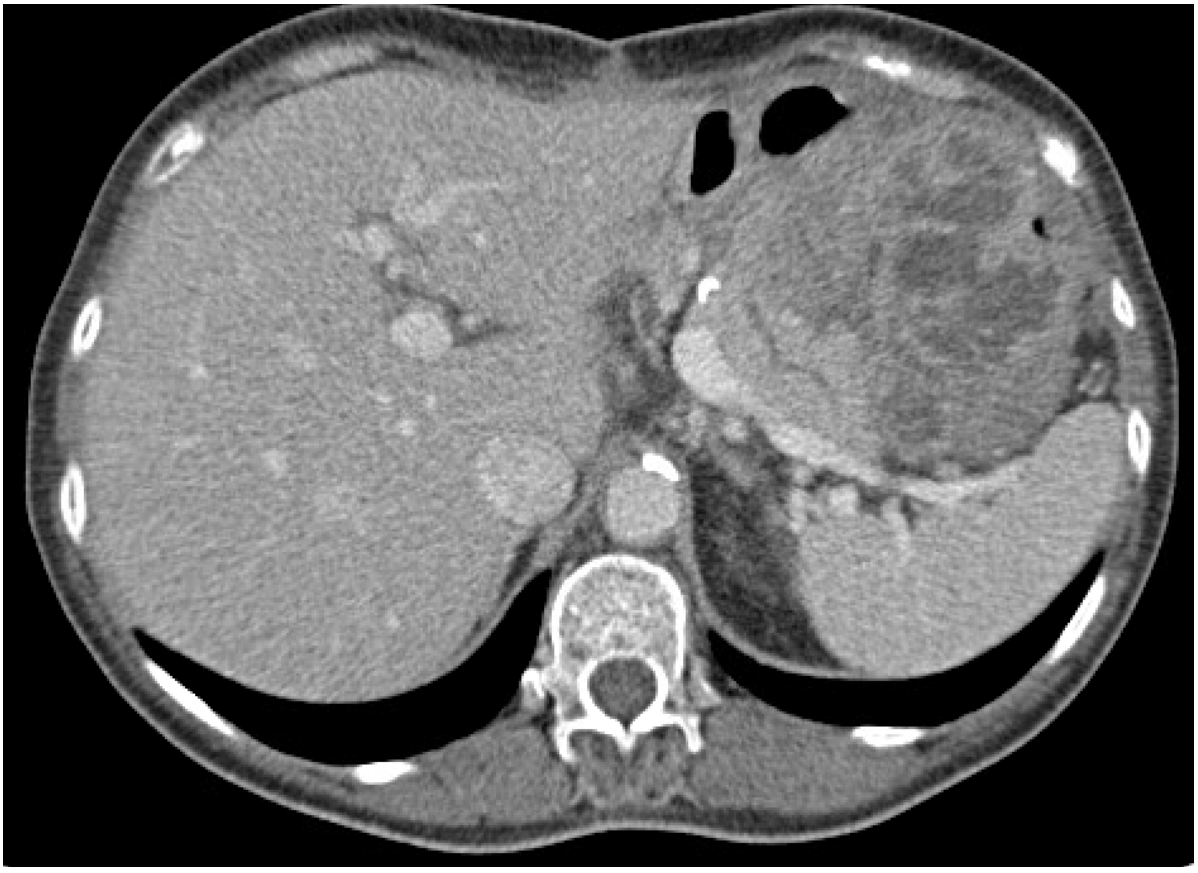

Figure 1. CT scan showing relapsed disease.

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