

Complete Pathologic Response in Advanced Primary Gastric Signet-Ring Cell Carcinoma: A Case Report

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Abstract

Background: Gastric signet ring cell carcinoma (SRC) is a poorly differentiated adenocarcinoma in which the tumour cells invade singly or in small groups.

The incidence of SRC has been reported in china as 13.9% (662 patients of 4,759) [1]. It is reported to occur more frequent among women and young patients.

A regimen of epirubicin, cisplatin, and infused fluorouracil (ECF) improves survival among patients with incurable locally advanced or metastatic gastric adenocarcinoma.

Case presentation: A 38-year-old female presented with a 3 weeks history of epigastralgia. Her medical history was unremarkable. The endoscopic findings of the stomach revealed an infiltrative lesion, which the guided biopsy yielded a positive pathologic diagnosis of signet ring cell carcinoma. Diagnostic imaging with an abdominal computed tomography (CT) scan revealed a gastric thickening, with lymph nodes. Induction chemotherapy was recommended, based on 6 cycles of ECX (Epirubicin 50 mg/m², Cisplatin 60 mg/m², Capecitabine 625 mg/m²). The total gastrectomy specimen showed a pathological complete response.

The patient, who is always followed in consultation, is in complete remission 19 months after the diagnosis.

Conclusion: SRC is a distinctive histological type of gastric cancer. The ECX or EOX (epirubicin, oxaliplatin, capecitabine) remains the standard treatment of advanced primary gastric signet-ring cell carcinoma.

Our case illustrates a complete pathologic response to ECX, which confirmed the effectiveness of this protocol on this histology.

Keywords: Gastric signet ring cell carcinoma, ECX, complete pathologic response

Abbreviations: CT: Computed Tomography; ECF: Epirubicin, Cisplatin, and infused Fluorouracil; ECX: Epirubicin, Cisplatin, Capecitabine, EOX: Epirubicin, Oxaliplatin, Xeloda; FAMTX: Fluorouracil, Doxorubicin and Methotrexate; SRC: Signet Ring cell Carcinoma; UICC: Union International Contra la Cancrum; WHO: World Health Organization

Background

Signet ring cell carcinoma (SRC) is a histological entity based on the microscopic characteristics, not on biological behavior. The clinicopathological characteristics and prognosis in patients with SRC carcinoma of the stomach are still controversial.

The incidence of SRC has been reported in china as 13.9% (662 patients of 4, 759) [1]. It is reported to occur more frequent among women and young patients.

A regimen of epirubicin, cisplatin, and infused fluorouracil (ECF) improves survival among patients with incurable locally advanced or metastatic gastric adenocarcinoma. Therefore, the present case illustrates a complete pathologic response to Epirubicin, Cisplatin and Capecitabine (ECX) in patient presented a metastatic gastric signet-ring cell carcinoma.

Case Presentation

A 38-year-old female presented with a 3 weeks history of epigastralgia. Her medical history was unremarkable.

The endoscopic findings of the stomach revealed an infiltrative lesion, which the guided biopsy yielded a positive pathologic diagnosis of signet ring cell carcinoma.

Diagnostic imaging with abdominal computed tomography (CT) scan revealed a gastric thickening, with lymph nodes (Figure 1).

Induction chemotherapy was recommended, based on 3 cycles of ECX (Epirubicine 50 mg/m², Cisplatin 60 mg/m², Capecitabine 625 mg/m²). Examination after this treatment showed remarkable reduction of tumor volume in the primary lesion and lymph nodes, which was defined as a partial response (PR) in abdominal CT scan (Figure 2). After 3 others cycles of ECX. The patient underwent total gastrectomy with lymph node dissection (D1, 5). The postoperative course was uneventful without surgical complications. At this time, no gastric cancer cells were detected in the resected specimen, including the

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primary lesion and lymph nodes, confirming a pathological complete response. Thus, this regimen described here may be a potent tool to control metastatic gastric carcinoma.

The patient, who is always followed in consultation, is in complete remission 19 months after the diagnosis.

Discussion

According to World Health Organization (WHO) classification, SRC is a histological type, primarily based on the microscopic characteristics of the tumor but not on the biologic behavior [2]. SRC has been classified as “diffuse type” by Lauren [3], “infiltrative type” by Ming [4], and “undifferentiated type” by Sugano et al. [5]. To establish a scale of tumor aggressiveness related to prognosis, the WHO [1] and the Union for International cancer control (UICC) [6] adapted a grading system in which SRC has been classified as high grade.

The histogenesis of a signet ring cell component is unclear. Signet ring cells are an intermediate form of squamous and adenocarcinoma cell or a glandular or mucin-secreting component arising in a squamous cell carcinoma as a result of field carcinogenesis, which involves both the covering squamous epithelium and the mucous gland [7].

Signet ring cells can often be confused with benign histiocytes when they show bland nuclei and are separated individually. In these circumstances, histochemical and immunohistochemical staining, such

as mucicarmine and cytokeratin, can be useful because histiocytes are negative for these staining [8]. Although there have been studies of the clinicopathologic characteristics including prognosis of SRC, the results were not consistent.

Advanced gastric carcinoma with SRC is characterized by the potential to infiltrate the gastric wall diffusely, and a higher rate of peritoneal dissemination than non-SRC [9,10]. It showed a rate of lymph node metastasis similar to or higher than other types of gastric carcinoma [7,9], unlike advanced cancer, early gastric carcinoma with SRC has a significantly lower lymph node metastasis rate than other histology [11].

The outcome among patients with gastric cancer is determined by the stage of the disease at presentation. Localized disease, limited to the mucosa and submucosa, is best treated surgically and has a five-year survival rate of 70 to 95 percent [12,13]. Once tumor cells have spread through the submucosa, the risk of lymph-node metastases increases and the likelihood of prolonged disease free survival decreases.

Western surgical and population-based series show that most patients present with a tumor that has penetrated the submucosa; they have a five-year survival rate of 20 to 30 percent [14]. In Japan, extended surgery prolongs survival in such cases, even in the presence of lymph-node metastases [3], but this effect has not been reproduced in Western trials [15,16].

The regimen of ECF, which was developed in the late 1980's, achieves response rates between 49 percent and 56 percent in randomized trials of the treatment of locally advanced gastric cancer [17,18]. As compared with a regimen of fluorouracil, doxorubicin, and methotrexate (FAMTX), the ECF regimen improves survival and response rates among patients with advanced esophagogastric cancer [17,19], and the side-effect profile is acceptable. These results have not been improved by substituting mitomycin for epirubicin [11]. A recent meta-analysis found that in advanced disease, epirubicin and cisplatin contribute independently to the efficacy of combination chemotherapy [20].

The MAGIC trial determined that a regimen of ECF given before and after radical surgery improves the outcomes of operable gastric cancer. The potential benefits of administering ECF preoperatively was as follows : increasing the likelihood of curative resection by downstaging the tumor, eliminating micrometastases, rapidly improving tumor-related symptoms, and determining whether the tumor is sensitive to the chemotherapy. The primary end point of this trial was overall survival; secondary end points were progression-free survival, surgical and pathological assessments of down-staging (i.e., tumor diameter, tumor stage, and nodal status), the assessments by the surgeons about whether the surgery was curative, and quality of life, but the pathologic complete response was not evaluated [21].

REAL-2 randomized multicenter phase III study showed that Capecitabine is as effective as fluorouracil in patients with previously untreated advanced esophagogastric cancer [22].

To our knowledge, no study has focused on induction chemotherapy of metastatic SRC, and the incidence of pathologic complete response for gastric cancer and especially for SRC. In consequence, we disposed a few treatment strategies specific to this histology, while newly developed treatment modalities have been introduced for gastric adenocarcinoma.

After a wide study of the medical literature, we found one case of pathologic complete response after chemoradiation in patient with advanced gastric cancer [23].

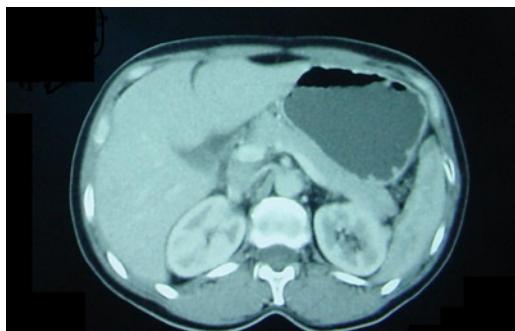


Figure 1: The baseline abdominal computed tomography scan.



Figure 2: Abdominal computed tomography scan after 6 cycles of chemotherapy.

In highly advanced gastric cancer with lymph node metastases, surgery may remove visible tumor masses but microscopic cancer cells may still exist in the blood, lymphatic system or peritoneal cavity. Resulting in local recurrence, distant metastases, or peritoneal dissemination after macroscopically curative surgery.

In the present case, a histological examination of the resected specimen showed no detectable cancer cells. Therefore, we believe that induction chemotherapy based on ECX, eradicated both the primary tumor and all the metastases in this patient. These encouraging results suggest that this regimen is an effective strategy, for the treatment of metastatic gastric signet ring cell carcinoma. Given the generally poor prognosis of these patients, our regimen should be further evaluated as induction chemotherapy to determine its efficacy and toxicity in a larger patient population.

Conclusion

SRC was a distinctive histological type of gastric cancer. The ECX or EOX (epirubicin, oxaliplatin, Capecitabine) remains the standard treatment of advanced Primary gastric signet-ring cell carcinoma.

Our case illustrates a complete pathologic response to ECX, which confirmed the effectiveness of this protocol on this histology.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review By the Editor-in-Chief of this journal.

Competing Interests

The authors declare that they have no competing interests.

Author's Contribution

AH participated in the treatment of the patient, collection of case details, literature search and drafted the manuscript. MN, KS, and YM participated in the treatment of the patient and data collection, and helped to revise the manuscript. All authors have read and approved the final manuscript.

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