

Multiple Visceral Resection after Signet Ring Cell Gastric Cancer Locoregional Recurrence - Case Report and Literature Review

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Rezumat

Rezecții multiviscerale pentru recidivă locoregională după adenocarcinom gastric cu celule în inel cu pecete operat – prezentare de caz și review al literaturii

Recurența reprezintă cea mai importantă cauză a eșecului tratamentului chirurgical la pacienții cu cancer gastric avansat, chiar și după rezecție radicală. Chirurgia joacă un rol important în tratamentul acestor pacienți, chiar și în cazul invaziei mai multor organe. În cazuri bine selecționate, cu condiție biologică bună, chirurgia este singura alternativă care asigură prelungirea supraviețuirii. Prezentăm cazul unei paciente în vârstă de 41 ani, diagnosticată cu recidivă tumorală cu implicare viscerală multiplă apărută la 15 luni după gastrectomie subtotală distală cu limfodisecție D2 pentru cancer gastric antral.

Cuvinte cheie: cancer gastric, gastrectomie radicală, recurență locoregională, celule în pecete

Abstract

Recurrence is the most important cause of treatment failure in patients with advanced gastric cancer, even after curative surgery. Surgery plays an important role in these patients, even in cases of multivisceral involvement. In selected cases

- good biological resources - surgery is the only viable choice to prolong survival. This report describes the case of a 41 year-old patient presenting a locoregional recurrence with multiple visceral involvement at 15 months after radical subtotal gastrectomy with D2 lymph node dissection for antral gastric cancer.

Key words: gastric cancer, radical gastrectomy, locoregional recurrence, signet ring cell carcinoma

Introduction

In Western countries, gastric cancer still represents a disabling disease and locoregional recurrence after surgery occurs in 22-50% of cases, especially in patients with advanced stage disease at the time of diagnosis, mostly within two years from the operation. Local recurrence may also occur in cases which had a R0 resection. Recurrence is the main cause of treatment failure in these patients, even after curative surgery. Unfortunately, the diagnosis of recurrence still remains difficult and the standard treatment has not been well established. Management of these cases is extremely difficult due to the involvement of regional structures. Since peritoneal carcinomatosis is the most prevalent form of recurrence at the time of diagnosis, chemotherapy has been the mainstay in the treatment of recurrent gastric cancer. Indications for surgery in the treatment of various types of recurrent cancer are limited to locoregional recurrence (1).

Solitary recurrence of gastric signet ring cell carcinoma is rare. We report a successful multivisceral surgical resection of a locoregional recurrence with multiple visceral involvement

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after radical subtotal gastrectomy with D2 lymph node dissection in a 41 year-old woman.

Case report

A 41 year-old patient was submitted to radical subtotal gastrectomy with Hoffmeister Finsterer anastomosis and D2 lymph node dissection for antral gastric cancer in march 2012 (T3N1M0 - signet ring cell carcinoma). After discharge (8th postoperative day), the patient underwent 6 cycles of adjuvant chemotherapy with ECF regimen (Epirubicin / Cisplatin/ 5 Fluorouracil). The patient's evolution was uneventful until July 2013 (16 months after surgery), when she presented for abdominal pain and vomiting with sudden onset. Abdominal CT scan found a recurrent tumor invading the abdominal wall, the head of the pancreas, the anterior wall of the portal vein, the gastro-jejunal anastomosis and transverse colon (Fig. 1). In the absence of effective alternative treatment and due to the fact that there were no other lesions we decided to perform a surgical intervention in order to assess the possibility of resection.

Intraoperatively, the peritoneal lavage fluid cytology was negative and the intraoperative echography confirmed the absence of liver metastases. We performed complete resection of the tumor (Figs. 2 and 3) *en bloc* with cephalic duodeno-pancreatectomy, parcellar resection of the portal vein, resection of the afferent limb, iterative gastrectomy, subtotal colectomy (Fig. 4), termino-lateral pancreatico-jejunostomy, hepatico-jejunostomy, gastrojejunostomy, ileocolostomy. The area of invasion in the abdominal wall was also resected and the wall was reinforced using a polypropylene mesh. The histopathological report confirmed signet ring cell recurrent tumor. Postoperative evolution was uneventful. At six months the postoperative control showed no signs of disease progression.

Discussions

Gastric cancer recurrence includes: loco-regional recurrence

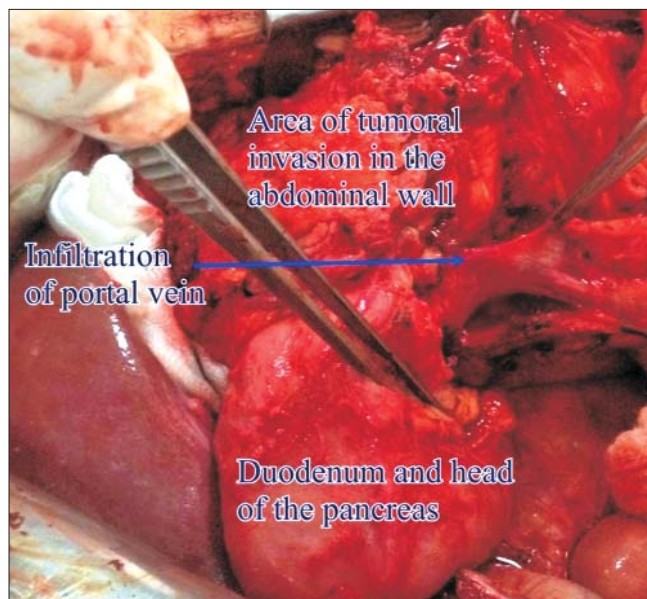
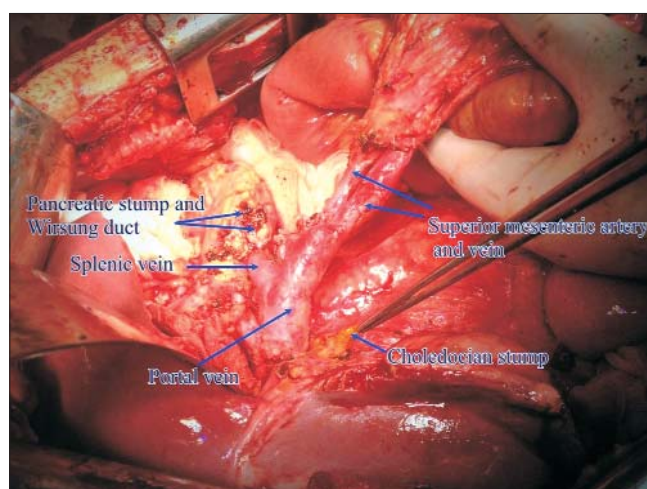
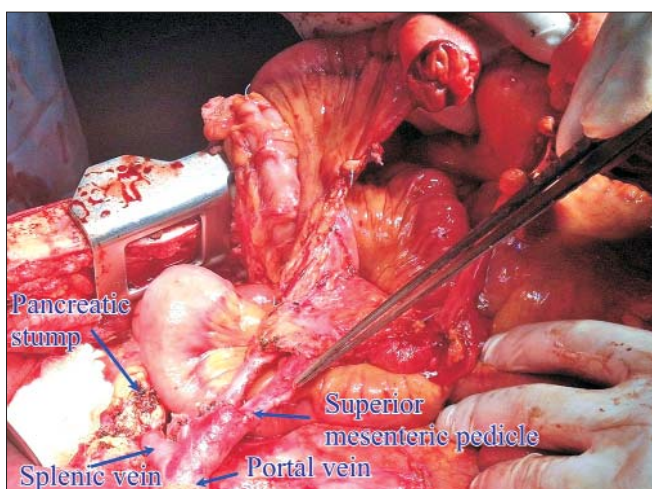


Figure 1. The initial intraoperative aspect: A large tumor invading the abdominal wall, the head of the pancreas and the anterior wall of the portal vein

(regional lymph nodes, perianastomotic region, gastric bed and stump or in an adjacent structure by direct extension), peritoneal recurrence (peritoneal carcinomatosis, Krukenberg tumor) or distant (including hematogenous) metastasis (liver, lung, bones, brain and skin)(1). In 1952 Thomson defined the stomach bed as immediately adjacent perigastric tissues including the entire pancreas. According to Thomson's classifications of recurrent tumors our case can be considered at the upper limit of what is called locoregional tumor (the tumor invaded the anterior abdominal wall, the pancreas and the anterior face of the portal vein and the transverse colon) (2). We decided to perform a multivisceral resection because the patient had a satisfactory general status, imagistic studies did not shown distant recurrence and the peritoneal lavage fluid



Figures 2, 3. The final aspect after complete R0 resection

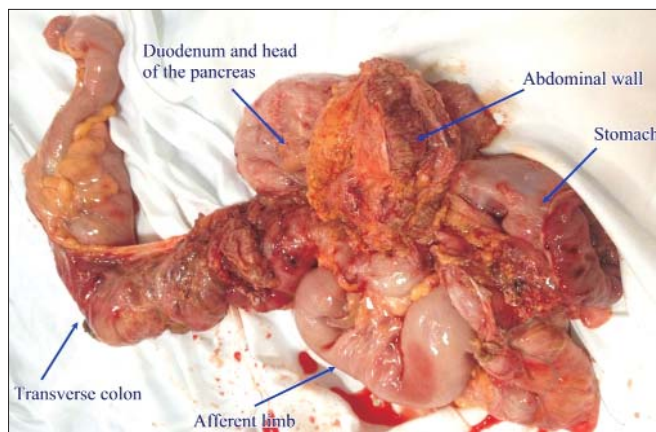


Figure 4. The Specimen

cytology was negative. The histopathological investigations of the resected specimen revealed a signet cell carcinoma.

An isolated loco-regional recurrence is reported in 12 % of cases in Fabio Carboni's series and in 11 % of Alvaro Diaz de Liano's series. (3,4) However, only a small part of patients with locoregional recurrence can undergo complete re-resection. In other series (Bohner et al, Yoo CH et al, Schwartz et al, D'Angelica et al) recurrence is reported in 6-46% of patients. Such differences may be explained by variations in the definition of recurrence, as well as the mode and timing of detection. (1,5) Clinicopathologic features of the primary tumor that predict loco-regional recurrence are: proximal location, advanced stage of the disease (T3-4, N+), infiltrative growth, degree of gastric wall penetration, diffuse type and stromal reaction. (3,6) In particular, extraluminal recurrence, which was classified into locoregional recurrence by Lenhert et al. was reported due to primary implantation of tumor cells into the resection area during gastrectomy (6,7).

Of the three patterns of spread - lymphatic, peritoneal and hematogenous - there is significant variation in the literature as to which recurrence route is most common. Japanese studies demonstrate a predilection towards peritoneal and hematogenous spread, while the American experience suggests that lymphatic spread is more frequent. There is some evidence that this difference is due to the common practice in Japan of performing a D2 or even more extended lymphadenectomy, thus lessening the chances of local recurrence. The recurrence pattern also seems to depend on its timing: early recurrence (<2 years from surgery) is usually due to lymphatic metastasis. Late recurrence is usually due to peritoneal implants or distant disease. There is a consensus within the literature that the extent of lymphatic spread at the time of initial surgery is the most important prognostic factor for recurrence and survival. A study by Sakar et al. further elucidated the temporal characteristics of lymph node metastasis. He divided 142 patients who developed recurrence following R0 resection into an early recurrence group (less than 2 years out from surgery) and a late group (2 years and beyond). Early recurrence was associated with N+ condition. Deng et al. reviewed 6,309 lymph nodes harvested from 308 patients undergoing R0

resection and found a threshold of nine positive lymph nodes to be a significant prognostic factor for recurrence. No patients in the study with nine or more positive lymph nodes survived more than 5 years. Patients with four or fewer lymph nodes had a 62% 5 year survival rate (8).

In South Korea, Gyeonggi Do et al. studied the pattern of body weight change after gastrectomy and its association with prognosis. More than 30% weight loss at 6 months post-operatively was significantly associated with early recurrence (9).

Nunobe et al reported a series of 109 patients with recurrent gastric cancer who were submitted to surgical intervention. 36 patients had locoregional recurrence and underwent different surgical interventions with curative intent. All of these 36 patients underwent D2 lymphadenectomy as their first procedure. One case had undergone hepatectomy for a solitary liver metastasis prior to surgery for the locoregional recurrence. Complete resection was possible in 29 patients (80.6%) with incomplete resection in the remaining 7 patients (19.4%). The median survival time was 23 months and overall 1-, 3-, 5- year survival rates were 73%, 36.7%, and 9.8% respectively. Complete resectability of the tumor was the only significant prognostic factor identified (10).

Roviello published a series of 441 patients who were submitted to radical gastrectomy for gastric cancer. 215 (49 %) of 441 patients developed recurrence: peritoneal recurrence in 36%, locoregional recurrence in 45%, hepatic recurrence in 27% and distant metastases in 9% The 5-year disease-free survival rate was 52%. There was a notable difference in 5-year disease-free survival rate according to pT stage (pT1, 89 %; pT2, 62 %; pT3-4, 25 %). Locoregional recurrence was found in 96 patients: in 13 cases the recurrence was located in the gastric stump, in 34 cases at the level of the gastric bed and 49 cases in the lymph nodes (11).

Diagnosis is improved with modern imaging and mainly suggested by endoscopy and CT scan. As occurred in our case, most patients are symptomatic and diagnosis is earlier in such cases.

Once the diagnosis of loco-regional recurrence has been made, curative surgical resection is only rarely possible. It appears that a curative resection is possible when a partial gastrectomy was performed. Approximately 20% of patients undergo surgical resection but in only 2-6% it may be considered curative with a mean survival lower than 2 years (3)

Yoo CH et al reported a series of 2,328 patients who underwent curative resection for gastric cancer; at operation either total or distal subtotal gastrectomy was performed depending on location and macroscopic type of gastric cancer, associated to extended lymphadenectomy (a minimum of 15 lymph nodes was retrieved). (5) Locoregional recurrence as single site recurrence was found in 98 patients: 54 at the level of anastomosis or stump, 34 in the lymph nodes and 10 in adjacent organs. The patients were divided into an early recurrence group (24 months or less) and a late recurrence group (more than 24 months) for correlation with clinicopathologic features. In the early recurrence group, patients with infiltrative or diffuse type of cancer, differentiated tumor, serosal invasion,

lymph node metastasis and who had undergone total gastrectomy were common in comparison with the late recurrence group. Locoregional recurrence was related to larger tumor size, infiltrative or diffuse type, proximally located tumor and subtotal gastrectomy. Reoperation and resection of the recurrence was possible in 19 patients and only 5 remained disease-free. Complete resection associated the longest survival with a mean of 21.6 months – compared to 12 months for palliative surgery (5).

Song et al analysed the role of surgery in the treatment of recurrent gastric cancer in a study on 1,697 patients who underwent curative resection for gastric cancer; 347 were endoscopically, radiologically or surgically diagnosed with recurrence. The recurrences were categorized as local (anastomosis and gastric stump), lymphatic (regional and distant lymph node metastasis), hematogenous (liver, lung, bone, brain and kidney) and peritoneal. Local recurrence was found in 19 patients: 16 cases presented a recurrence at the level of the gastric remnant and 3 cases had a recurrence localised on the anastomosis. The types of surgery for recurrence were categorized as complete resection, incomplete resection, bypass or enterostomy and laparotomy only. Complete resection was defined as “macroscopically no residual tumor and negative margin surgical resection” and it was achieved in 15 cases. The mean survival after re-resection was significantly longer - 52.2 months for complete resection - and 13 months for palliative procedures. (12)

D'Angelica et al analysed recurrence patterns in 1,172 patients who underwent an R0 gastrectomy over a 15-year period. These patients were largely treated by an extended lymph node dissection. 80% of recurrences occurred within 2 years and only 10% were alive 2 years after the diagnosis of recurrence. Approximately two thirds of the patients had recurrence in a single area. (1)

The incidence of signet ring cell carcinoma (SRC) is increasing, especially in Western countries. Because of its infiltrating character and lack of clinical symptoms, SRC is often discovered in an advanced stage and seems to be, consequently, associated with poor prognosis. In his study, Piessen G. Et al tried to test the hypothesis that SRC histology is an independent predictor of poor prognosis in gastric advanced gastric cancer. They demonstrated that SRC is associated with worse survival when compared with non-SRC because of three aspects: 1. higher prevalence of peritoneal carcinomatosis and lymph node invasion at initial diagnosis, 2. lower R0 resection rate due to its infiltrating character leading to more positive vertical margins despite more extensive surgery, and 3. earlier relapse primarily in peritoneal carcinomatosis form. Of 215 patients, a final histologic diagnosis of SRC was made in 70 (32.5%) and non-SRC in 145 (67.5%). 35 patients were not resected due to diffuse metastatic illness and/or neoplastic ascites, leading to 180 gastric cancer resected patients. The study group was composed of all patients with resected SRC (SRC group, n = 59). The median time to recurrence after surgery in the R0 patients was 11 months (range, 5–25) in the SRC group versus 14 months (range, 4–68) in the non-SRC group ($P = 0.009$).

A nonsignificant trend toward more recurrences in the SRC group compared with the non-SRC group (73.9% vs. 54.8%, $P = 0.129$) was observed. Locoregional, distant and both distant and locoregional recurrence were found in 33.8%, 18.5%, and 9.2% of patients, respectively. Locoregional, especially peritoneal carcinomatosis, recurrences occurred more frequently in the SRC group (43.5% vs. 28.6%, $P = 0.016$ and 52.2% vs. 21.4%, $P = 0.011$, respectively). (13)

Once the radical resection of the recurrence is achieved, especially in patients with diffuse-mixed type of gastric cancer and involvement of the serosa, and signet ring cell carcinoma, an adjuvant chemotherapy can be useful due to a high risk of peritoneal recurrence. (11)

Conclusions

Surgery plays an important role in the treatment for isolated loco-regional recurrences of gastric cancer. Staging laparoscopy can be used for the detection of early stage recurrence in patients with equivocal radiologic findings. A minimal approach with laparoscopy would be an alternative to the complicated second-look laparotomy. In low risk patients, especially if symptomatic and for whom surgery is indicated by multidisciplinary assessment, an attempt at resection may be justified in specialized centers with acceptable postoperative mortality and morbidity as there are no effective alternative therapies. If complete resection can be accomplished with low perioperative risk for the extended surgery, long term survival can be expected. (10,14) Therefore, for the case of resectable lesions, aggressive surgical approaches are strongly recommended. (12) According to Takeyoshi's study, surgical resection for non-hepatic intraabdominal recurrence of gastric cancer is the treatment of choice for selected patients. Surgical resection followed by adjuvant chemotherapy may improve the outcome of these patients, with a free of disease period between 1 and 3 years. (15)

In the absence of effective alternative treatment for recurrent gastric cancer, surgical options should be pursued especially for late and solitary recurrence. (6,14) When surgical resection is performed, a 20% 5 year survival can be expected (4,7,16,17).

As long as a recurrence of gastric cancer can be considered locoregional, even in cases of multivisceral involvement, surgery in selected cases for patients with good biological resources is the only viable choice to prolong survival.

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