Complete response of a metastatic gastroesophageal adenocarcinoma on irinotecan-based chemotherapy in a dialysis patient

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Abstract: We present the first case report of a complete response of metastatic gastroesophageal cancer in a chronic hemodialysis patient with irinotecan-based chemotherapy. An elderly dialysis patient presented with diffuse liver metastases by a gastroesophageal adenocarcinoma. He received combination chemotherapy with 5 fluorouracil and irinotecan. After six months of chemotherapy, liver scans show complete remission. The principles, practice, and experience of chemotherapy with irinotecan during dialysis are discussed.

Keywords: gastroesophageal cancer, irinotecan, chemotherapy, dialysis

Introduction and background

Metastatic gastric and gastroesophageal carcinoma are known as chemotherapy-sensitive tumor types. Many different chemotherapy regimens were therefore developed. However, little is known on the feasibility and efficiency of chemotherapy for these cancer types in patients with severe renal failure. Only case reports on the pharmacology of irinotecan in patients with colon or rectal cancer are available at present. We present the first case of combination chemotherapy in metastatic gastroesophageal cancer in a dialysis patient.

Case report

A 73-year-old patient with a longstanding history of ischemic heart disease had been on dialysis for two years for vascular renal insufficiency. In September 2004 he was admitted for gastrointestinal blood loss. An upper gastrointestinal (GI) endoscopy showed a tumor at the gastroesophageal junction. Biopsy revealed adenocarcinoma. The computed tomography (CT) scan of the liver showed important liver metastases. CA 19.9 was very high: 24,925 U/mL (nL < 37 U/mL).

The patient was started on chemotherapy, the regimen consisting of L-leukovorin 250 mg/m², irinotecan 50 mg/m² followed by 5-fluorouracil (5 FU) 2 g/m²/24 h, six weeks out of eight. There was neither significant nausea nor diarrhea. Dialysis was continued three times a week, (the patient was on a Monday – Wednesday – Friday schedule of dialysis) and chemotherapy was given on the Monday, just after dialysis. Only one dose was omitted owing to neutropenia. After four weeks of chemotherapy he also underwent a right carotid endarterectomy for an intercurrent transient ischemic attack in the right carotid region.

Six months after starting chemotherapy the CT scan of the liver showed a complete response of the numerous metastases. (Figures 1 and 2) Endoscopy showed only
minimal tumor remnants. Marker studies showed a remarkable drop in CA 19.9. (Table 1) Nine months after initiation of treatment, however, the liver metastasis and tumor marker were progressive again. Second line chemotherapy with paclitaxel was started. Doses of chemotherapy were based on a number of case reports on paclitaxel for ovarian cancer in dialysis patients.\textsuperscript{14,15} CT scan after two months showed further progressive disease. The patient died in hospice 13 months after initial start of chemotherapy.

**Discussion**

The increase in solid tumors in a patient undergoing dialysis poses specific problems,\textsuperscript{16} especially in the choice and pharmacology of anticancer drugs, bearing in mind that all

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**Figure 1** A) Initial situation with massive liver metastases in left, right, and caudate lobe of the liver. B) Complete response of diffuse liver metastases after four months of irinotecan-based chemotherapy.

**Figure 2** Evolution of CA 19.9 under chemotherapy.
of these drugs were developed in patients with normal liver and kidney function. For gastric cancer, 5FU has always been the backbone of treatment.1,2 In chronic hemodialysis, there are some data on dose reductions with 5FU weekly.17,18 For gastric cancer, combination chemotherapy is, however, necessary to obtain prolonged disease control and even for prolonging overall survival.1,2 Combinations of 5FU + cisplatin and either docetaxel or epirubicin have therefore become standard chemotherapy regimens in gastric cancer.19,20

Besides the aforementioned regimens, irinotecan-based combinations were shown to be active in first21 and second line gastric cancer.22 Its equivalence (in combination with 5FU) in first-line metastatic gastric cancer was recently established in two studies, both comparing this regimen with a combination chemotherapy with cisplatin and 5FU.23,24

Irinotecan is metabolized in the liver to its active metabolite SN-38, followed by biliary excretion.6 There is no significant renal elimination. The drug was evaluated in patients with serum creatinin between 1.6 and 5 mg/dL and no unexpected toxicities were seen.25 There are a number of case reports on the use of irinotecan during hemodialysis, all of which are on patients with metastatic colon cancer.

A first report mentions the use of irinotecan at a dose of 50 mg/m² without significant toxicity.7 In two other case reports on dialysis patients, both patients were started with irinotecan at 50 mg/m². Both reports mention that by increasing the dose, prohibitive diarrhea was the consequence.8,9

The worst outcome in higher irinotecan doses (above 125 mg/m²) was demonstrated in two other dialysis patients, where these dosages led to extreme GI toxicities and even death.9

It can be concluded that irinotecan in terminal renal insufficiency should not be given at a dose above 50 mg/m². Korean authors have made pharmacologic evaluations on the use of irinotecan in small-cell lung cancer patients during dialysis. They increased the dose up to 100 mg/m² without diarrhea. They noted however that these doses were only feasible in patients of Korean descent.26

There is a very recent case report on the combination of irinotecan at a dose of 50 mg/m² weekly combined with FU1600 mg/m²/24 h/week, leading to disease stabilization at six months in a dialysis patients with diffuse bone, cerebral and liver metastases of colon cancer.10

Our case report builds on this knowledge of the use of irinotecan in metastatic colorectal cancer during dialysis. This case report discusses both the weekly dose of irinotecan and the 24-hour administration of 5FU in a gastroesophageal cancer patient.

Conclusion

This is the first report on the efficacy of irinotecan- and fluorouracil-based chemotherapy in a dialysis patient with liver metastases of a gastroesophageal carcinoma. Combination chemotherapy of irinotecan and FU was extremely well tolerated, without significant delays in administration. It produced radiographically complete remission of the liver metastases, and a normalization of CA 19-9 tumor marker, leading to a remarkable overall survival.

Disclosures

The authors report no conflicts of interest in this work.

References


Table I Biochemistry and CA 19.9 evolution during therapy. (Normal Range LDH/lactate dehydrogenase: 200–585 U/L AP/Alkaline Phosphatases: 38–135 U/L CA 19.9 <37 U/mL)

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