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Safe use of capecitabine-cisplatin in metastatic gastric carcinoma with severe liver dysfunction: a case report from Algeria

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Abstract
Due to its high incidence and poor prognosis, gastric cancer is an important health problem worldwide. The liver is the most frequent site of metastases. Advanced cancer in the setting of liver dysfunction poses a dilemma for physicians, as many cancer chemotherapeutic agents undergo hepatic metabolism. This paper reports the case of a patient with liver failure due to liver metastases of gastric cancer. The initial liver function tests showed an elevation of transaminases (aspartate amino transferase 180 IU/l, alanine aminotransferase 110 UI/l), hyperbilirubinemia (total bilirubin at 24 mg/dl), alkaline phosphatase at 1127 UI/l and elevation of tumor markers (carcinoembryonic antigen >1000 ng/ml and CA19,9 at 180 UI/l). We initiated capecitabine/cisplatin based combination chemotherapy. Our data supports the safety and feasibility of cisplatin-capecitabine regimen in patients with severe liver dysfunction secondary to liver metastases of gastric cancer.
Keywords: Gastric cancer, Liver dysfunction, Capecitabine, Cisplatin

1. Introduction

In Algeria, incidence of stomach cancer was estimated at 3.7/100000 in women and 7.6/100000 in men, according to GLOBOCAN 2012, making it the fifth most common malignancy, after cancer of the lung, breast, colorectal and prostate (1). The liver is the most frequent site of metastases in gastric cancer. Metastatic liver involvement may result in liver dysfunction, indicated by increased bilirubin (hyperbilirubinemia), increased level of cholestatic parameters (gamma-glutamyl transferase and alkaline phosphatase) and transaminases as well as impaired liver synthesis (e.g. low albumin). Liver has a very important role in the metabolism of drugs; thus, the administration of chemotherapy to gastric cancer patients with liver dysfunction requires careful consideration (2). We report here, on a patient with extensive liver metastasis and secondary liver dysfunction who was treated with capecitabine and cisplatin with manageable toxicity.

2. Case presentation

A 64-year-old patient presented with four months' history of epigastralgia after weight loss which had been ongoing for a year. His performance status was estimated to be ECOG 2. The physical examination showed a hepatomegaly and scleral icterus. Computerized tomography (CT) scan and ultrasonography of the abdomen and pelvis revealed thickening of the lesser gastric curvature and multiple solid masses in the liver (Figure1). Endoscopy and biopsy confirm a cancer of the antrum of stomach. The liver function tests showed increased transaminases (aspartate amino transferase 180 IU/l, alanine aminotransferase 110 UI/l) hyperbilirubinemia (total bilirubin at 24 mg/dl), alkaline phosphatase at 1127 UI/l, and elevation of tumor markers (carcinoembryonic antigen >1000ng/ml and CA19,9 at 180 UI/l). The patient was treated with cisplatin (75 mg/m^2) on day 1, and capecitabine (1,000 mg/m2

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orally twice daily) on days 1~14 of a 21-day cycle. Nausea, emesis and diarrhea grade 2 were noted during the first cycle but these toxicities were manageable. Total bilirubin, which was high (24 mg/dl) on admission, decreased to 10 mg/dL and aspartate amino transferase 32 IU/l after the first cycle. After three cycles of chemotherapy, his total bilirubin decreased to within the normal range (1.05 mg/dL). CT scan revealed that the tumor nodes were markedly reduced (Figure2); his carcinoembryonic antigen levels decreased to 300 ng/ml from 1000ng/ml and CA19-9 to 1.09ng/ml from 378 ng/ml. He has received 9 cycles of capecitabine-cisplatin with ongoing clinical benefit and good tolerance of treatment.

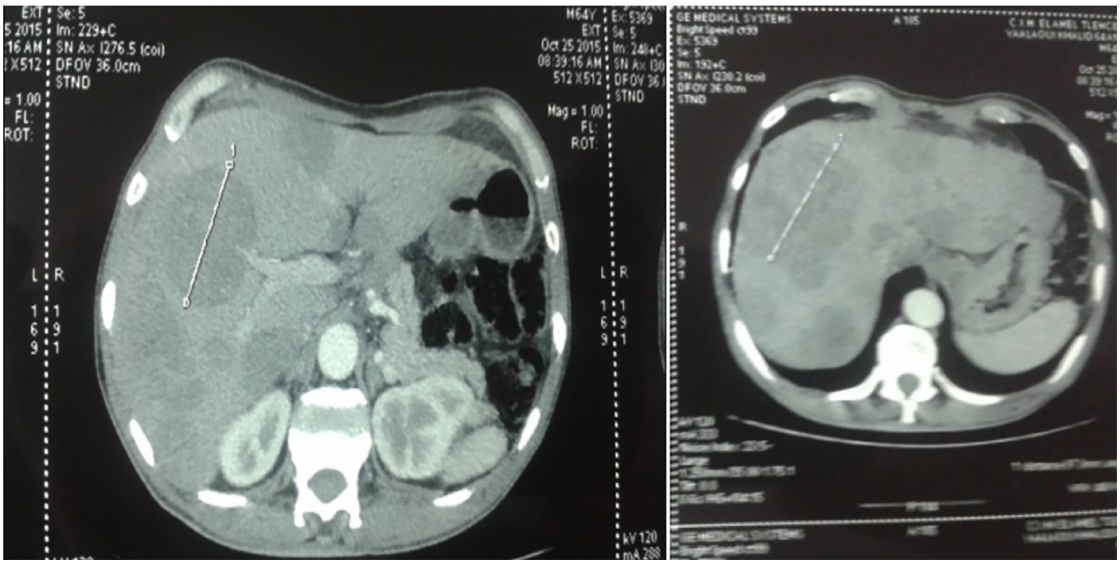

Figure 1. CT scan of the abdomen (A and B) shows multiple variable-sized metastatic nodular lesions in the liver.

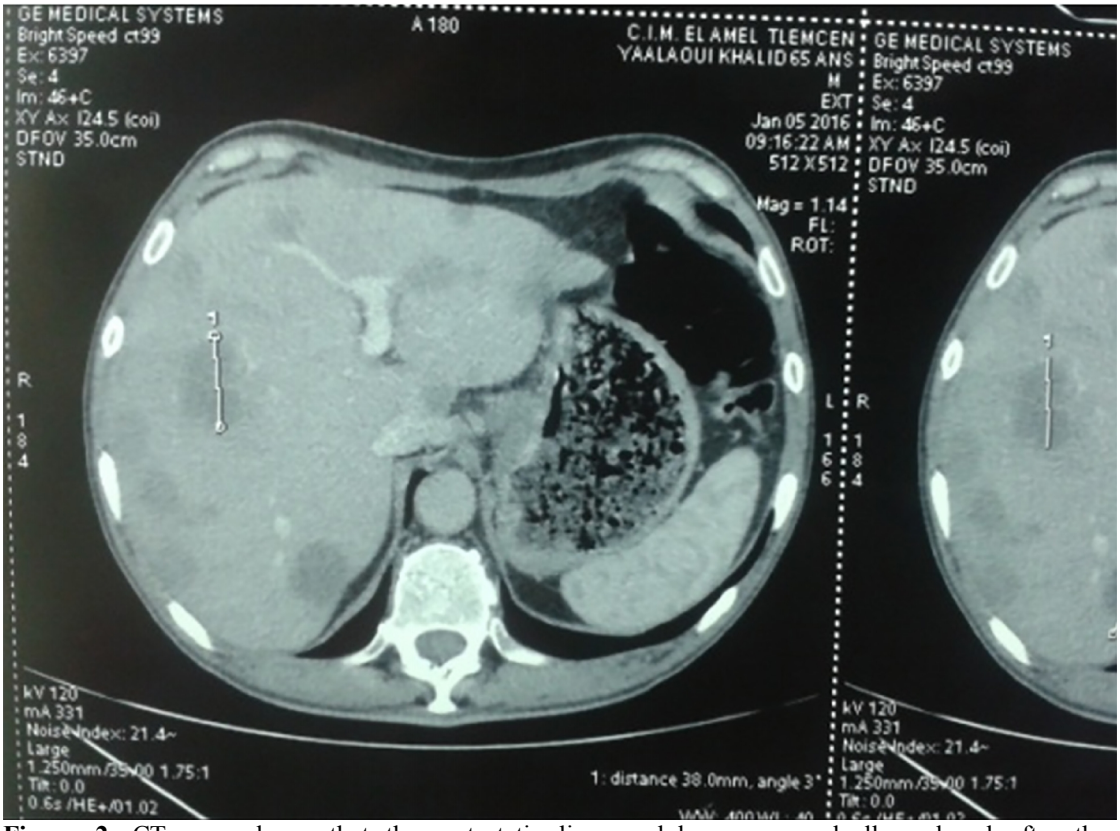

Figure 2. CT scan shows that the metastatic liver nodules were markedly reduced after three cycles of chemotherapy

3. Discussion

Chemotherapy has been shown to improve survival and quality of life in patients with metastatic gastric carcinoma. Several chemotherapeutic agents have activity in gastric cancer (3, 4). These include 5-FU, capecitabine, cisplatin, oxaliplatin, irinotecan, and taxane. 5-FU is a uracil analogue and antimetabolite that is metabolized mainly in the liver by dihydropyrimidine dehydrogenase (DPD). Although 5-FU is fairly safe to use in patients with liver dysfunction, regular monitoring of liver tests is advised (5). Capecitabine, a prodrug of 5-Fluororuracil (5-FU) is activated through three enzymatic reactions. Twelves et al. (6) have compared the use of capecitabine in patients with moderate hepatic dysfunction secondary to liver metastases to patients with normal liver function. Results have demonstrated that there are no significant differences in the pharmacokinetic parameters in the two groups, thus no need for adjustment of dose in this category of patients. Many studies have demonstrated that cisplatin is a pilot molecule in the treatment of metastatic gastric cancer; its exclusive renal excretion allow its administration without adjustment dose in patients with liver dysfunction. In a study of 11patients with liver failure caused by metastatic breast cancer treated with cisplatin at doses of 75 mg/m^2 every 21 days, and vinorelbine at 20 mg/m2 on days 1 and 8 of a 21-day of cycle, results demonstrated an improvement in liver failure in 10 patients and partial response in 7 cases (7). One death, from intracerebral hemorrhage, was recorded. The BC cancer agency has declared that no adjustment dose is required in patients with liver dysfunction. Oxaliplatin is a third-generation platinum which can replace, with the same efficiency, the cisplatin in the treatment of metastatic gastric cancer. A “phase 1 study” conducted by The Organ Dysfunction Working Group of the National Cancer Institute demonstrated that oxaliplatin administrated at the standard dose of $130mg/m^2$ was well tolerated for patients with all liver failure without alteration in the clearance of the platinum species from the plasma, but they did not report the rate of bilirubin in the severe liver dysfunction group (8, 9). According to BC cancer agency, no adjustment dose is required for mild to moderate failure (10, 11).

4. Conclusions

This report suggests that capecitabine-cisplatin may be a safe and efficacious treatment for patients with hepatic dysfunction, but more clinical data is needed to confirm these results. Liver dysfunction resulting from liver metastases in patients with gastric carcinoma should not lead to therapeutic delay, but the indication of chemotherapy for this category of patient must be cautious because no recommendations are available and clinical data in this clinical situation are limited.

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Conflict of Interest:

There is no conflict of interest to be declared. We declare that this article is published for free funded by the journal because it wins the price of best presentation at ICHSMT'16.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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