CASE REPORT

mFOLFOX-based Chemotherapy Can Augment Survival in Advanced Gastric Cancer Patient with Disseminated Intravascular Coagulation

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ABSTRACT

Although gastric cancer is a frequent cancer type, disseminated intravascular coagulation is a very rare but serious complication of this disease. We report a 65-year-old man who complained of weight loss, nausea and vomiting, fatigue and dyspnoea for three days. He was diagnosed as having advanced gastric cancer complicated with disseminated intravascular coagulation, which was successfully treated with mFOLFOX chemotherapy regimen. After one cycle of mFOLFOX therapy, thrombocytopenia was improved and serum lactate dehydrogenase levels decreased. Remarkable remission was seen. After 12 cycles of chemotherapy, remarkable remission was seen in the primary tumour and multiple metastatic bone lesions.

Keywords: Advanced gastric cancer, disseminated intravascular coagulation, mFOLFOX-based chemotherapy

INTRODUCTION

Gastric cancer is the fifth most common cancer and the second most common cause of cancer deaths worldwide (1). Disseminated intravascular coagulation (DIC), a clinicopathological syndrome that always occurs as a consequence of an underlying disease, is a rare and serious complication of this disease, with an incidence rate of 1.6% (2–4). It may cause thrombotic complications or a fulminant course with widespread bleeding and serious organ dysfunctions.

The major causes of DIC are sepsis, serious trauma, obstetric complications and neoplasms such as gastrointestinal, pancreatic, liver, ovarian, breast, lung and prostatic carcinomas (5). The prognosis of advanced gastric cancer (AGC) with acute DIC is extremely poor and survival time is usually no more than one month despite best supportive care (6).

Here, we present a case of disseminated intravascular coagulation diagnosed as advanced gastric cancer treated with mFOLFOX-based chemotherapy. He had survived for about one year.

CASE REPORT

A 65-year-old man was admitted to the emergency room with weight loss, nausea, vomiting and fatigue for the last month and dyspnoea for the last three days. His Eastern-Cooperative-Oncology-Group status was 3. His arterial blood pressure was 170/110 mmHg, his pulse rate was 116/min, his respiratory rate was 28/min, and his oxygen saturation was 85% in the room air. From his physical examination, his skin and conjunctivas were pale, his liver was palpable and bilateral pretibial oedema (++) was observed. His haemoglobin level was 7.7 g/dL, his leukocyte number was 9400/mm^3, and his platelet number was 59,000/mm^3 in blood count. His liver function tests showed albumin of 2.6 g/dL, total bilirubin of 1.5 mg/dL, aspartate aminotransferase of 98 IU/L, alanine aminotransferase of 34 IU/L and alkaline phosphatase of 546 IU/L. Lactate dehydrogenase level was 1373 IU/L, his Prothrombin time was 18.5 sc with 1.53 international normalized ratio, his aPTT was 37.7 sc, his fibrinogen level was 197 mg/dL, and his D-Dimer level was 6786 ng/mL. His peripheral smear showed thrombocytopenia, fragmentations of erythrocytes, and reticulocytosis. The patient was diagnosed as DIC with present findings.

The pathological examination of his gastric biopsy showed signet ring cell adenocarcinoma. His tumour marker levels were CEA 115 ng/mL, CA19-9 1303 U/mL. The initial positron emission tomography-computed

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tomography (PET-CT) scan showed gastric cancer in his pyloric end, multiple liver, bilateral adrenal and widespread bone metastasis in his maximum intensity projection (Figure A). Under supportive therapy and replacement transfusions with thrombocyte and erythrocyte suspensions and fresh frozen plasmas, his platelet number and haemoglobin level were decreased to 36 000/mm^3 and 7.8 g/dL, respectively. mFOLFOX was given to him, which was composed of oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2 day 1 followed by 400 mg/m^2 bolus 5-FU and a 46-h 2,400 mg/m^2 5-FU infusion which were repeated every two weeks for 12 cycles. After the administration of the first chemotherapy, his haematologic and biochemical parameters improved and there was no evidence of DIC. At the end of 12 cycles of chemotherapy, his PET-CT scan showed nearly complete remission of gastric cancer and metastatic areas. (Figure B). CEA and CA-19-9 levels decreased to 5 ng/mL and 78 U/mL, respectively. During his chemotherapy, no serious adverse effects were observed. Following with partial response, the patient lived 14 months and died due to cancer progression.

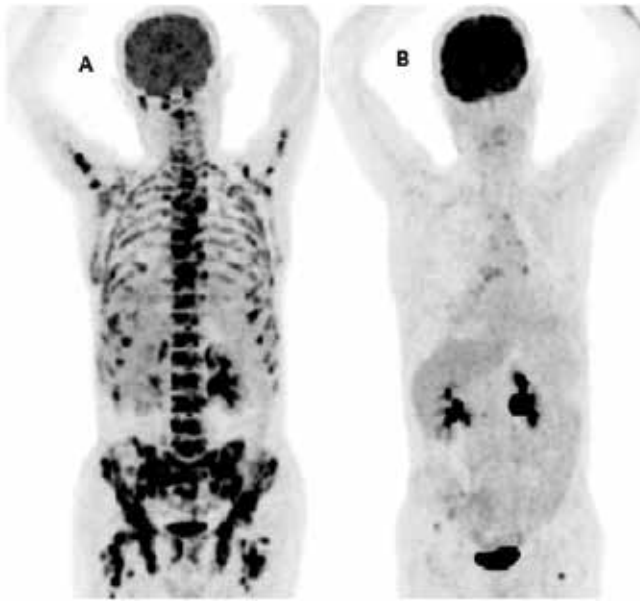

Figure: (A) Initial positron emission tomography–computed tomography (PET–CT) scan showed gastric cancer in the pyloric end, multiple liver, bilateral adrenal and widespread bone metastasis in the maximum intensity projection. (B) After 12 cycles of mFOLFOX-based chemotherapy, the follow-up PET-CT scan showed the nearly complete remission of gastric cancer and metastatic areas.

DISCUSSION

Disseminated intravascular coagulation, in which the coagulation system is activated and widespread intravascular coagulation appears (4), is a rare and serious complication of gastric cancer. DIC always occurs as a consequence of an underlying disease and has an uncertain course from asymptomatic disease to a fulminant course with widespread bleeding and serious organ dysfunctions (5, 7). DIC associated with gastric adenocarcinoma occurs through the exacerbation of the blood clotting process by which procoagulant materials such as mucin extracts derived from the tumour cells directly stimulate coagulation factor X or damage red blood cells and platelets by direct contact with the tumour cells on the micro-vessels (8). There is the evidence of the consumption and the proteolytic degradation in DIC. The common laboratory abnormalities in chronic DIC in solid tumours include thrombocytopenia and circulating fibrin degradation products. Microangiopathic haemolytic anaemia may occur in the absence of other DIC laboratory abnormalities, usually in association with disseminated mucin-secreting adenocarcinoma (9).

The initial presentation of DIC with gastric cancer has a poor prognosis. The supportive treatment, such as replacements of platelets and erythrocytes, fresh frozen plasma transfusions has a little effect on DIC. In a study, which included AGC patients who initially presented with DIC, the median survival time (MST) was only 16 days with best the supportive care, but significantly longer with 98 days in the patients who received systemic chemotherapy. This study suggested that systemic chemotherapy is the only effective therapy for DIC caused by malignancy and that chemotherapy treatment prolongs MST (10). Similarly, when we administered supportive therapy to our patient, the hematologic and biochemical parameters got worse.

The optimal treatment option for DIC is the management of the underlying disease (4). For this reason, to improve DIC in AGC, combination chemotherapy is the preferred option. Cisplatin and 5-FU are the most commonly used drugs in combination (11). But in such patients, it is a complicated situation to perform combination chemotherapy because of DIC-induced thrombocytopenia and bleeding. Even though many studies had been done to determine the best agent, it is still unclear which agent is better (12). In our clinic, we generally prefer to admit docetaxel, cisplatin, 5-FU (DCF) in AGC. Because of the general status of our patient and the instability of laboratory parameters, we preferred mFOLFOX instead of DCF. mFOLFOX therapy is an effective and tolerable regimen in AGC even in patients with impaired general status (13). In our case, we observed that the administration of mFOLFOX regimen improved DIC, provided partial remission of malignant

mass of stomach, bilateral pleural effusion and metastasis of the liver, bones and bilateral adrenal glands. Most of the studies about gastric cancer accompanied DIC included small numbers of patients (between 5 and 18) as this circumstance is rare (14). Furthermore, there had been few studies comparing the prognosis between patients who received the best supportive care and palliative chemotherapy (8).

With this case, we observed that applying early and dense chemotherapy could improve DIC and augment survival in AGC accompanied DIC. However, more effective and less toxic regimens need to be investigated in further studies.

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