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□ Case Report □

A Case of Gastric Cancer Presenting Acute Disseminated Intravascular Coagulation Palliated with Combination Chemotherapy of Irinotecan and Cisplatin

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Acute disseminated intravascular coagulation (DIC) associated with gastric cancer is not common and has short survival of 1 to 3 weeks. Systemic chemotherapy in spite of hematologic unstability for gastric cancer may prolong survival time. A 47-year-old woman who complained of dyspnea, vaginal bleeding and easy bruisibility was diagnosed to stage IV gastric cancer with acute disseminated intravascular coagulation based on the laboratory data. She also had multiple bone metastases and bone marrow involvement. This is the first case treated with combination chemotherapy of irinotecan and cisplatin for advanced gastric cancer complicated by disseminated intravascular coagulation at the time of diagnosis. With systemic chemotherapy, some of the bleeding symptoms and the DIC process improved, even not completely recovered. However the patient died of disease progression and survival time was 12 weeks.

Key Words: Gastric cancer, Irinotecan, Disseminated intravascular coagulation

INTRODUCTION

Acute disseminated intravascular coagulation (DIC) may be complicated during the clinical course of cancer including solid tumors.(1,2) Gastric cancer associated with acute DIC is not common and has dismal prognosis.(3) However recently life prolongation has been induced by effective systemic chemotherapy for underlying gastric cancer in spite of hematologically unstable condition.(3-6) We report a case of advanced gastric cancer having disseminated intravascular coagulation and multiple bone metastasis at the time of diagnosis, who survived 12 weeks with irinotecan-cisplatin chemotherapy.

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CASE REPORT

The patient was a 47-year-old woman, previously in good health, presented with several episodes of back pain, hip pain, dyspnea, dizziness, and weakness of 2 days duration. She complained of vaginal bleeding since a few days ago. Her past history & family history was unremarkable. On physical examination palpebral conjunctivae were pale and there were multiple ecchymoses at whole body. She had very critical appearance. The blood pressure was 130/70 mmHg, the pulse rate 115/min, the respiratory rate 28/min and the body temperature 36.8°C. Laboratory tests revealed pancytopenia (WBC $2.84\times10^3/mm^3$, normal: $4\sim5\times10^3/mm^3$, Hb 5.8 g/dl, normal: 12~16 g/dl, platelet $27\times10^3/mm^3$, normal: $150\sim450\times10^3/mm^3$), prolonged prothrombin time (PT 22.2 sec, normal: 11.1~13.1 sec), elevated fibrinogen degradation products level (FDP 99.15 ug/ml, normal: less than 5 ug/ml), D-dimer (104.20 ug/ml, normal <0.5 ug/ml) and lactate dehydrogenase level (LDH 4666 IU/L, normal: 218~472 IU/L).

Gastrofiberscopy showed a 1.5 cm sized active ulcer with irregular margin at greater curvature of mid body (Fig. 1). Biopsies from the margins of ulcer demonstrated moderately differentiated signet ring cell carcinoma (Fig. 2). Abdominal computed tomographic scan showed small nodules in the paraaortic

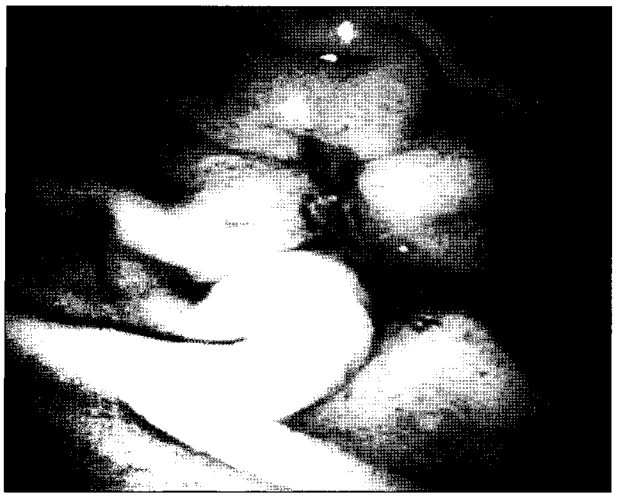

Fig. 1. Gastrofiberscopy demonstrates a 1.5 cm sized active ulcer with irregular margin at greater curvature of mid body.

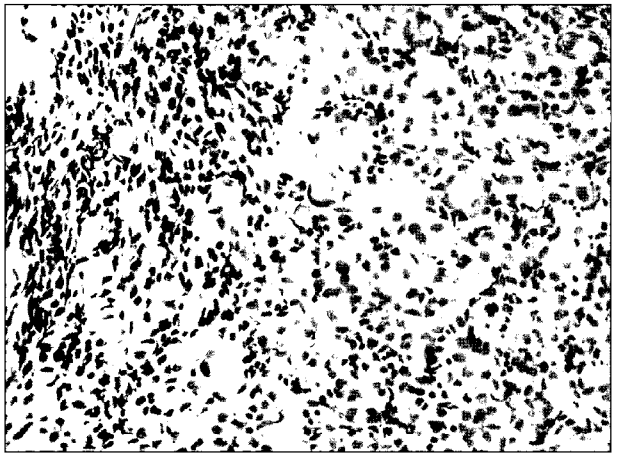

Fig. 2. Gastrofiberscopic biopsy shows signet ring cell type adenocarcinoma (H&E, ×200).

space and mesentery with moderate amount of pelvic fluid collection, suggesting carcinomatosis peritonei. Bone scintigraphy revealed extensive, numerous hot uptakes in the calvarium, facial bones, sternum, both clavicles, both scapulae, both rib cages, the nearly entire vertebrae, both pelvic bones and both humeri and femurs (Fig. 3). Based on these findings, a diagnosis was made as stage IV gastric cancer having multiple bone and bone marrow metastasis with DIC. With consent of the patient and her family, we performed irinotecan-cisplatin chemotherapy to control the underlying gastric cancer. Systemic combination chemotherapy was composed of irinotecan 70 mg/m^2 on day 1 and day 15 and cisplatin 70 mg/m^2 on day 1. Chemotherapy was repeated every four weeks. After two cycles of chemotherapy, hematologic profile some improved but not

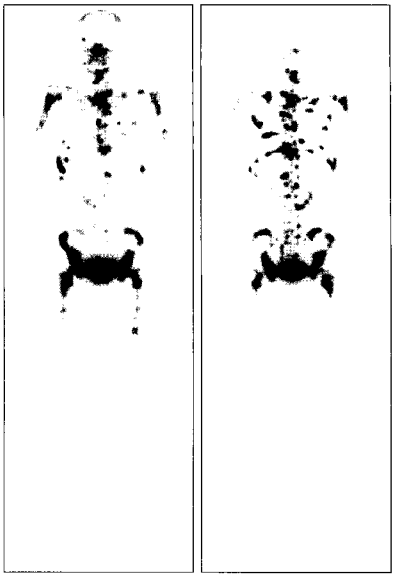

Fig. 3. Bone scintigraphy reveals extensive, multiple hot uptakes over bone.

resolved to normal: WBC $3.9\times10^3/mm^3$, platelet $62\times10^3/mm^3$, PT 14.4 sec, FDP 20.4 ug/ml, D-dimer 18.5 ug/ml, and LDH 353 IU/L. She felt better than before chemotherapy, vaginal bleeding stopped and the ecchymosis of anterior trunk disappeared. Grade 2 emesis with chemotherapy was tolerable. However, tumor response could not be assessed because she had not measurable lesion. After third cycle of chemotherapy, she admitted via emergency room complaining of gross hematuria. WBC $4.4\times10^3/mm^3$, platelet $4\times10^3/mm^3$, FDP 69.9 ug/ ml, D-dimer 36 ug/ml. Three days later after admission, she expired of progression of cancer associated disseminated intravascular coagulation.

DISCUSSION

The incidences of DIC are reported to be 0.68% of patients with gastric cancer.(5) DIC associated with cancer has been reported in gastric cancer, breast cancer, prostate cancer and high-grade non-Hodgkin lymphoma.(2) Tissue factor on their surface of tumors activates intrinsic and extrinsic pathway. DIC in cancer is a consequence of thrombin formation linked to the release into circulation of procoagulant material which activates the extrinsic coagulation pathway by converting factor X to factor Xa. Thrombin catalyzes the activation and the consequent consumption of fibrinogen and other coagulant proteins, as well as the production of fibrin thrombi. Continued fibrin formation and fibrinolysis lead to hemorrhage from the depletion of co-

agulation factor and platelet and the antihemostatic effects of fibrin degradation products.(1) Clinical features of DIC are abnormal thrombosis, abnormal bleeding and rapidly fatal course. DIC associated with a large tumor burden or with metastatic disease is difficult to manage when the tumors are not sensitive to treatment. The role of heparin in the treatment of acute DIC is controversial. The transfusion of blood components may be a way to support complication of acute DIC transiently. The underlying cancers should be controlled to manage acute DIC complicated by cancers. Gastric cancer is moderately sensitive to systemic chemotherapy. Systemic chemotherapy improves survival and quality of life (QOL) in patients with advanced gastric cancer compared with the best supportive care alone.(7,8) There have been several reports on disseminated gastric cancer with DIC that showed prolonged survival with systemic chemotherapy in spite of coagulopathy and severe thrombocytopenia.(3, 4,6) Two phases chemotherapy for gastric cancer associated DIC resulted in survival time of 6 months.(3) In that report, high dose 5-fluorouracil and leucovorin were used as an initial nonmyelosuppressive regimen and myelosuppressive chemotherapeutic drug, etoposide and cisplatin were added after successful control of DIC process. Hironaka et al reported sequential methotrexate and 5-fluorouracil therapy as feasible regimen for gastric cancer with DIC showing 113 days of median survival time.(9) A phase II study of monthly cisplatin (80 mg/m^2/4 weeks) and bimonthly irinotecan (70 mg/m^2/2 weeks) in patients with metastatic gastric cancer have shown overall response rate 48%.(10) We planned combination chemotherapy of cisplatin (70 mg/m^2/4 weeks) and bimonthly irinotecan (70 mg/m^2/2 weeks) and 75% of each of the drugs were administered at first cycle because the hematologic laboratory finding was unstable including severe thrombocytopenia. She felt better than that time of initial diagnosis, and the ecchymosis and vaginal bleeding was controlled. All patients with gastric cancer associated with acute DIC died within 1~3 weeks of diagnosis. But our patient survived 12 weeks after we first made the diagnosis of stage IV gastric cancer complicated by DIC. The irinotecan/CDDP chemotherapy may be a potential palliative regimen. Systemic chemotherapy for gastric cancers with acute DIC could be helpful to prolong survival and improve quality of life.

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위암과 동반된 급성 파종성 혈관 내 응고증에 대하여 Irinotecan, Cisplatin 복합화학요법으로 완화요법을 시행한 1예

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이상훈 · 우인숙 · 김선영 · 송명준 · 노상영 · 고수진 · 이명아 · 강진형 · 홍영선 · 최명규 · 이경식

위암과 관련된 급성 파종성 혈관 내 응고증의 발병 빈도는 0.68%로 보고되고 있으며 생존 기간은 1~3주로써 예후가 매우 불량하다. 본 증례는 47세된 여자가 호흡곤란과 질출혈을 주소로 내원하여 위암4기(골 및 골수전이)로 진단됨과 동시에 검사실 소견상 급성 파종성 혈관 내 응고증 소견을 보인 예이다. 현재 위암과 동반된 급성 파종성 혈관 내 응고증에 대한 표준 복합 항암화학요법 약제는 정립되어 있지 않다. 본 예에서는 irinotecan과 cisplatin 복합화학요법을 시행하여 환자의 증상 및 급성 파종성 혈관 내 응고증 소견이 호전되고 생존기간이 연장된 1예를 보고하는 바이다. 따라서 위암과 동반된 급성 파종성 혈관 내 응고증의 경우에는 혈액학적으로 불안정하더라도 대한 전신 항암화학요법을 시행함으로써 생존기간을 연장하고 환자의 삶의 질을 향상시킬 수 있다. **(J Korean Gastric Cancer Assoc 2006;6:189-192)**

중심 단어: 위암, Irinotecan, 파종성 혈관 내 응고증