Disseminated Carcinomatosis of Bone Marrow from Submucosal Carcinoma in Adenoma of the Rectum

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A 62-year-old man was admitted because of paresis of the legs and a bleeding tendency. He was diagnosed as metastatic bone cancer with disseminated intravascular coagulation (DIC). In spite of treatment, his general condition progressively deteriorated and he died of respiratory failure 13 days later. Autopsy revealed a carcinoma in adenoma in the rectum. Although the depth of cancer invasion was confined to the submucosal layer, disseminated carcinomatosis of the bone marrow and tumor emboli in blood vessels of the lung were present.
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Key words: bone marrow metastasis, disseminated intravascular coagulation (DIC), rectal cancer

Introduction

Disseminated carcinomatosis of the bone marrow is often accompanied by disseminated intravascular coagulation (DIC) (1), and the clinical course is rapid. Most cases of disseminated carcinomatosis of the bone marrow derive from the stomach (1, 2); but carcinomatosis arising from the colon is rare (3–7). In this paper, we describe a case of disseminated carcinomatosis of the bone marrow with DIC arising from submucosal carcinoma in adenoma of the rectum.

Case Report

A 62-year-old man was admitted to the hospital on January 11, 1991 because of paresis of the legs, macrohematuria and nasal bleeding. He had a history of pulmonary tuberculosis of 6 years of age. Three months before admission the patient first noticed lumbago, which gradually worsened. One month before entry he could not walk, and he was unable to stand up one week before admission. Furthermore, he noticed macrohematuria, tarry stool and nasal bleeding two days before admission.

Body temperature was 37.8°C, pulse 74 beats/min, respiratory rate 18 breaths/min, and blood pressure 122/72 mmHg. On physical examination the patient was gaunt, showing nasal bleeding and petechia in the anterior chest and abdomen. Neither superficial lymph nodes nor struma was palpated. The lungs were clear, and the heart beat

sounds were regular with no murmur. The liver and spleen were not palpated. The genital, prostata and rectum were normal.

The urine showed macrohematuria, giving a 2+ test for protein. Peripheral blood examination showed a red blood cell count of 4,590,000/mm³, hemoglobin of 14.1 g/dl, hematocrit of 42.7%, and a white blood cell count of 15300/mm³, consisting of 7% myelocytes, 1% metamyelocytes, 62% neutrophils, 2% basophils, 4% eosinophils, 3% monocytes and 21% lymphocytes, in addition, the platelet count was 71000/mm³. Moreover, red cell fragmentation was observed. The erythrocyte sedimentation rate was 36 mm/h. The bleeding time was over 15 minutes, and the coagulation time 13 minutes. The prothrombin time was 13.3 seconds (46%) and the activated partial thromboplastin time 44.0 seconds (62%). Fibrinogen content of plasma was 142 mg/dl, and the fibrin/fibrinogen degenerative product (FDP) was over 40 µg/dl, with anti-thrombin III of 70.2%. The results of blood chemistry were as follows: total bilirubin 0.7 mg/dl, GOT 166 IU/l, GPT 17 IU/l, LDH 3434 IU/l, ALP 1161 IU/l, total protein 7.1 g/dl, serum albumin 3.6 g/dl, creatinine 1.1 mg/dl, Na 142 mEq/l, K 3.6 mEq/l, Cl 102 mEq/l, Ca 5.0 mEq/l, FBS 99 mg/dl. The results of serological tests were as follows: C-reactive protein 14.1 mg/dl, Ig G 1440 mg/dl, Ig A 229 mg/dl, Ig M 129 mg/dl, CEA 67.9 ng/dl, CA 19-9 14 U/ml, αFP 2 ng/dl, DUPAN II 28 U/ml, calcitonin 73 pg/ml. A chest X-ray film showed calcification in the left upper lobe. The bone X-ray showed a compression fracture in the

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lumbar spine (Fig. 1).

Based on the above findings, we diagnosed his illness as metastatic bone cancer with DIC. There were no tumors in the liver, pancreas, adrenal gland, kidney or bladder, as revealed by computed tomography, ultrasound echography and intravenous pyelography. Gastrofiberscopy showed no tumor, only erosion, in the stomach. Since barium enema and colonoscopic examinations were not performed because of the patient's poor condition, we could not rule out colonic cancer.

To treat DIC, the administration of heparin (10000 U/day), gebexate mesilate (20 mg/kg/day) and anti-thrombin III was started. However, the bleeding tendency did not improve and microhemangiopathic hemolytic anemia (MHA) developed. His general condition worsened rapidly and dyspnea occurred. He died of respiratory failure on January 22, 1991.

At autopsy, there was a polypoid lesion, measuring $2.5 \times 1.8 \times 2.0$ cm, in the rectum 12 cm distant from the anus. Macroscopically it was the subpedunculated type (Ips)

Fig. 1. Bone X-ray of the spine showing a multiple compression fracture.

Fig. 2. Resected specimen showing a subpedunculated polypoid lesion (arrow) (a). Cross-section of the tumor showing moderately differentiated adenocarcinoma in adenoma; the depth of invasion reached the submucosal layer (b, hematoxylin-eosin stain, $\times 1$). Close-up view of the tumor (c, $\times 100$). Lymphatic and venous (d, $\times 40$) permeation are seen in the submucosal layer.

Fig. 3. Microscopic bone marrow section showing a diffusely infiltrative metastatic carcinoma (a, hematoxylin-eosin stain, $\times 40$). Microscopic lung section showing tumor emboli in blood vessels (b, HE stain, $\times 40$).

early colonic cancer (8). Histological examination revealed that it was moderately differentiated adenocarcinoma in adenoma, and that the depth of cancer invasion was confined to the submucosal layer. However, marked cancer infiltration was found in the lymphatic and venous vessels in both the submucosal layer and serosa (Fig. 2). Moreover, regional lymph node involvement was present. Cancer metastasis in the bone marrow was remarkable, especially in the spine. Microscopic lung sections revealed tumor emboli in the blood vessels (Fig. 3). There were no metastases in the liver, adrenal glands or other organs. Although there were erosions in the stomach, there was no evidence of tumor involvement.

Discussion

Jarcho (9) first reported diffusely infiltrative carcinoma in 1936. Hayashi et al (1) reviewed 40 cases of disseminated carcinomatosis of the bone marrow in Japan. The three major symptoms are anemia, lumbago or/and back pain, and a bleeding tendency. Hematological findings are severe anemia, leukoerythroblastosis and DIC and/or MHA.

Biochemical findings are mild to moderate hyperbilirubinemia, elevation of serum GOT and GPT, and marked elevation of ALP and LDH. Most of the primary cancers are in the stomach (over 90%). Mucin-forming, diffusely infiltrative, or poorly differentiated carcinomas are most frequently seen histologically (1, 2). Metastases to the bone marrow are diffusely infiltrative rather than of a nodular pattern. The present case is in accordance with these clinical features of disseminated carcinomatosis of the bone marrow.

Disseminated carcinomatosis of the bone marrow is often accompanied by DIC or MHA (1, 2), and its clinical course is rapid. Brain et al (10) reported that mucin-forming carcinoma is related to DIC or MHA. It has been proposed that the pathogenesis of DIC and/or MHA in cancer is due to tissue thromboplastin-like substances derived from tumor cells and disseminated hematogenous metastases, thus causing damage to vascular endothelial cells (1, 2). The pathology is also accelerated by other factors such as infection, anemia and acidosis.

Reports on carcinomatosis of the bone marrow from the colon are rare in Japan (3–7); histological examination revealed that all of these were advanced cancers and mucin-forming or poorly differentiated adenocarcinomas in the presented case, moderately differentiated adenocarcinoma in adenoma was seen. Although the depth of invasion was confined to the submucosal layer, lymphatic and venous permeation and diffusely infiltrative bone marrow metastases were found. It is known that the percentage of lymphatic vessel invasion is 5 to 10% and distant metastasis is very rare even in submucosal invasive carcinoma of the colon (11, 12). To our knowledge, this is the first report showing disseminated carcinomatosis of the bone marrow from submucosal carcinoma in adenoma of the rectum.

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Carcinomatosis and Rectal Cancer

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