



Cytokeratin 면역조직화학염색으로 확진된 대장암의 골수 전이 1예

A Report of Bone Marrow Metastasis of Colon Cancer as a Primary Diagnosis, Supported by Cytokeratin Immunohistochemical Staining

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Bone marrow metastasis of colon cancer is rare. Here, we report a 56-year-old female patient who presented with pancytopenia. She was diagnosed with colon cancer accompanied by lung and axial skeleton metastasis. The bone marrow study showed metastatic carcinoma. Immunohistochemical (IHC) staining with anti-cytokeratin 7 (CK7) and anti-cytokeratin 20 (CK20) antibodies showed that the bone marrow samples were negative for CK7 and positive for CK20, consistent with metastatic colon cancer. To the best of our knowledge, there has been only one other reported case of bone marrow metastasis of colon cancer as the primary diagnosis in an adult patient in Korea. Bone and bone marrow metastases of colon cancer are regarded as uncommon. However, for proper management, bone marrows should be promptly examined in patients with solid tumors when unexplained cytopenia is noted, even if the origin of the tumor is known to be rarely metastatic to bone marrow. In addition, the use of cytokeratin IHC staining is helpful for determining the origin of metastatic carcinoma.

Key Words: Bone marrow, Colon cancer, Metastasis, Immunohistochemistry, Cytokeratin

CASE REPORT

Bone marrow metastasis of colon cancer is an uncommon finding. Here, we report a rare case of a patient who presented with bone marrow metastasis of colon cancer as primary diagnosis, along with pancytopenia. A 56-year-old woman visited the hematology-oncology outpatient department due to pancytopenia (white

blood cells $2.95 \times 10^6/L$, reference range $4.0-10.0 \times 10^6/L$; hemoglobin 90 g/L, reference range 120-160 g/L; platelets $97 \times 10^6/L$, reference range $150-400 \times 10^6/L$). She also complained of back pain and weight loss (5 kg per month). Magnetic resonance imaging of the spine showed diffuse signal changes in the first and second thoracic vertebrae, with heterogeneous enhancement of the whole spine, which was suggestive of malignant bony metastasis. Abdominal and pelvic computed tomography (CT) and colonoscopy revealed a large mass that completely obstructed the ascending colon. A biopsy identified moderately differentiated adenocarcinoma, and molecular analysis of the biopsy specimen detected a missense mutation in the 12th codon of the *KRAS* gene. Subsequent chest CT and positron emission tomography-CT showed metastasis of colon cancer to the lymph nodes, lungs, and the axial skeleton. Peripheral blood morphology showed pancytopenia with leukoerythroblastosis. Bone marrow aspiration and biopsy were performed. The aspirate was markedly diluted, and the biopsy revealed hypercellular marrow with patchy infiltration of

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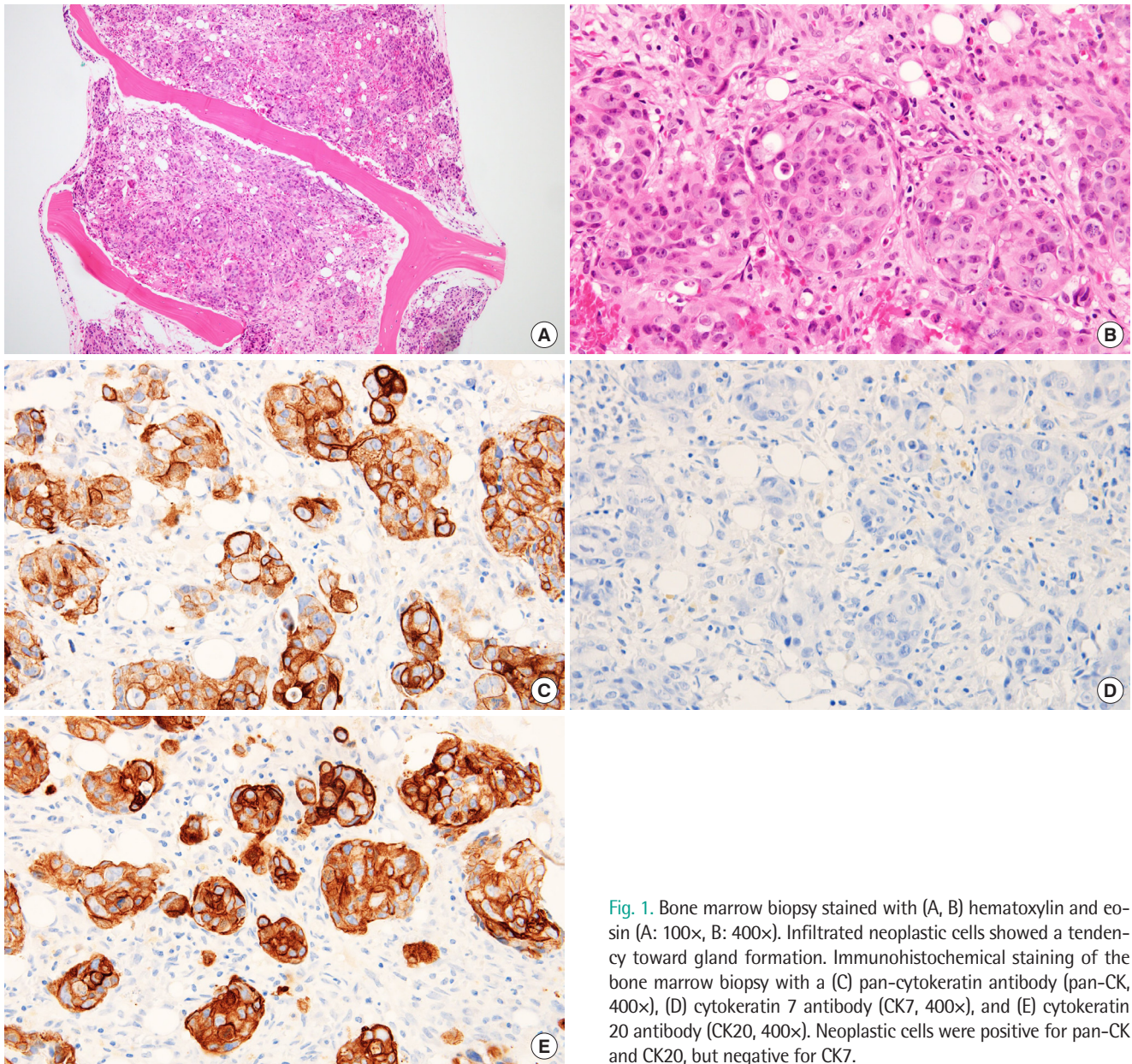


Fig. 1. Bone marrow biopsy stained with (A, B) hematoxylin and eosin (A: 100x, B: 400x). Infiltrated neoplastic cells showed a tendency toward gland formation. Immunohistochemical staining of the bone marrow biopsy with a (C) pan-cytokeratin antibody (pan-CK, 400x), (D) cytokeratin 7 antibody (CK7, 400x), and (E) cytokeratin 20 antibody (CK20, 400x). Neoplastic cells were positive for pan-CK and CK20, but negative for CK7.

malignant cells and glandular formation. The presence of metastatic carcinoma was subsequently confirmed by positive immunohistochemical (IHC) staining with an anti-pan-cytokeratin (pan-CK) antibody. Then, we performed additional IHC staining with anti-cytokeratin 7 (CK7) and anti-cytokeratin 20 (CK20) antibodies. The sample was positive for anti-CK20 IHC staining, but negative for anti-CK7 IHC staining, strongly suggesting that it originated from colon cancer (Fig. 1). She is undergoing chemotherapy using bevacizumab, 5-fluorouracil, leucovorin, and irinotecan, and is in the fourth cycle without significant adverse events.

DISCUSSION

Colon cancer is the third most common cancer in Korea [1]. The most common metastatic sites are the liver and lungs, and the incidence of bone and bone marrow metastases from colon cancer is quite low [2, 3]. In a study of 252 patients with colorectal cancer, only 5.5% were diagnosed with bony metastases [4]. The most frequent histological types are poorly differentiated adenocarcinoma and signet-ring cell carcinoma [5]. To the best of our knowledge, only two cases of bone marrow metastasis of colon cancer have

been reported in Korean adults. In the first case, bone marrow metastasis was the primary diagnosis [6], and in the other case, the bone marrow was the first site of recurrence [3]. In our patient, the bone marrow metastasis was not highly suspicious because the histological type was moderately differentiated adenocarcinoma, and the sites of metastases were limited to the lungs and axial bones. Bone and bone marrow metastases of colon cancer are regarded as clinically uncommon.

Cytokeratins are filamentous proteins found in epithelial cells that are expressed in a tissue-specific manner [7]. The expression patterns of CK7 and CK20 have been found to be useful for the differential diagnosis of carcinomas of epithelial origin [8]. CK7 is expressed in carcinomas originating from tumors in the lung, breast, ovary, and bile ducts. CK20 is expressed in all colorectal carcinomas, and in a majority of gastric and pancreatic carcinomas. Carcinomas originating from the prostate and kidney, sarcomas, and hepatocellular carcinomas have been found to be negative for both CK7 and CK20 staining [7, 8]. In our patient, the IHC staining was positive for pan-CK and CK20 and negative for CK7, which is consistent with carcinoma originating from the colon.

The prognostic significance of bone marrow metastasis of colon cancer is still controversial, because of the limited number of cases that have been reported, and comparison of the data is difficult due to somewhat different disease definitions and evaluation methods [9-11]. There is emerging evidence that bone marrow micrometastasis of stage I-III colon cancer is related to poor prognosis for disease-free and overall survival [12, 13]. Our patient has been treated with the standard chemotherapy regimen for stage IV colon cancer. Frequent follow-ups regarding the response status of the disease are necessary because the clinical presentation of the metastatic pattern is unusual.

In conclusion, a bone marrow study should be promptly performed when unexplained cytopenia is detected in patients with solid tumors, even if the origin of the carcinoma is known to rarely metastasize to bone marrow. In the case of metastatic carcinoma, IHC staining with anti-CK7 and anti-CK20 antibodies is useful for determining the origin of carcinoma, especially in the case of metastatic carcinoma of unknown origin.

요약

대장암의 골수 전이는 드문 것으로 알려져 있다. 범혈구감소증

으로 내원한 56세 여자 환자가 폐와 뼈 전이만을 동반한 대장암으로 진단되었다. 골수검사상 전이암이 관찰되었고, 항-CK7과 항-CK20 항체를 이용한 면역조직화학염색을 통해 CK7 음성, CK20 양성을 보이는 대장암의 골수 전이를 확인할 수 있었다. 국내에서는 성인 대장암 환자에서 진단 시 골수 전이가 발견된 경우는 단지 한 증례만이 보고되어 있다. 폐를 제외하면 뼈와 골수 전이만 동반된 대장암은 흔하지 않은 임상적 상황이다. 이처럼 골수 전이가 드물다고 알려진 고형암을 진단받은 환자라 하더라도, 원인을 알 수 없는 혈구감소증이 관찰된다면 빠른 골수검사를 시행하는 것이 적절한 치료를 위해 반드시 필요하다. 또한 cytokeratin 면역조직화학염색을 이용하면 전이암의 기원을 밝히는 데 도움이 될 것이다.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

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