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A RARE CASE OF RECURRENT SIGNET RING CELL CARCINOMA PRESENTING WITH THROMBOCYTOPENIA

Sezin Sayın[1], Elçin Kasapoğlu[1], Ali Gökyer[2]

[1]Trakya University School of Medicine, Edirne, TURKEY
[2]Division of Medical Oncology, Department of Internal Medicine, Trakya University School of Medicine, Edirne, TURKEY

ABSTRACT

Aims: Signet ring cell carcinoma is a rare type of gastric cancer most commonly seen in the stomach. There is a 60% systemic recurrence rate of gastric cancer after curative resection, and it most commonly recurs in the liver, peritoneum, and lungs. Bone metastasis is extremely rare in gastric cancer. We aim to present a rare case of signet ring cell carcinoma with thrombocytopenia as a primary symptom of bone marrow metastasis years after the patient's primary diagnosis with gastric adenocarcinoma. ***Case Report:*** A 52-year-old male patient was admitted to the Medical Oncology Division of Trakya University Hospital with dyspeptic complaints six years ago, whereupon gastroscopy revealed an ulcerated lesion in the antral region of the stomach, and the pathological biopsy revealed adenocarcinoma. The patient underwent subtotal gastrectomy and lymph node dissection, combined with adjuvant chemoradiotherapy. In the follow-up, a complete blood count revealed thrombocytopenia, and poorly differentiated adenocarcinoma metastasis with a signet ring cell component was demonstrated through imaging studies and pathological examination. Treatment with cisplatin and 5-fluorouracil was initiated after the diagnosis of human epidermal growth factor receptor-2 negative, stage 4 gastric adenocarcinoma. The patient showed clinical and laboratory response to the treatment and will continue with the current regimen. ***Conclusion:*** In this case, the primary tumor was in the stomach, and he had signs of thrombocytopenia only. When the prognosis of the patient was evaluated, it was thought that there was tumor residue at a cellular or clonal level in the stomach after gastrectomy, or an asymptomatic metastasis present and unnoticed in the bone marrow during the surgical treatment. In conclusion, this case shows that physicians should be alert to the changes in blood parameters in terms of recurrence with bone marrow involvement even if there is no visible recurrence in the patient. ***Keywords:*** Bone marrow, gastric cancer, metastasis, signet ring cell carcinoma, thrombocytopenia

INTRODUCTION

Signet ring cell carcinoma (SRCC) of the stomach is a diffuse type of gastric adenocarcinoma, which is a rare condition with a poor prognosis due to being commonly diagnosed at advanced or metastatic stage (1). In gastric adenocarcinoma, neoplastic cells produce mucin that fills the cytoplasm and displaces the cell nucleus to the periphery, creating the signet ring cell pattern (2). According to the World Health Organization classification, if this signet ring cell pattern is seen in more than 50% of the cells, the diagnosis is SRCC, whereas if this pattern is present in less than 50% of the cells, it is only referred to as "adenocarcinomas with a signet ring cell component" (3).

Signet ring cell carcinoma is most commonly seen in the stomach but can also be seen in almost any part of the gastrointestinal tract, or the breast, prostate, and bladder (4). While the overall incidence of gastric carcinomas is decreasing, the incidence of SRCC is increasing even though it is a rare subtype of gastric adenocarcinoma (5). A study conducted by Benesch et al. (1) showed that signet ring cell carcinomas constitute 16.8% of gastric cancer cases. Clinical management of metastatic SRCC is difficult due to the rarity of cases and poor chemosensitivity (6). The most common first-line treatment for advanced SRCC is triplet chemotherapy with docetaxel-5FU-oxaliplatin known as TEFOX (7).

There is a 60% systemic recurrence rate of gastric cancer after curative resection and it most commonly recurs in the liver, peritoneum, and lungs (8, 9). Bone metastasis is extremely rare in gastric cancer, accounting for 0.9-3.8% of overall metastases in gastric cancer patients (10).

In this case report, we aim to present a patient with gastric SRCC who presented with thrombocytopenia due to bone marrow metastasis six years after his primary diagnosis.

CASE REPORT

A 52-year-old male patient was admitted to the Medical Oncology Division of Trakya University Hospital with dyspeptic complaints six years ago, whereupon gastroscopy revealed an ulcerated lesion in the antral region of the stomach, and the pathological biopsy revealed adenocarcinoma. Since distant metastasis was not detected in thoracoabdominal computed tomography, which was performed for staging, the patient underwent subtotal gastrectomy and lymph node dissection. Postoperative pathological examination documented gastric adenocarcinoma located in the antrum, and it was classified as pT1bN2M0, according to the TNM Classification of the Union for International Cancer Control Eighth Edition.

The patient underwent combined treatment with FUFA (combination of calcium folinate and 5-fluorouracil) and radio-

Address for Correspondence: Sezin Sayın, Trakya University School of Medicine, Edirne, TURKEY
e-mail: seziniyas@gmail.com
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ORCID iDs of the authors: SS: 0000-0001-7892-5992; EK: 0000-0001-7888-1053; AG: 0000-0002-1653-6155.

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therapy. Afterward, treatment was continued for 6 months by receiving FOLFOX (combination of folinic acid, fluorouracil, and oxaliplatin) chemotherapy regimen in the following 4 months. After adjuvant therapy, the patient was followed up with gastroscopy and systemic imaging studies, to assess whether recurrence had occurred.

The complete blood count in August 2020 revealed the following values: Platelet count was 83x103/uL, hemoglobin 12.8 g/dL, leukocyte 5x103/uL, and neutrophil 2.6x103/uL. Upon detection of these values, positron emission tomography/computed tomography imaging was performed in September 2020 to evaluate if any recurrence had occurred. There was mild to moderate Fluorodeoxyglucose uptake, commonly observed in the bone marrow with a maximum standardized uptake value of 4.15, and reactive bone marrow activation or metastases were investigated. Pathological fluorodeoxyglucose involvement was not detected in other parts of the body. The pathological examination of the bone marrow biopsy documented poorly differentiated adenocarcinoma metastasis with a signet ring cell component. In addition, molecular analysis was performed on the bone marrow specimen and was negative for programmed cell death ligand-1 and human epidermal growth factor receptor-2; stable status for microsatellite instability was determined.

Cisplatin and 5-fluorouracil treatment was initiated with the diagnosis of human epidermal growth factor receptor-2 negative, stage 4 gastric adenocarcinoma. The thrombocyte count of the patient, who received the 5th cycle, was measured as 130x103/uL at the last follow-up examination during the treatment. The patient, who has shown clinical and laboratory response to the treatment, will continue with the current regimen.

DISCUSSION

Signet ring cell carcinoma of the stomach is a rare form of gastric adenocarcinoma (7). According to Lauren classification, the most frequently used classification of gastric cancer, SRCC is a diffuse-type gastric cancer (11). Diffuse type gastric cancer consists of poorly cohesive and poorly differentiated cells, which explains its malignant nature (11).

Metastasis from primary tumors to the bone is a rare condition, and bone marrow involvement is even rarer (12). According to a study, the incidence of bone marrow metastasis in advanced gastric cancer, confirmed by bone marrow biopsy, is 0.024% (13). Although bone marrow metastases with the primary tumor in the stomach are rare, they are usually seen in young patients and patients with aggressive histology, such as SRCC or poorly differentiated adenocarcinoma (14). In our patient, the primary tumor was in the stomach and had the molecular characteristics of human epidermal growth factor receptor-2 negative, programmed cell death ligand-1 negative, and microsatellite instability stable.

In the study conducted by Ekinci et al. (15), 245 patients with advanced gastric cancer were assessed and the findings were that 5 patients had bone marrow metastases, and the median age of the patients was 45 years. Pain and hemorrhagic symptoms were frequently observed as main complaints along with serum alkaline phosphatase elevation in 28 cases of diffuse carcinomatosis of the bone marrow associated with gastric cancer (16). In addition, bone marrow metastasis of gastric adenocarcinoma is mostly manifested by hematological imbalances such as anemia, thrombocytopenia, and high alkaline phosphatase and lactate dehydrogenase levels (14). In a case presented by Fonocho et al. (17), the patient had new-onset pancytopenia without evidence of systemic disease despite normal blood counts in the postoperative follow-up; thus, carcinomatosis of the bone marrow associated with recurrent gastric cancer was considered. In the study of Takayasu et al. (12), a case presented with weight loss, back pain, bicytopenia without reticulocytosis, and leukoerythroblastosis, which are all compatible with bone marrow infiltration. In our case, the patient only had signs of thrombocytopenia. There were no additional physical examinations or laboratory findings. The patient was 52 years old and was compatible with the findings of the study conducted by Ekinci et al. (15).

When the prognosis of the patient was evaluated, it was thought that there was a tumor residue at a cellular or clonal level in the stomach after gastrectomy, or an asymptomatic metastasis present and unnoticed in the bone marrow during the surgical treatment. Since distant metastasis was not detected in the thoracoabdominal computed tomography, the patient was considered as an early-stage gastric adenocarcinoma, and subtotal gastrectomy and lymph node dissection were performed because the lesion was close to the antrum. In addition, combined therapy with the FUFA regimen was used to increase the effectiveness of radiotherapy given as adjuvant therapy. Because our patient was human epidermal growth factor receptor-2 negative, programmed cell death ligand-1 negative, and microsatellite instability stable; fluorouracil plus cisplatin was chosen as the treatment regimen. Spontaneous recovery of the platelet count during treatment was considered as a response to treatment, and the patient's treatment is ongoing.

In conclusion, even if there is no visible recurrence of gastric cancer in the patient, physicians should be alert to the changes in blood parameters in order to eliminate recurrence with bone marrow involvement.

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