J Gastric Cancer 2014;14(1):54-57 • http://dx.doi.org/10.5230/jgc.2014.14.1.54 | Case Report

Gastric Carcinoma with Bone Marrow Metastasis: A Case Series

Ahmet Şiyar Ekinci, Öznur Bal, Tahsin Özatlı, İbrahim Türker, Onur Eşbah, Ayşe Demirci, Burçin Budakoğlu, Ülkü Yalçıntaş Arslan, Emrah Eraslan, and Berna Öksüzoğlu

Department of Medical Oncology, Ankara Onkoloji Training and Research Hospital, Ankara, Turkey

Gastric cancer is a major cause of cancer-related mortality. At the time of diagnosis, majority of the patients usually have unresectable or metastatic disease. The most common sites of metastases are the liver and the peritoneum, but in the advanced stages, there may be metastases to any region of the body. Bone marrow is an important metastatic site for solid tumors, and the prognosis in such cases is poor. In gastric cancer cases, bone marrow metastasis is usually observed in younger patients and in those with poorly differentiated tumors. Prognosis is worsened owing to the poor histomorphology as well as the occurrence of pancytopenia. The effect of standard chemotherapy is unknown, as survival is limited to a few weeks. This report aimed to evaluate 5 gastric cancer patients with bone marrow metastases to emphasize the importance of this condition.

Key Words: Stomach neoplasms; Bone marrow metastasis; Poor prognosis

Introduction

In Turkey, gastric cancer is the second most common cause of cancer-related mortality in men, and the fourth most common cause in women.[1] It is very important to assess the presence or absence of metastases to establish appropriate treatment plans for gastric cancer. Gastric cancer generally metastasizes to the peritoneal surfaces, liver, and distant lymph nodes; metastasis to the spleen, adrenal glands, ovaries, lung, brain, or even the skin has also been noted frequently. There is limited data on the frequency and clinical significance of bone marrow metastasis in gastric cancer. Bone marrow metastases are frequently observed with solid tumors and these may negatively affect patient survival. Malignancies of the prostate, breast, lung, kidney, thyroid, and stomach are the most common neoplasms that may metastasize and involve the bone marrow.[2-10] There are limited published data from the Far East about gastric cancer with bone marrow involvement. In the last 4 years, 420 patients with gastric cancer were admitted at our clinics, of which 245 had metastatic cancer. Of these, only 5 patients had bone marrow metastasis. We have evaluated the characteristics of these patients and reviewed the literature.

Correspondence to: Ahmet Şiyar Ekinci
Department of Medical Oncology, Ankara Onkoloji Training and Research Hospital, Mehmet Akif Ersoy Neighborhood, 13 Street Number: 56, 06200 Yenimahalle, Ankara, Turkey
Tel: +90-312-3360909-5713, Fax: +90-312-312336-9681
E-mail: a.siyar@hotmail.com
Received January 8, 2014
Revised February 12, 2014
Accepted February 20, 2014

Case Report

We evaluated 5 (2%) patients with bone marrow metastasis out of 245 patients with advanced gastric cancer. The median age was 45 years (range, 22~55), which was lower than that of the overall population of gastric cancer patients. All patients were male; 3 patients had signet-ring cell type, 1 had undifferentiated type, and 1 had tubular type tumor, according to the World Health Organization classification. Four patients had primary tumors located in the corpus and 1 patient had neoplasm of the cardia. The most common sites of synchronous metastasis in gastric cancer patients with

Table 1. Clinicopathological features of gastric carcinoma patients with bone marrow metastases

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (yr)/sex	55/male	47/male	22/male	45/male	42/male
Tumor differentiation (WHO)	Undifferentiated	Signet ring cell	Signet ring cell	Signet ring cell	Tubular
Gastric localization	Cardia	Corpus	Corpus	Corpus	Corpus
Other sites of metastases	Bone	Liver, bone	Liver, lung, bone	Liver, bone, surrenal	Peritoneum
Duration between diagnosis of gastric cancer and bone marrow metastasis	32 months	Synchronously	Synchronously	Synchronously	5 months
Treatment after the diagnosis of bone marrow metastasis	BSC	BSC	CDDP, 5-FU	Docetaxel, CDDP, 5-FU	BSC
Survival after the diagnosis of bone marrow metastasis (d)/alive or dead	61/alive	47/dead	20/dead	53/dead	34/dead

WHO = World Health Organization classification; BSC = best supportive care; CDDP = cisplatin; 5-FU = 5-fluorouracil.

bone marrow involvement were the bone (4/5 patients), followed by the liver (3/5 patients). All patients with bone marrow metastasis were diagnosed on the basis of bone marrow biopsy reports, and all patients had cytopenia at the time of admission. Three patients were diagnosed with bone marrow metastasis and gastric cancer synchronously. One patient had peritoneal metastasis at the time of diagnosis, and bone marrow metastasis developed 5 months later. Only 1 patient had recurrence with bone and bone marrow metastasis after curative surgery and adjuvant chemoradiotherapy at the 32nd month of diagnosis. Two patients received chemotherapy after the diagnosis of bone marrow metastasis. The median duration of survival after the diagnosis of bone marrow involvement was 47 days. The range of survival duration after diagnosis of bone marrow metastasis was 20~53 days among the 4 patients who died; 1 patient was alive at 61 days after diagnosis. Clinicopathological features of the 5 patients are summarized in Table 1. Only 2 patients underwent chemotherapy. Unfortunately, 1 patient died after the first cycle, and the other patient died after the second cycle of treatment.

Four patients had both anemia and thrombocytopenia, and 1 patient had only thrombocytopenia. All patients had elevated levels of alkaline phosphatase (ALP) with a median value of 615 U/L (normal range, 40~150 U/L), and lactate dehydrogenase (LDH) with a median of 628 U/L (normal range, 125~220 U/L). However, no patient developed hypercalcemia, although 4 patients had bone metastases. Laboratory findings are summarized in Table 2.

Table 2. Laboratory findings of gastric carcinoma patients with bone marrow metastases at the time of diagnosis

	Cytopenia	LDH at diagnosis	ALP at diagnosis	Calcium level at diagnosis
Case 1	Thrombocytopenia, anemia	556	781	9.0
Case 2	Thrombocytopenia	1,523	615	8.1
Case 3	Thrombocytopenia, anemia	1,783	1,432	8.4
Case 4	Thrombocytopenia, anemia	628	528	7.6
Case 5	Thrombocytopenia, anemia	524	583	7.4

Normal range: LDH at diagnosis, 125~220 U/L; ALP at diagnosis, 40~150 U/L; Calcium level at diagnosis, 8.4~10.2 mg/dl. LDH = lactate dehydrogenase; ALP = alkaline phosphatase.

Discussion

Bone marrow infiltration with malignant cells is frequently observed in patients with solid organ malignancies. Carcinomatosis of the bone marrow can originate from the primary prostate, lung, or breast carcinoma,[2-11] and rarely from gastric carcinoma.[3] There is limited data regarding the incidence and clinical significance of bone marrow metastasis in gastric carcinoma. This case series is one of the largest in the literature compared to other case series reported from the Far East. Kim et al.[12] reported the prevalence of bone morrow metastasis to be 0.024, which was confirmed by bone marrow biopsy reports. Kusumoto et al.[13] reported 9 gastric cancer patients with bone marrow metastases, and concluded that all patients had more aggressive histopathology (signet ring cell or poor differentiated) and were younger than patients without bone

marrow metastasis. They also reported an elevation of ALP and/or LDH levels in gastric cancer patients with bone marrow involvement, and 6 of 9 patients had disseminated intravascular coagulopathy.

In gastric cancer cases, bone metastasis is usually rare compared to liver and peritoneal metastasis. In the 5 cases of gastric cancer with bone marrow involvement reported here, 4 patients had bone metastasis, which was consistent with reports from published literature. In the study by Kwon et al.[14] that included gastric cancer patients with bone marrow involvement, the incidences of metastases to the bone, lung, and liver were 57% (15/26), 11% (3/269), and 3.8% (1/26), respectively. Of the 2,150 patients with advanced cancer in the study by Ahn et al.,[15] there were 19 patients (0.9%) with bone metastases; however, another study revealed a higher incidence (13.4%, 33/246 patients) among autopsy cases.[16] In both series, bone metastasis was associated with poorly differentiated histology. All these findings suggest that there may be a relationship between bone and bone marrow metastasis, and possibly between poor differentiation and unusual metastatic sites, including the bone and bone marrow. Kong et al.[17] reported that there were 193 (0.96%) patients with pulmonary metastases among 20,197 patients with advanced gastric cancer; further, 34 (17%) of the patients with lung metastasis also had bone metastasis and 11 (5.7%) patients had bone marrow metastasis as well as lung metastasis. Besides, 58% of the patients had poorly differentiated or signet ring cell histopathology.

Chemotherapy is known to prolong survival as compared to best supportive care (BSC), for the management of advanced gastric carcinoma.[18] However, these reports in published literature were limited to patients with adequate bone marrow function; in other words, patients with bone marrow involvement were excluded. The incidence of bone marrow metastases in gastric cancer patients is low; therefore, the clinical features and optimal treatment options for such patients has not yet been established. In the present study, 4 patients died approximately within 2 months after the diagnosis of bone marrow metastasis. In the study by Kusumoto et al.,[13] the median survival was only 3 months in the chemotherapy group and 2 months in the BSC group, with borderline significance in gastric cancer patients with bone marrow metastasis. Kwon et al.[14] published the largest case series in 2011. In that report, 15 patients received palliative chemotherapy and 10 patients received BSC. The median survival was 11 days in the BSC group compared to 121 days in the palliative chemotherapy group ($P<0.001$). Because of the lack of prospective studies of gastric cancer patients with bone marrow metastases, an optimal chemotherapy regimen is still unknown.

Bone marrow metastases in gastric cancer patients are characterized by aggressive histology and a younger age of onset. They are diagnosed on the basis of bone marrow biopsy findings and treated like cases of metastasis to other sites. Unfortunately, patients have poor prognosis, characterized by short survival times.

References

1. Ministry of Health, Public Health Agency Turkey. T.C. Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu [Internet]. Ankara: Ministry of Health, Public Health Agency Turkey; 2008. Available from: http://www.kanser.gov.tr.
2. Anner RM, Drewinko B. Frequency and significance of bone marrow involvement by metastatic solid tumors. Cancer 1977;39:1337-1344.
3. Kiliçkap S, Erman M, Dinçer M, Aksoy S, Harputluoglu H, Yalçin S. Bone marrow metastasis of solid tumors: clinicopathological evaluation of 73 cases. Turk J Cancer 2007;37:85-88.
4. Mehdi SR, Bhatt ML. Metastasis of solid tumors in bone marrow: a study from northern India. Indian J Hematol Blood Transfus 2011;27:2:93-95.
5. Mohanty SK, Dash S. Bone marrow metastasis in solid tumors. Indian J Pathol Microbiol 2003;46:613-616.
6. Tasleem RA, Chowdhary ND, Kadri SM, Chowdhary QA. Metastasis of solid tumours in bone marrow: a study from Kashmir, India. J Clin Pathol 2003;56:803.
7. Frisch B, Bartl R, Burkhardt R. Bone marrow biopsy in clinical medicine: an overview. Haematologia (Budap) 1982;15:245-285.
8. Penchansky L. Bone marrow biopsy in the metastatic work-up of solid tumors in children. Cancer 1984;54:1447-1448.
9. Wong KF, Chan JK, Ma SK. Solid tumour with initial presentation in the bone marrow--a clinicopathologic study of 25 adult cases. Hematol Oncol 1993;11:35-42.
10. Clifton JA, Philipp RJ, Ludovic E, Fowler WM. Bone marrow and carcinoma of the prostate. Am J Med Sci 1952;224:121-130.
11. Finklestein JZ, Ekert H, Isaacs H Jr, Higgins G. Bone marrow metastases in children with solid tumors. Am J Dis Child 1970;119:49-52.
12. Kim HS, Yi SY, Jun HJ, Lee J, Park JO, Park YS, et al. Clinical outcome of gastric cancer patients with bone marrow metasta-

ses. Oncology 2007;73:192-197.
13. Kusumoto H, Haraguchi M, Nozuka Y, Oda Y, Tsuneyoshi M, Iguchi H. Characteristic features of disseminated carcinomatosis of the bone marrow due to gastric cancer: the pathogenesis of bone destruction. Oncol Rep 2006;16:735-740.
14. Kwon JY, Yun J, Kim HJ, Kim KH, Kim SH, Lee SC, et al. Clinical outcome of gastric cancer patients with bone marrow metastases. Cancer Res Treat 2011;43:244-249.
15. Ahn JB, Ha TK, Kwon SJ. Bone metastasis in gastric cancer patients. J Gastric Cancer 2011;11:38-45.
16. Nishidoi H, Koga S. Clinicopathological study of gastric cancer with bone metastasis. Gan To Kagaku Ryoho 1987;14:1717-1722.
17. Kong JH, Lee J, Yi CA, Park SH, Park JO, Park YS, et al. Lung metastases in metastatic gastric cancer: pattern of lung metastases and clinical outcome. Gastric Cancer 2012;15:292-298.
18. Ajani JA, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, et al; V-325 Study Group. Clinical benefit with docetaxel plus fluorouracil and cisplatin compared with cisplatin and fluorouracil in a phase III trial of advanced gastric or gastroesophageal cancer adenocarcinoma: the V-325 Study Group. J Clin Oncol 2007;25:3205-3209.