CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 37 (2017) 165–168

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Recurrent gastric cancer metastasizing to the bone marrow: A case report of a rare presentation

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ARTICLE INFO

Article history:
Received 17 May 2017
Received in revised form 13 June 2017
Accepted 13 June 2017
Available online 24 June 2017

Keywords:
Recurrent gastric cancer
Bone marrow metastasis
Case report

ABSTRACT

INTRODUCTION: Gastric cancer notoriously recurs post curative surgical resection. While there may be visceral metastasis to peritoneal surfaces, bone marrow involvement may also occur although with rarity. We present a case report of recurrent gastric cancer with bone marrow metastasis in a patient with no evidence of systemic disease on follow-up for two years post surgical resection. This case demonstrates the need of heightened clinical suspicion in these patients.
METHODS: We reviewed the medical records of a patient who presented with metastatic gastric adenocarcinoma to the bone marrow two years post R0 subtotal gastrectomy with Roux-en-Y gastrojejunostomy without evidence of systemic disease on follow up for two years.
RESULTS: Laboratory and imaging studies of the patient on presentation two years post R0 subtotal gastrectomy with Roux-en-Y gastrojejunostomy is as follows; elevated alkaline phosphatase (ALP) of 472 U/L, CT chest/abdomen/pelvis that showed multiple new sclerotic lesions throughout osseous structures suspicious for metastasis, PET/CT that showed many sclerotic lesions throughout the axial and appendicular skeleton, some FDG-avid and suspicious for active osseous metastasis. Bone marrow biopsy showed metastatic poorly differentiated carcinoma consisted with known history of gastric cancer.
CONCLUSION: Gastric cancer has a high rate of recurrence post curative surgery. Despite the rarity of bone marrow metastasis, a high level of suspicion should be maintained in patients presenting with elevated ALP and evidence of pancytopenia post curative surgery.

1. Introduction

Surgical resection is the mainstay of treatment for gastric cancer [1]. Recurrence of gastric cancer post curative resection is well documented [2–5] and is attributed most commonly to haematogenous spread and spread of cancer cells at the time of surgery [6]. Clinicopathological characteristics determine the type of recurrence in gastric cancer [7]. While overt bone and skeletal metastases are rare in gastric cancer, bone marrow involvement is more common than predicted by clinical findings [8]. Physicians working at both an academic and community centers were involved in the care of the patient reported. In line with the SCARE criteria, we present a case of recurrent gastric cancer with bone marrow metastases presenting with new onset pancytopenia in a patient who had no evidence of systemic disease on follow-up for two years post curative surgery [9]. This case demonstrates the need for heightened clinical suspicion in such patients.

2. Methods

We reviewed the medical records of a patient with metastatic gastric cancer to the bone marrow presenting two years post R0 resection of the primary tumor.

3. Results

Detailed case presentation is as follows: Patient is a 66-year old Hispanic female whose preoperative workup included an esophagogastroduodenoscopy (EGD) that showed a linear ulcer in antrum and a deformed pylorus with biopsy consistent with adenocarcinoma. Computed tomography (CT) of the abdomen and pelvis showed thickening of the distal portion of the stomach without evidence of metastasis or lymph node involvement. Positron emission tomography (PET) scan showed FDG-avid mass in the gastric antrum without evidence of loco-regional or distant metastasis (Fig. 1). The patient underwent subtotal gastrectomy with R0 resection with Roux-en-Y gastrojejunostomy. Pathology

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http://dx.doi.org/10.1016/j.ijscr.2017.06.025

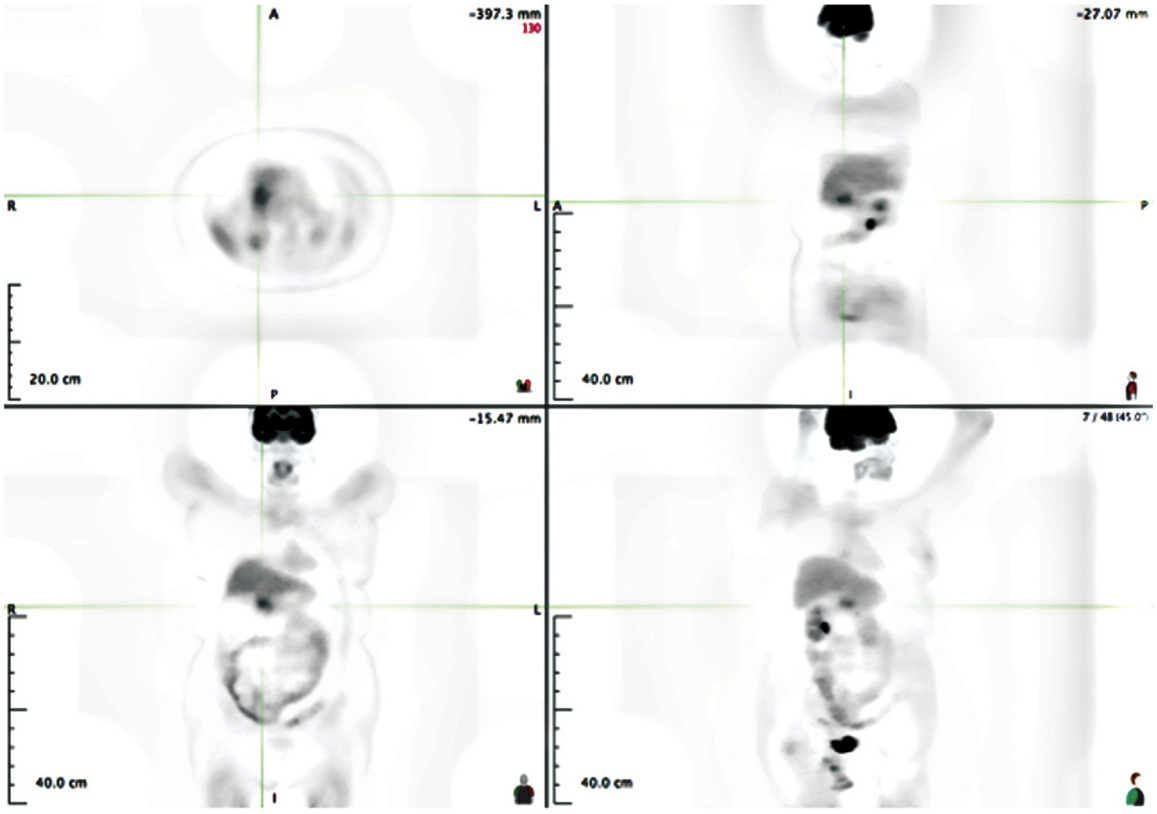

Fig. 1. PET/CT: FDG-avid mass in antrum.

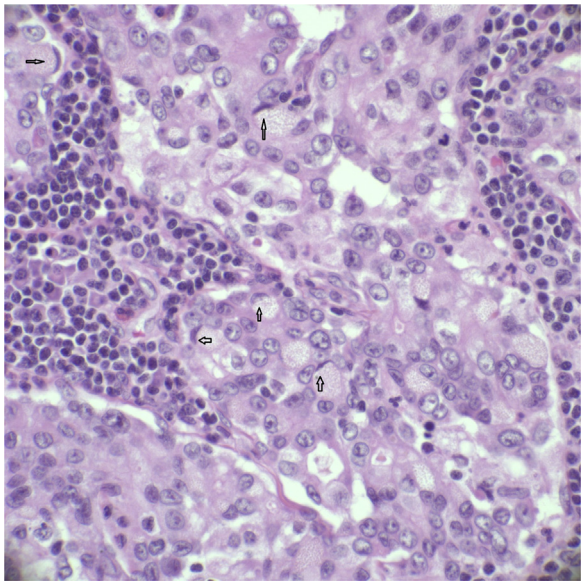

Fig. 2. Poorly differentiated gastric carcinoma, notice signet ring cells (arrows).

reported a G3 diffuse poorly differentiated gastric carcinoma with signet ring cell components; pT3, N3a, M0 consistent with stage III B (Fig. 2). A 4.0*3.5*1.1 cm tumor invading the muscularis propria was observed with metastasis involving 7/14 greater curvature and 1/1 lesser curvature nodes. Immediate postoperative recovery was uncomplicated. Further treatment included adjuvant 5-Fluorouracil infusion with concomitant radiation therapy. Chemoradiation therapy was delayed until resolution of dysphagia with nausea and vomiting that developed about a month postoperatively. Despite having normal blood counts on postoperative follow-ups, she presented about two years later with new onset pancytopenia and severe mucositis requiring broad-spectrum antibiotics and Neupogen. Other significant labs include an elevated alkaline phosphatase (ALP) at 472 U/L and a sodium level of 138 mmol/L. Imaging studies during hospitalization include a CT of the chest/abdomen/pelvis that showed multiple new sclerotic lesions throughout osseous structures suspicious for metastases and a PET/CT that showed multiple sclerotic lesions throughout the axial and appendicular skeleton, some FDG-avid and suspicious for active osseous metastases (Fig. 3). Bone marrow biopsy showed metastatic poorly differentiated carcinoma consisted with known history of primary gastric cancer (Fig. 4). HER-2 was negative and patient was started on palliative chemotherapy with FOLFIRI (Folinic acid-Fluorouracil-Irinotecan) and Zoledronic acid that was well tolerated.

4. Discussion

Gastric cancer remains a significant source of cancer morbidity and mortality worldwide. Disease progression is usually loco-regional to systemic with distant metastasis. Systemic disease recurrence after curative surgical resection is estimated at 60% [10,11]. Gastric cancer typically metastasizes to visceral and peritoneal surfaces with liver and distant nodes among the most common sites [12].

While overt bone or skeletal metastases are rare with gastric cancer, bone marrow involvement occurs more often than clinical findings might predict [8]. Despite the rarity, bone marrow metastasis in gastric cancer is typically seen in younger patients and those with aggressive histology, i.e. presence of signet ring cells or poorly differentiated [13]. The incidence of metastatic gastric cancer to osseous structures is not well established; various studies report values ranging from 0.9% to 57% [14–16]. Surgical extirpation of

Fig. 3. PET/CT: Sclerotic lesions, some FDG-avid.

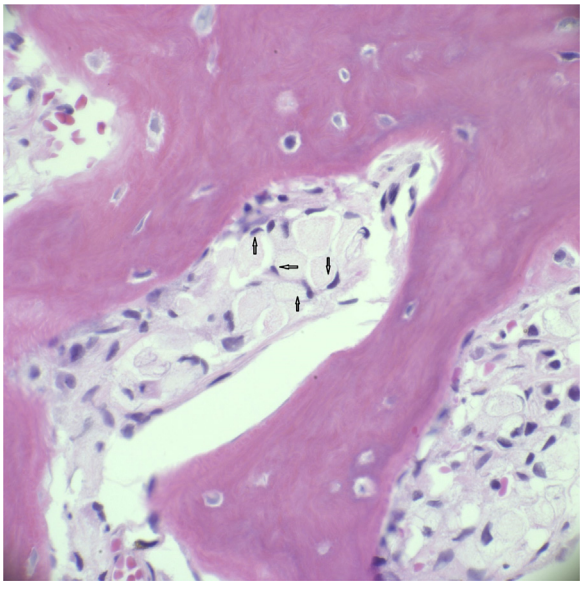

Fig. 4. Bone marrow biopsy: Poorly differentiated gastric carcinoma, notice signet ring cells (arrows).

the primary gastric cancer seems to correlate inversely with bone involvement as one study showed a 13.4% incidence in autopsy cases as opposed to only 1.5% in resected cases [17]. Another study showed a prevalence of 0.024% in advanced gastric cancer with bone marrow metastasis confirmed by bone marrow biopsy [18]. Ekinci et al. found 5 out of 245 patients with advanced gastric cancer to have bone marrow metastasis with a median age of 45 years old [12].

Gastric cancer can disseminate to the bone marrow as early as several months to more than 20 years post curative resection of early gastric cancer [19,20], presenting mostly with haematologic disorders including anemia, thrombocytopenia, elevated alkaline phosphatase and lactate dehydrogenase [13]. In addition to poorly differentiated adenocarcinoma, signet ring cell is also common warranting the consideration of lymphoma given their association [21]. Iguchi [22] reviewed 28 of such cases reported in Japan from 2003 to 2013 noting a male predominance (18–20) with an average age of 54.4 opposed to 64.5 for females. Pain and haemorrhagic symptoms were the most commonly presenting complaints. Of the haematologic abnormalities, disseminated intravascular coagulopathy (DIC) was the most frequent (n = 23) followed by anemia (n = 22). Elevated alkaline phosphatase (ALP) was noted in all the patients averaging 4305 IU/L with mild to moderate lactate dehydrogenase (LDH) averaging 706 IU/L in most of the patients. Despite the predominance of haematologic disorders, tumor progression (45%), brain haemorrhage (25%), infection (21%) and DIC (4%) were identified by Kwon et al. [14] as the most common causes of mortality in these patients.

Despite improved survival in patients with disseminated disease to bone marrow associated with gastric cancer, prognosis remains poor warranting prompt and adequate treatment. Treatment considerations include addressing haematologic disorders, especially DIC, chemotherapy for gastric cancer, and treatment of bone lesions with bone modifying agents [22]. The myriad of chemotherapy or supportive care regimens attest to the lack of a standard treatment for disseminated gastric cancer to the bone marrow [13,23]. While optimal treatment for such patients is yet to be established, the Kwon et al. study [14] suggests a preference of palliative chemotherapy over supportive care in patients with advanced gastric cancer with bone marrow metastases.

In gastric cancer patients with bone metastases, factors such as history of smoking, poor performance status, poorly differentiated adenocarcinoma, elevated levels of LDH, carcinoembryonic antigen (CEA) and cancer antigen (CA 19-9) portend a poor prognosis while chemotherapy and zoledronic acid treatment are associated with improved survival [16]. In cases with bone marrow involvement, low sodium (<133 mmol/L), peritoneal seeding, and lung metastasis have been shown to be adverse prognosticative factors [14]. In patients who underwent curative resection, bone marrow tumor-cell content has been used to predict both disease-free and overall survival [24]. This suggests both the consideration of adjuvant chemotherapy in such patients and bone marrow sampling for disease surveillance.

5. Conclusion

This case highlights another example of a rare presentation of gastric cancer. Given the high rate of recurrence post curative surgery, a high degree of suspicion should be maintained for post-resection patients presenting with elevated ALP and evidence of pancytopenia.

Conflicts of interest

None.

Funding source

None.

Ethical approval

Not Applicable.

Consent

Consent was obtained from the patient.

Authors contribution

Ernest Fonocho, MD – Wrote manuscript, involved in analysis of patient and literature.

Subhasis Misra, MD, FACS – Involved in treatment of patient.

Dr. Nail Aydin, MD, FACS – Involved in analysis of patient and literature, and also assisted with manuscript preparation and its approval.

Guarantor

Nail Aydin, MD.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijscr.2017.06.025.

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