

Diffuse Bone Marrow Involvement of Gastric Cancer Diagnosed by Positron Emission Tomography Computed Tomography

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1. Abstract

Bone metastases from gastric adenocarcinoma are rare, accounting for less than 2% of cases. Bone marrow (BM) metastases are even less frequent. For those patients suspected for bone and bone marrow metastases, a biopsy is normally the method of choice for diagnosis. In our case, bone and BM metastases were diagnosed using PET-CT, revealing 18F uptake throughout the whole skeleton in a 61 years old patient with gastric cancer. Following that finding, a bone marrow aspiration was done from the posterior superior iliac spine, which showed a signet ring cells, originating from the primary adenocarcinoma in the stomach.

2. Introduction

Globally, gastric cancer accounts for almost 1 million deaths each year [1]. Recurrence of gastric cancer often appears early, commonly within the first 2 years after gastrectomy [2]. With more than 930 000 cases per year, Eso-Gastric Adenocarcinoma (EGA) is the second most diagnosed cancer in the world [3].

Among all the different histological subtypes, Signet Ring Cell carcinoma (SRC) represents 32-70% of all EGA in Western countries with an increasing incidence. SRC carcinoma is defined by the World Health Organization (WHO) as an adenocarcinoma in which more than 50% of the tumor is represented by isolated or small groups of malignant non-cohesive cells containing intracytoplasmic mucin [1,2]. SRC is an independent predictor of poor prognosis, with a median survival of less than half of the median

survival observed in non-SRC GA [2]. This is linked to higher rates of positive lymph nodes and Peritoneal Carcinomatosis (PC) at initial diagnosis and to higher rate of PC Recurrence (PCR) that occurs in up to half of the patients [4].

Recurrences usually present in the abdominal cavity, peritoneum, lymph nodes, and liver [4, 5]. Recurrence limited to bone and bone marrow is rare, and prognosis in such cases is poor [6].

Bone metastases in patients with gastric cancer are observed in fewer than 2% of patients after curative surgical resection [7]. The proportion is higher for patients who present with advanced disease, with autopsy studies suggesting that the incidence is as high as 20% [8]. Bone metastasis is more commonly associated with disease involvement at other sites. Isolated recurrence in bone is rare. Prognosis for patients with bone metastasis is very poor, approximately 4 months [5]. A recent retrospective study by Park et al. reported a benefit for palliative chemotherapy in patients with bone metastasis: median overall survival was 167 days compared with 43 days for patients treated with radiotherapy and best supportive care [9]. In that study, the chemotherapy regimens varied widely; most protocols consisted of either taxanes, anthracyclines, fluoropyrimidines, or a platinum agents.

3. Case

A 61 year old man with Barrett's syndrome, hypertension, hyperthyroidism and psoriasis. He referred to a routine follow up gastroscopy, being suffering of Barrett's syndrome and helicobacter

pylori. Gastroscopy revealed a 4 cm wound with raised margins in the angulus of his stomach. Biopsy from the lesion yielded a diagnosis of gastric poorly differentiated mucin producing adenocarcinoma, positively stained with keratin and cytokeratin 7 (Figure 1). Human epidermal growth factor receptor-2 (HER-2) determined by Immunohistochemical (IHC) test was found to be negative. Complete blood count, renal and liver function tests were normal. A positron emission tomography/computed tomography scan (PET-CT) demonstrated [18F] fluorodeoxyglucose uptake only in the gastric mass (Figure 2A). He underwent a subtotal gastrectomy at January 2013. In pathology the tumor was invading the serosa and metastases were found in 14 out of 15 resected lymph nodes. The patient received adjuvant treatment with Epirubicin, Cisplatin and 5-Fluorouracil (ECF) every 3 weeks. As a result of continuous neutropenia he received only 2 courses of ECF within 2 months.

Four months following the operation (1 month after chemotherapy with ECF) an elevation in CEA and CA19-9 was observed. His complete blood count was normal. Renal and liver function tests were also normal apart from elevated alkaline phosphatase (2207 IU/l). His performance status was 2 (ECOG: Eastern Cooperative Oncology Group), no clinical findings were found. Repeated PET-CT revealed, 18F uptake in blastic lesions in the skeleton and bone marrow involvement in the whole skeleton (Figure 2B). A bone marrow aspiration was done from the posterior superior iliac spine. Bone marrow was found to be infiltrated by metastatic gastric adenocarcinoma (Figure 3). Tumor cells were positively stained with keratin and cytokeratin 7. HER-2 negative by IHC. The patient was treated with Paclitaxel 80mg/m² intravenously once a week and Pamidronate 90 mg intravenously every 4 weeks. Treatment was continued for 3 months. CEA and CA19-9 levels were elevated during the first month of paclitaxel, decreased during second month and elevated thereafter during the third month. Chemotherapy was stopped due to weakness, anemia, thrombocytopenia, increased tumor markers and poor performance status. The patient died with progression of disease at August 2013.

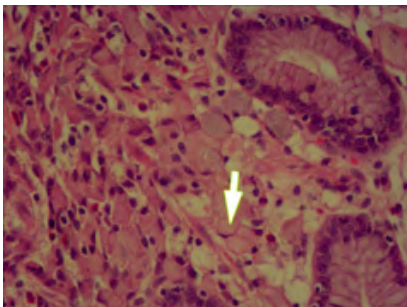


Figure 1: Biopsy from stomach: the lamina propria shows infiltrates of signet ring cell carcinoma (x 20)

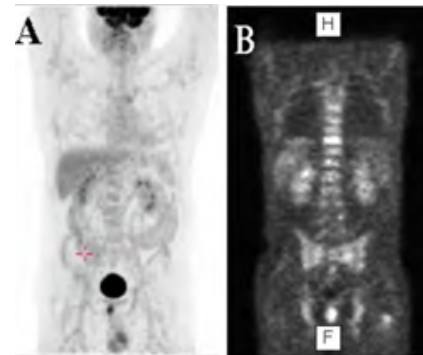


Figure 2: A: PET-CT prior to gastrectomy showed fluorodeoxyglucose uptake only in the gastric mass. B: PET-CT 4 months after gastrectomy showed 18F uptake in plastic lesions in and bone marrow involvement in the whole skeleton.

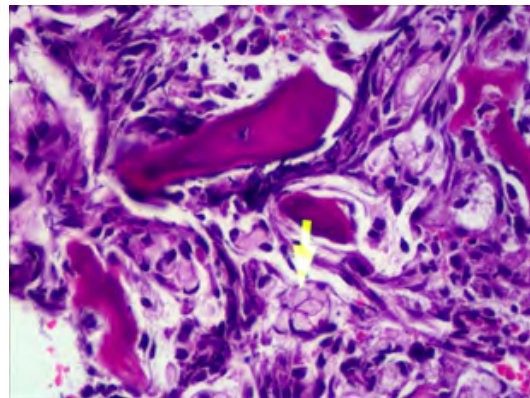


Figure 3: Biopsy from bone marrow: at high magnification the signet ring cells can be seen infiltrating bone marrow (x 40)

4. Discussion

BM may be an important reservoir of tumor cells, from which they recirculate into distant organs such as liver or lungs. The detection of disseminated cancer cells in bone marrow was first described in gastric cancer by Schlimok et al using immunocytochemistry with an anti-CK18 antibody [10]. They reported that tumor cells in bone marrow were detected in 34 of 97 patients (35%). Thereafter, several investigators also demonstrated the presence of disseminated tumor cells in bone marrow using the same method and reported positivity rates of 33%–53% [11, 12,13]. Soeth et al [14] reported that CK20 mRNA-positive samples were detected in 11 of 49 (22%) gastric cancer patients using nested RT-PCR. Compared with these results, the present data exhibit an extremely low positivity rate in bone marrow disseminated cells.

The incidence of bone marrow metastases may be underestimated in gastric cancer patients because bone marrow biopsy is not a routine clinical practice. Mostly, CT image is used for staging of gastric cancer. PET-CT is not used routinely in gastric cancer patients although it is used in many other solid tumors and in malignant lymphomas. In their systemic review and meta-analysis, Adams et al found a sensitivity and specificity of PET-CT 87.5-100% and 86.7-100% respectively, for the detection of bone marrow involvement in 955 patients with Hodgkin's lymphoma who

had also bone marrow biopsy [15]. There are no publications in the literature with big number of patients on the use of PET-CT in gastric cancer.

Two points make this case interesting. First, the bone marrow involvement by gastric cancer diagnosed by blind bone marrow biopsy of the posterior superior iliac crest. Second, as far as we know, it is the first case reported in the literature on bone marrow metastases from gastric cancer diagnosed by PET-CT. The possibility of bone metastases and bone marrow involvement in gastric cancer, although not common, should be kept in mind in patients with advanced gastric cancer. PET-CT may be helpful for diagnosis and avoiding bone marrow biopsy.

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