Case Report
A sudden elevated phyma as the first symptom of the recurrence of early gastric cancer: a case report and review of literature

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Abstract: Patients with early gastric cancer (EGC) without lymph node metastasis have low rates of recurrence. In this case, we describe a patient without lymph node metastasis five years ago but presenting with a sudden elevated phyma as the first symptom of the recurrence now. Though it is an individual case, whether the patients of EGC with some risk factors in clinical practice need systemic adjuvant chemotherapy is worth discussing. Furthermore, we propose a recommendation if the tumor invade the submucosa, this population need systemic adjuvant chemotherapy regardless of lymph node metastasis.

Keywords: Early gastric cancer, bone metastasis, systemic adjuvant chemotherapy

Introduction
Early gastric cancer (EGC) is defined as the presence of a lesion confined to the mucosa or submucosa, regardless of the presence of regional lymph node metastasis [1]. Although the prognosis of early gastric cancer has been improved, there are still some cases developed into distant metastasis like bone metastasis.

In this report, we describe a patient presenting with a sudden elevated phyma as the first symptom of the recurrence of EGC five years after curative surgery and without lymph node metastasis. Moreover, in order to have a further knowledge about the process of metastasis, we examined the clinical significance of bone metastasis in EGC by reviewing the literature on the subject.

Methods
Two authors systematically searched PubMed and Embase for relevant studies published up to November 2014, independently, to identify studies for inclusion in this review. The search was limited to studies conducted in humans. Search terms were individualized for each database. Search terms used included (“early gastric cancer” OR “EGC”) AND (“bone” OR “osteolytic”) AND (“metastases” OR “metastasis”). We also searched the relevant conferences, trial databases, the reference lists of identified trials, and major reviews.

Case presentation
A 62-year-old man was referred with a 5-month history of an elevated phyma. Five years previously, a diagnosis of EGC had been established, and a radical subtotal distal gastrectomy was performed. The pathological examination revealed a poorly differentiated tubular adenocarcinoma, with 0 of 15 lymph nodes positive. The tumor invaded the submucosa and no vascular or lymphatic invasion. When he discharged, CT revealed no tendency of metastasis. Then, he took low dose of 5-fluorouracil by oral administration. Five months before admission, he found a phyma on his right shoulder unintentionally. It was about 2×2 cm, soft and aponia. The doctor in the locality mistook it for fibroma and resected it at that time. Then, the phyma increased quickly. Now, it was about 4×5 cm, hard and pain (Figure 1). The result of the needle aspira-
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The phyma on patient’s right shoulder. The phyma was about 4×5 cm, hard and pain. A sudden elevated phyma as the first symptom of the recurrence of EGC.

Discussion

A review in 2011 collated all reported cases with bone metastasis in EGC in the English literature to that date by H. Ubukata et al. We reviewed a total of 15 cases, which were already reported in the literature and tabulated together with our case [2-13] (Table 1). In this review, we conclude the features of bone metastasis in EGC.

Characteristics

Several studies have suggested that bone metastasis from EGC were related to some clinicopathologic characteristics including signet ring cell or undifferentiated adenocarcinoma histology [14, 15], relatively younger age, elevated levels of serum alkaline phosphatase [15, 16]. Moreover, intensive management and support should be taken into account to improve survival [17, 18].

Mechanisms

Usually, bone metastasis of GC was considered to occur last, after liver metastasis or lung metastasis, for the reason that hematogenous metastasis was thought to progress into portal vein system first and then systemic venous system [19]. While a gradually increasing of GC patients, who developed with overt bone metastases but without either peritoneal metastasis or liver metastasis, were reported recently.

It is still unclear that the mechanisms of bone metastasis in EGC occurred after long period follow-up. A notion called “tumor dormancy” could explain this phenomenon possibly, which indicates a state in which the normal, healthy tissues of the hosts bearing cancer are concomitant with cancer cell. When the dormancy is disturbed, the prognosis of the cancer-bearing patients is poorer, regardless of the duration of the disease-free interval. Most cases of EGC emerged metachronous bone metastases have tumor dormancy with long intervals. However, like the case reported by Anagnostopoulos et al [9], those cases of EGC with synchronous metastases may have either only very short dormancy periods or even no periods of dormancy. Bone metastasis, especially micrometastasis to the bone marrow, may occur more frequently with GC than our clinical experience suggests. It may be more prominent that patients with bone metastasis but without other overt metastases in EGC than that in advanced GC.

Diagnosis

More and more biomarkers were found in diagnosis for bone aspiration biopsy. Maehara Y et al [20] have found that cytokeratin-positive cells were present in the bone marrow of their patients with EGC and those presenting with disseminated cytokeratin-positive cells at the time of primary surgery can be followed to detect any distant metastasis. Therefore, they suggested that cytokeratin might be a biomarker for patients with EGC who should receive postoperative adjuvant trials. Recently, several studies recommended that Bone Morphogenesis Protein-2 (BMP-2) associated with progression to metastatic disease in GC [21-23]. Moreover, the use of elevated alkaline phosphatase levels for the detection of bone metastasis and recommend bone scintigraphy in positive cases by Kobayashi, M et al [14].
Figure 2. Extensive bone metastasis. (A) (PET/CT) and (B) (ECT) revealed extensive bone metastasis. A sudden elevated phyma as the first symptom of the recurrence of EGC.
Table 1. Review of the cases with bone metastasis in EGC in the English literature

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author-year</th>
<th>Age</th>
<th>Gender</th>
<th>Histology</th>
<th>lymph node metastasis</th>
<th>Depth of invasion</th>
<th>Metastatic site</th>
<th>Recurrence time (Year)</th>
<th>Treatment</th>
<th>Survive time (month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yasuna-1986 [2]</td>
<td>39</td>
<td>M</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>Yasuna-1986 [2]</td>
<td>47</td>
<td>M</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>9</td>
<td>Soufleris-2007 [7]</td>
<td>70</td>
<td>M</td>
<td>Diffuse</td>
<td>-</td>
<td>M</td>
<td>B</td>
<td>8</td>
<td>NS</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>Kang-2008 [8]</td>
<td>71</td>
<td>M</td>
<td>Diffuse</td>
<td>-</td>
<td>M</td>
<td>B</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>11</td>
<td>Anagnostopoulos-2010 [9]</td>
<td>45</td>
<td>M</td>
<td>Diffuse</td>
<td>+</td>
<td>M</td>
<td>B</td>
<td>3 Week</td>
<td>5-Fu + folinic acid + Radiotherapy</td>
<td>18</td>
</tr>
<tr>
<td>12</td>
<td>Saito-2011 [10]</td>
<td>75</td>
<td>F</td>
<td>Diffuse</td>
<td>+</td>
<td>SM</td>
<td>B</td>
<td>3</td>
<td>5-FU + paclitaxel + Radiotherapy</td>
<td>78</td>
</tr>
<tr>
<td>15</td>
<td>Kawabata-2013 [12]</td>
<td>67</td>
<td>M</td>
<td>Diffuse</td>
<td>-</td>
<td>M</td>
<td>B</td>
<td>8</td>
<td>MTX + 5-Fu</td>
<td>16</td>
</tr>
<tr>
<td>17</td>
<td>Our case-2014</td>
<td>62</td>
<td>M</td>
<td>Diffuse</td>
<td>-</td>
<td>SM</td>
<td>B</td>
<td>5</td>
<td>5-Fu</td>
<td>NS</td>
</tr>
</tbody>
</table>
Recurrence of EGC

Treatment

S-1 and cisplatin were recommended for disseminated carcinomatosis of bone metastasis especially to EGC patient [24, 25]. In our case, we treated the patients with six cycles of chemotherapy with 5-fluorouracil i.v. and found that he was in remission from the metastasis status markedly.

Conclusion

EGC without lymph node metastasis have low rates of recurrence. Most studies reported that this kind of patient didn’t need adjuvant chemotherapy. But considering the patient in our report, whether the patients of EGC with some risk factors in clinical practice need systemic adjuvant chemotherapy is worth discussing. Maybe we should think highly of the patients with submucosal invasion or poorly differentiated carcinomas. It may suggest a promising therapeutic strategy such as development of diagnostic procedures for micrometastases, especially bone metastasis, and creation of convenient and sensitive methods of examination are required further consideration to against EGC and improvement of the survival rates of EGC.

Disclosure of conflict of interest

None.

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References


