

Isolated Bone Lytic Lesions as a Form of Presentation of Gastric Cancer with Signet Ring Cells

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Abstract Gastric cancer (GC) is still the second most common cause of cancer-related death worldwide. In addition, gastric cancer is the most commonly diagnosed malignancy in Korea, Japan, China, South America and Eastern European nations, with the lowest frequency observed in the United States and Canada. Metastatic gastric cancer is a therapeutic challenge for medical oncologists, especially those with bone marrow metastases. Bone marrow metastases occur in many solid tumors such as breast, lung, prostate and gastric cancer [1]. Our case is about a woman diagnosed of gastric adenocarcinoma with signet ring cells presenting with bone marrow infiltration.

Keywords: gastric cancer, signet ring cell, bone marrow metastasis; lytic bone metastasis

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1. Case Presentation

Our patient is a 73-year-old woman with a history of Alzheimer's dementia, presenting pain for the last three months which was mostly located in the rachis, refractory to first-step analgesic medical treatment scheduled by her primary care physician. She was initially evaluated in a private center, analytical and image studies were carried out highlighting alkaline phosphatase (AP) values greater than 2000U/L, as well as findings of disseminated lytic lesions along the rachis in a thoracoabdominal tomography, being referred to our Internal Medicine department to continue study. The patient presented with hyporexia and unintentioned weight loss, in addition to referred rachidial pain with an inflammatory pattern. She had no relevant alterations in her physical examination, no lymph node enlargement or visceromegalies were detected. Analytically we confirmed a sustained increase in AP (2800U/L), as well as a mild anaemia (haemoglobin 11.1 g/dL) with an iron pattern suggesting chronic disorder anaemia, maintaining the normality of the other series. We also found a carcinoembryonic antigen (CEA) value of 13.6 ng/ml. Proteinogram, globular sedimentation rate, liver profile (except AP), urine examination, 24-hour proteinuria, calcium and B2 microglobulin were normal. The bone x-ray study showed lytic lesions in humerus, proximal regions of both femurs, as well as in cervical and lumbar rachis. Chest and abdomen tomography reports spinal infiltration in the almost entire skeleton without

major findings at other levels. (Figure 1 and Figure 2). A dorsal nuclear magnetic resonance was also performed, finding a generalized alteration in the bone marrow presenting as a low signal in the T1 (Figure 3) and a high signal in T2 (Figure 4) and Stir (Figure 5), showing gadolinium capitation (Figure 6). Upper and lower endoscopic studies were finally performed, finding a small overelevation in gastric angular notch. Biopsy of this lesion reported gastric adenocarcinoma with signet ring cells. Bone marrow aspiration and biopsy also revealed massive signet ring cell infiltration. With the diagnosis of disseminated gastric neoplasm the patient was considered not being candidate for active chemotherapeutic treatment so she was transferred to Palliative Care Unit for follow-up. She finally died one month after the diagnosis.



Figure 1.



Figure 2.



Figure 3.



Figure 4.



Figure 5.



Figure 6.

2. Discussion

Gastric cancer (GC) is the third leading cause of cancer related mortality among males and the fifth leading cause of cancer related mortality among females worldwide, with 1 million new patients diagnosed every year [2]. There are two distinct types of gastric adenocarcinoma, intestinal (well-differentiated) and diffuse (undifferentiated), which have distinct morphologic appearance, epidemiology, pathogenesis, and genetic profiles [3]. The histologic shift from intestinal type gastric cancer to diffuse type will have important clinical implications. Diffuse type gastric cancer occurs at a younger age, and is more advanced at presentation, particularly when compared to well or moderately differentiated intestinal type gastric cancer. [4]

The traditional risk factors for stomach cancer do not play as great a role in diffuse type gastric cancer, and studies have described the importance of familial syndromes such as hereditary diffuse gastric cancer [5]. This is of particular importance to our case because our patient had the signet ring cell type of gastric adenocarcinoma, which is a type of diffuse gastric cancer.

At the time of diagnosis, majority of the patients usually have unresectable or metastatic disease. The most common sites of metastases are the liver, lymph nodes and the peritoneum, but in the advanced stages, there may be metastases to any region of the body [6].

Bone metastasis is an uncommon event in advanced gastric cancer patients and bone metastases are rarely detected as isolated lesions. Advanced stage cancer patients demonstrate a significantly higher incidence of bone cancer recurrence. Solitary bone metastases are only observed in one third of cases [7]. If bone marrow involvement is discovered, it is usually during the workup for metastatic disease [8]. When bone marrow metastasis occurs, it is more commonly a signet ring cell subtype of gastric carcinoma and occurs in younger patients.

The prognosis for bone marrow involvement with gastric adenocarcinoma is very poor, specially when these metastases are present at the moment of the diagnosis [9], as we observed in the case we are presenting.

Interestingly, our patient only had a light normocytic anaemia. She did not have leukopenia or thrombocytopenia, the latter of which was determined to be indicative of bone marrow involvement in any study. Bone pains and the analytical increase of the alkaline phosphatase were nearly the only signs of the disease.

This case is significant for two reasons. First, it highlights the importance of a broad differential diagnosis when approaching a patient with lytic bone lesions. Second, bone marrow involvement is more common in

patients with diffuse type gastric cancer and occurs in particularly young patients. The increasing incidence of diffuse type gastric adenocarcinoma means bone marrow metastases will likely play a greater role in the presentation and management of gastric cancer.

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