Microangiopathic Hemolytic Anemia and Diffuse Bone Metastasis by Signet Ring Cell Adenocarcinoma

Andrés J. Muñoz Martín, Pilar García Alfonso, María Carmen Riesco Martínez, Virginia Martínez Marín, Yolanda Jerez Gilarranz, Rebeca Mondejar Solís, Miguel Martín Jiménez

Medical Oncology Service, Hospital General Universitario “Gregorio Marañón”, Madrid, Spain.
Email: andresmunmar@hotmail.com

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ABSTRACT

Microangiopathic hemolytic anemia (MAHA) is a rare paraneoplastic syndrome and is typically associated with gastric adenocarcinoma. We report a 47-year-old woman who presented with asthenia, lower back pain and bleeding. Twelve years ago the patient underwent total gastrectomy due to gastric adenocarcinoma and achieved complete remission. The patient was diagnosed with MAHA and diffuse bone metastasis of signet ring cell adenocarcinoma of unknown origin and was treated successfully with polychemotherapy based on cisplatin and 5-fluorouracil.

Keywords: Microangiopathic Haemolytic Anemia, Gastric Cancer, Paraneoplastic Syndrome, Chemotherapy, Signet Ring Cell Adenocarcinoma

1. Introduction

MAHA was first described in 1962 by Brain et al. [1] and is an uncommon haematological disorder which can appear in different diseases (thrombotic thrombocytopenic purpura, haemolytic uremic syndrome, vasculitis and paraneoplastic syndrome in cancer) [2]. It is defined as a severe haemolytic anemia with negative Coombs test and fragmentation of red cells in the peripheral blood smear. MAHA occurs in patients with metastasized signet cell carcinoma of stomach but it’s been described in breast and lung carcinoma [3]. The pathogenesis of cancer-related MAHA is not well understood. Typically, it’s associated to diffuse bone metastasis by signet ring cell adenocarcinoma. MAHA can be the first manifestation of metastatic carcinoma and is associated to extremely poor prognosis [4,5]. Sometimes is the first sign of recurrence after a curative surgery even many years later [6,7].

In this report we describe the case of a 47-year-old woman with a medical history of gastric cancer twelve years ago who was diagnosed with MAHA and massive infiltration of bone marrow by signet cell carcinoma. After careful workup the primary site could not be identified. The patient responded dramatically to polychemotherapy and long-term partial response was achieved.
per GI endoscopy, colonoscopy, mammography and abdominal ultrasound were normal. Bone marrow biopsy disclosed metastasis of a signet ring cell adenocarcinoma. Immunohistochemical staining was positive for CA19.9, CEA, cytokeratins (AE1, panCK, 8,18,19) and negative for cytokeratins AE3, CD45, CD20, CD30, ALK1, CD68, CA125, c-erb-2, estrogen receptor, progesterone receptor, bcl-2, p53. The Ki67 rate proliferation was low. PET scan was not available.

Therefore a diagnostic of metastatic signet cell carcinoma of probably gastric origin with paraneoplastic MAHA was established and the patient was treated with multiagent chemotherapy cisplatin 80 mg/m² intravenous (iv) on day 1 and 5-FU 1.000 mg/(m²·day) continuous infusion on days 1-5, zoledronic acid and intensive blood and platelet transfusions. After the first cycle of chemotherapy, the vaginal bleeding and epistaxis stopped and the hemoglobin level stabilized (> 8 g/dL) and platelet increased over 30.000/μL. Six courses of chemotherapy were delivered and clinical and laboratory response was evident (haemoglobin 11 g/dL, WBC 3.900 with 54% neutrophils, normal platelets, alkaline phosphatase 340 U/L,LDH 522 U/L). A bone scan and CT scan showed a partial response in the number and intensity of bone lesions. Chemotherapy was then stopped and the patient started a follow-up program in our service. Three months later, the bone metastases progressed and the patient was treated with antialgic radiotherapy over L4-L5 (total dose 20 Gy). She received second line treatment with FOLFIRI, four cycles were delivered with progression of disease. Third line multiagent chemotherapy DCF (docetaxel 75 mg/m² iv day 1, cisplatin 75 mg/m² iv day 1, 5-FU 750 mg/m²/day continuous infusion on days 1-5) with a 20% dose reduction was started. She received 4 cycles with excellent clinical, biochemical and radiological response. After the fifth cycle, the patient came to the emergency room with an evident progression of the disease with severe pain, grade IV anemia, leucopenia and thrombocytopenia. PET with conventional diagnostic test. Unfortunately, in this clinical case PET scan was not performed due to we lacked this technique at the time of the patient was diagnosed.

Gastric cancer usually relapses in the first three years after surgery [12], however similar clinical cases have been reported with long periods of time between the primary tumor and the recurrence [5,6]. Some authors have suggested the origin of the metastasis in dormant tumor cells in the bone marrow and lymph ducts of the gastric wall in spite of normal gastric mucosa [6]. Our clinical case may support this hypothesis, however it is unclear why tumor cells remain dormant for as long as 12 years and which mechanism let them grow.

4. Conflict of Interest

The authors declare that they have no conflict of interest relating to the publication of this manuscript.

REFERENCES


