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Microangiopathic Hemolytic Anemia (MAHA), High Alkaline Phosphatase and D-dimer Levels and Bone Marrow Infiltration as the First Presentation of Metastatic Signet Ring Cell Carcinoma of Gastric Origin: A Rare Case Report

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Abstract

Microangiopathic haemolytic anaemia (MAHA) occurs seldom as a paraneoplastic syndrome in some solid tumors, but MAHA companionship by signet ring cell carcinoma (SRCC) of gastric origin is very rare. This case report describes a 46-year-old man who initially presented with unendurable back and abdomen pain, he has also jaundice, anaemia, thrombositopenia, elevated bilirubin-D-dimer and alkaline phoshatase levels. He was diagnosed with MAHA on the basis of the laboratory findings that revealed anaemia with schistocytes, and a negative direct Coombs' test. Bone marrow and peripheral blood smear examinaton of the patients revealed out the diagnosis which was performed because of the progression of anaemia and thrombositopenia. However, the primary origin of this signet ring cell carcinoma (SRCC) was found in the stomach.

Keywords: Bone marrow infiltration; Microangiopathic haemolytic anaemia; Signet ring cell carcinoma

Introduction

Microangiopathic haemolytic anaemia (MAHA) was first described by Brain et al. [1], nowadays used to describe any haemolytic anaemia related to red blood cell (RBC) fragmentation, occurring in association with small vessel disease. Many different disease and disorders, including preeclampsia, infections, adverse drug reactions, hematopoietic stem cell transplantation, autoimmune diseases, and malignancies (particularly gastric, breast, and lung cancers), can cause MAHA [2-7]. MAHA can occur as a paraneoplastic syndrome in cancer patients, and it may present as the first manifestation of a malignant tumor. However, the pathogenesis of secondary MAHA is unclear.

Thereby, only a few cases of MAHA associated with SRCC of gastric origin have been reported.

In this case report, we describe a 46-year-old male patient who presented with extremely high alkaline phosphatase and D-dimer levels and bone marrow infiltration as the first presentation of metastatic signet ring cell carcinoma of gastric origin.

Case Report

A 46-year-old man was admitted to the hospital with a 3 days history of recurrent and unendurable back and abdomen pain, jaundice. The patient denied further symptoms, like weakness. On physical exam, the patient has a distended abdomen but nothing else.

The patient was diagnosed with MAHA on the basis of the laboratory findings, which showed anaemia with schistocytes and polychromasia, nucleated red blood cells on the peripherial blood smear , a negative direct Coombs' test, and elevated serum levels of total bilirubin (5.48 mg/dl), lactate dehydrogenase (LDH) (933 IU/L), and alkaline phosphatase (ALP) (768 IU/L), D-dimer (65.600 ng). Also the vitamin B12 levels were very low (114 mg/dl). The tumor markers CEA, CA 19-9, PSA, AFP, beta HCG were in normal ranges.

In order to rule out the possibility of solid or haematological tumor origin, endoscopic examinations of the upper and lower gastrointestinal tract and abdominal ultrasonography were performed, with unremarkable findings. No abnormal findings were in the thoracic, abdominal, and pelvic computed tomography scans of the patient. On positron emission tomography-computed tomography (PET-CT) there was found a mild hyperactivity at C4, T9 and L5 vertebral corpus region, but nothing else. A magnetic resonance imaging of the thoracic and lumbar spine showed massive vertebral infiltration and during the hospitalisation the patients analysis showed progression of MAHA, thrombocytopenia, and hyperbilirubinemia, bone marrow examination was performed. Clusters of abnormal large non-hematopoietic cells with exantric nucleolus were observed in the bone marrow aspirates. The bone marrow biopsy sections showed infiltration of signet ring-shaped atypical large cells with increase osteoblastic activity, megaloblastic changes in the erythroid chain and hyperplasia in erythroid-granulocytic-megakaryocytic series. So

endoscopic examination of the stomach was done and the result of gastric biopsy was SRCC. Finally, we diagnosed the patient with SRCC of gastric origin.

The patient received red blood cell and platelet transfusions because of the low platelet count (23 × 109/L) and low haemoglobin level (5.4 g/dl). However, the haemoglobin level and platelet count did not increase even after transfusions. Persistently high serum levels of bilirubin, LDH, and ALP, D-dimer were observed. The patient's general situation setback and he died after 1 week of admission.

Discussion

SRCC is an epithelial malignancy characterized by the histologic appearance of signet ring cells. It is a form of adenocarcinoma that produces mucin. When the adenocarcinoma contains more than 50% signet rings it is referred to as a signet ring cell carcinoma. It is most often found in the glandular cells of the stomach, but it may develop in other areas of the body (e.g., the prostate, bladder, gallbladder, breast, colon, ovarian stroma and testis) [8-11].

MAHA can present as the first manifestation of a malignant tumor. The most common tumors associated with MAHA are gastric, breast, and lung cancers and malignancies of unknown origin [2,9,13]. In a study it is reported that 14 (25.5%) out of 55 MAHA patients had gastric cancer [14]. In our patient, MAHA, elevated total bilirubin, lactate dehydrogenase, alkaline phosphatase, D-dimer levels were the initial finding of SRCC of gastric origin.

Among patients with bone marrow metastases from cancer, MAHA patients have a worse prognosis than patients without MAHA. If bone marrow involvement is reported, it is usually during the workup for metastatic disease [13].

Most patients with cancer and MAHA die within a few weeks after the diagnosis [15], and the most common cause of death is infection. Our patient was diagnosed with cancer associated microangiopathic haemolytic anaemia (CA-MAHA) on the basis of the findings of bone marrow examination (Figure 1).

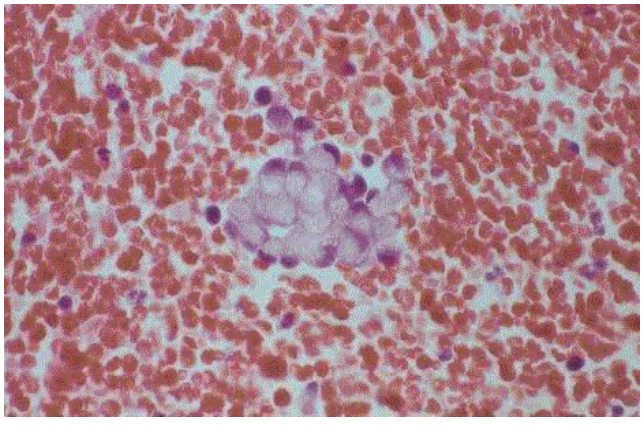

Figure 1: Infiltration of Bone Marrow by a Signet-Ring–Cell gastric carcinoma.

Characteristic laboratory findings of CA-MAHA are anaemia with schistocytes, thrombocytopenia, leukoerythroblastic anaemia, decreased haptoglobin levels, and elevated serum levels of ALP, LDH, like our patient. We found leukoerythroblastic changes in the peripheral blood smear of the patient. MAHA is also seen in many different diseases such as idiopathic thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), haemolytic uremic syndrome (HUS), and vasculitis. Patients with these diseases have similar laboratory findings and clinical manifestations; therefore, the underlying diseases are important for appropriate treatment. Bone pain and respiratory symptoms can be seen more frequently in CA-MAHA than in non-CA-MAHA [12].

Some studies have reported that a decrease in the levels of the von Willebrand factor (vWF), ADAMTS13 plays a role in CA-MAHA. However in our case ADAMTS13 was in normal range [14].

Here is no definitive treatment of choice for CA-MAHA. The low platelet count and haemoglobin level make red blood cell and platelet transfusion obligatory. Chemotherapy is the most ascendant treatment of choice for the underlying cancer [15].

The most common origins of SRCC are the stomach and unknown origins in 10 of the previously reported cases of metastatic SRCC that showed MAHA as an initial clinical finding [10,11]. The patients all showed bone marrow and/or bone metastasis, and therefore, bone marrow examination played an important role in the diagnosis as in this case. In the present case, CA-MAHA on the basis of the findings of bone marrow examination leads us to the diagnosis of the patient.

MAHA, as a paraneoplastic syndrome in cancers, can be seen in gastric cancers usually accompanied by multiple bone or bone marrow metastases. Unfortunately, the prognosis of patients with CA-MAHA is generally poor and despite chemotherapy the mortality is very high.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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