Adrenal Crisis and Disseminated Intravascular Coagulation Associated With Disseminated Carcinomatosis of the Bone Marrow From Gastric Cancer

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Abstract

Gastric cancer is the third leading cause of cancer deaths worldwide. Disseminated carcinomatosis of bone marrow (DCBM) originating from gastric cancer is rare and associated with poor prognosis. We present the first reported case of gastric adenocarcinoma with DCBM leading to concomitant disseminated intravascular coagulation (DIC) and adrenal crisis refractory to treatment. Computerized tomography of the chest, abdomen and pelvis showed diffuse sclerosis of the axial and proximal appendicular skeleton, suggestive of metastatic disease. Bone marrow biopsy demonstrated infiltrative signet ring cells, consistent with metastatic adenocarcinoma from gastric primary. Laboratory tests showed severe anemia, thrombocytopenia, and coagulopathy, compatible with DIC.

Introduction

Gastric cancer is an important cause of cancer-related mortality and is the third leading cause of cancer deaths worldwide. Metastatic spread is most often observed in the liver and peritoneum, less likely in the lungs and bone. Disseminated carcinomatosis of bone marrow (DCBM) manifests as widespread bone metastasis and occurrence is rare, therefore usually described as case reports and case series in the literature. We present a case report of gastric adenocarcinoma with disseminated carcinomatosis of the bone marrow leading to disseminated intravascular coagulation (DIC) and adrenal crisis refractory to treatment.

Case Report

The patient is a 57-year-old female with past medical history of central hypopituitarism, secondary adrenal insufficiency, and untreated gastric adenocarcinoma, who presented to the emergency room with diffuse cramping abdominal pain and generalized weakness. Additionally, she complained of fatigue, poor appetite, confusion, nausea & vomiting, and upper & lower extremity swelling. These symptoms had persisted intermittently for 1 week. Her gastric adenocarcinoma was diagnosed in 2017, but she declined surgical resection of the tumor at that time. In 2020, she underwent upper endoscopy, which showed an ulcerated intramural (subepithelial) lesion in the lesser curve of stomach, at 6 cm distal to the gastroesophageal junction. Sonographically, the lesion was hypoechoic and appeared to originate from the superficial luminal mucosa with invasion into the serosa. Two abnormal lymph nodes were observed in gastrohepatic ligament. Biopsies taken from the lesser curve ulcer, antrum, and pyloric channel revealed signet ring cell adenocarcinoma (Fig. 1).

Initial vitals in the emergency department demonstrated blood pressure 81/45, heart rate 79, respiratory rate 18, and peripheral capillary oxygen saturation of 96% on room air. Physical exam showed scattered ecchymoses on the back and pitting edema in bilateral upper and lower extremities. Initial laboratory results were significant for sodium of 118 mmol/L, potassium 6.8 mmol/L, hemoglobin 6.5 mg/dL, platelet count 17 K/uL. Liver enzymes were mildly elevated with alanine aminotransferase 37 mg/dL, aspartate transaminase 48 mg/dL, and significant elevation in alkaline phosphatase to 1901 mg/dL.
Given the bicytopenia, a peripheral smear was obtained which demonstrated normocytic, normochromic anemia suggestive of hypoproliferation and anemia of chronic disease. Computerized tomography of the chest, abdomen and pelvis showed bilateral pleural effusions and anasarca reflecting total body fluid overload, as well as diffuse sclerosis of the axial and proximal appendicular skeleton suggestive of metastatic disease (Fig. 2). Endocrinology was consulted and recommended stress dose steroids for acute adrenal insufficiency. Sodium rapidly increased to 129 mmol/L but dropped to 122 the following day. Since the administration of hydrocortisone temporarily restored the sodium level, undertreated adrenal insufficiency was thought to have induced the hyponatremia. Further hyponatremia workup showed albumin 3.2 mg/dL, serum osmolality 256 mOsm/kg, urine osmolality 195 mOsm/kg, and urine sodium < 11 mmol/L, which suggested a component of hypoalbuminemia and consequential reduced intravascular effective volume.

Thrombocytopenia persisted throughout the patient’s hospital course despite several transfusion attempts. Hematology-oncology was consulted, and a bone marrow biopsy was obtained on day 3 which showed clusters of glandular epithelioid cells, some with signet ring cell morphology, consistent with metastatic gastric adenocarcinoma (Fig. 3). On day 4, the patient developed worsening diffuse ecchymoses over entire body, epistaxis, oral mucosal bleed, and bleeding from peripheral intravenous sites. DIC was confirmed with elevated D-dimer > 20.0 ug/mL, prolonged PT of 24.6s (INR 2.1), prolonged PTT of 37s, as well as decreased fibrinogen of 191 mg/dL. Given the bone marrow findings, the DIC was thought to be caused by bone marrow carcinomatosis and bone marrow failure. As the clinical status continued to worsen, the patient decided to pursue hospice care.

**Discussion**

DCBM is a rare disease with low incidence\(^3,4\). Most cases of DCBM are caused by solid tumor metastasis and as many as 90% of cases are associated with a primary gastric cancer\(^5,6\). The pattern of DCBM is often diffuse and widespread throughout the skeleton, as cancer cells infiltrate the bone marrow but do not readily form tumors\(^3\). Imaging findings suggestive of osteosclerosis on x-ray and CT may be a sign of DCBM and can be correlated with PET-CT in patients with solid organ malignancy\(^7,8\). Our patient's finding of diffuse skeletal sclerosis noted on CT was consistent with the pattern of infiltration in DCBM.

DCBM is often associated with hematologic disorders such as DIC, leukoerythroblastosis, or hemolytic anemia\(^4,6,9\).

Much of the published literature on DCBM associated with gastric cancer is in the form of case reports. Iguchi reviewed 28 cases in 2015 which characterized the clinical features associated with DCBM originating from gastric cancer. Of the hematologic manifestations, DIC (n = 23) and anemia (n = 22) were the most common\(^3\). Anemia was attributed to either microangiopathic hemolytic anemia or gastrointestinal hemorrhage in most cases\(^3\). Notably, marked elevation of alkaline phosphatase occurred in all patients\(^3\). Our patient presented with many of the key features associated with DCBM, including anemia, thrombocytopenia, DIC, and elevated alkaline phosphatase.
To our knowledge, DCBM complicated by refractory adrenal crisis has not been reported in the literature. Many reasons could be considered to explain our patient's adrenal insufficiency and refractory hyponatremia, in the context of advanced malignancy and hematologic abnormalities. Bilateral metastases to the adrenal glands has been reported to adrenal insufficiency in patients with advanced gastric cancer. However, our patient had no evidence of adrenal metastasis or enlargement on CT scan. Our patient's DIC and severe anemia could have led to adrenal gland failure due to reduced perfusion, thrombosis, and/or bleeding. In our case, the severe anemia on presentation was not due to hemolysis or bleeding but likely due to bone marrow invasion by the DCBM, which could sensitize the adrenal glands to ischemic injury. Malnutrition associated with gastric cancer can also cause hypoalbuminemia, which can result in hypovolemic hyponatremia, as the patient will overproduce antidiuretic hormone to compensate for the decreased intravascular volume.

**Declarations**

*Conflict of Interest:*

The authors have no financial or other conflicts of interest concerning this study.

*Ethics approval:*

The local IRB has confirmed that no ethical approval is required for case reports.

*Informed Consent:*

The patient described in our case report is deceased. All attempts have been exhausted in trying to contact the patient's next of kin for informed consent to publish their information, but consent could not be obtained. However all identifying information has been removed from this case report to protect patient privacy.

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