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*Case Report*

# Gastric cancer with bone marrow necrosis: a case report and review of the literatures

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**Abstract:** Bone marrow necrosis (BMN) is a serious and rare complication of many diseases, which is induced by necrosis of hemopoietic cells and matrix tissue with large areas by special reasons. Until now, its pathogenesis is not clear. The clinical symptoms of BMN include bone pain, fever, blood cell diminish, liver, spleen and superficial lymph node enlargement and so on. Multi-site bone marrow aspiration and biopsy frequently adopted to diagnosis of BMN. Prognosis of BMN is poor, and its survival period is not more than six months. The therapy of BMN depends on diagnosis and treatment in the early stage. The basic measurement to prolong the survival of BMN patient is to actively cure the original disease, and with adjuvant therapy by blood transfusion, anti-infection, bleeding and other symptomatic treatments.

**Keywords:** Gastric cancer, bone marrow necrosis, literatures

## Introduction

Bone marrow necrosis (BMN) is a severe and rare complication of many diseases, which is induced by necrosis of hemopoietic cells and matrix tissue with large areas by special reasons [1]. In 1924, BMN was firstly discovered in autopsy of a patient with sickle cell anemia by Graham. Then several cases of BMN were reported [2, 3]. Dunnp [4] and Kiraly [5] found that the incidence rate of BMN was 0.15% and 0.37% in bone marrow aspiration and biopsy, among which the primary disease of cancer accounted for 100% and 98% respectively. Once diagnosed with BMN, many patients usually died in short term, and the median survival time was about 2 months. No more than 40 cases about gastric cancer merged with BMN were reported in recent 20 years worldwide, and all patients had poor prognosis [4-9]. In this case report, we described a case of BMN in gastric cancer and reviewed the associated literatures.

## Case report

A 44 years old male came to Wenzhou Central Hospital with the complaints of abdominal pain, fatigue, and fever more than 20 days, body pain, and swollen lymph nodes for more than 10 days in April 28, 2014. On clinical examination, body temperature was 37.8°C and the blood pressure were 102/62 mmHg. The patient appeared severe anemia with slightly yellow of skin and sclera. He was examined and noted with following symptoms: sternal tenderness, superficial supraclavicular lymph node enlargement with diameter about 1.0-1.5 cm and moderate quality, none tenderness, ability to move, soft abdomen, upper abdominal tenderness and umbilical week tenderness, and no rebound tenderness.

This patient was advised to undergo a haematological investigation. The leukocyte count was 2.9~12.1 × $10^9$/L, and haemoglobin was 29~68 g/L, while blood platelet count was 4~36 × $10^9$/L and the percentage of reticulocyte was 14.5~19.1%. The unit of alanine transaminase (ALT), aspartate aminotransferase (AST) and alkaline phosphate (ALP) was 60, 68 and 260 U/L respectively. The concentration of total bilirubin (STB), direct bilirubin (CB) and indirect bilirubin (UCB) were also detected and the values were 55.1, 36.5 and 18.6 μmol/L,

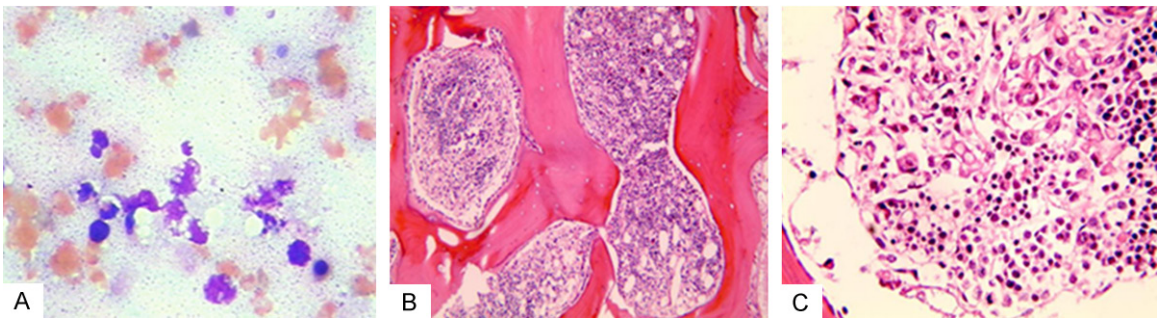


**Figure 1.** The smear of bone marrow with gastric cancer under microscope. A. The smear of bone marrow stained with Wright Giemsa dying (1000 ×). B. Pathological image of bone marrow at low magnification (HE staining with 40 ×). C. Pathological image of bone marrow at high magnification (HE staining with 400 ×).

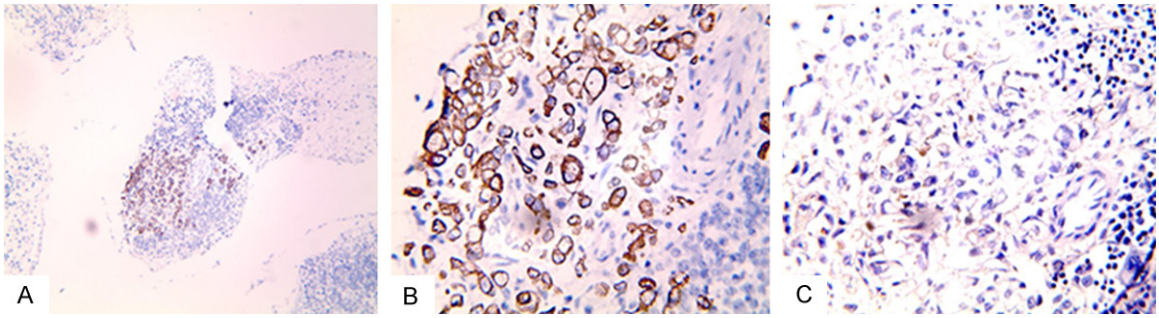


**Figure 2.** IHC analysis of suspicious cells from bone marrow. A. IHC analysis of CK protein of bone marrow cells under microscope (100 ×). B. IHC analysis of CK protein of bone marrow cells under microscope (400 ×). C. IHC analysis of CEA protein of bone marrow cells under microscope (100 ×).

respectively. Lactate dehydrogenase (LDH) was 1457 U/L and C-reactive protein was 141.6 mg/L. Some antigens were also detected, among which: carcinoembryonic antigen (CEA) was 12.9 μg/L, CA125 was 35.8 kU/L, CA199 was 5386.0 kU/L, CA15-3 was 59.3 kU/L, CA724 was 1476.0 kU/L. Cytokeratin 19 fragment was 16.9 μg/L and neuron specific enolase (NSE) was 59.3 μg/L. The concentration of ferritin was more than 1500.0 μg/L and the prothrombin time (PT) was 13.9 s. The fibrinogen was 0.75 g/L. The prothrombin time (PT) was 39.4 s and activated partial thromboplastin time (APPT) was 29.6 s. D-dimer was 9395 μg/L.

In view of the above findings a bone marrow aspiration was planned. Dry tap bone marrow aspiration was applied in the first time. In the second bone marrow aspiration, marrow liquid was dark red. Wright-Giemsa staining results showed that the background of slide was filled with dust particles (**Figure 1A**), the quantity of nucleated cells was moderate, the structure of cells were blurred, nucleus were vague, the cytoplasm showed soluble state, plasma membrane were dissolved and the contents were spilled out. The background of slide was filled with dust particles (**Figure 1A-C**). The diagnosis of BMN was rendered. Bone marrow biopsies and pathology results further suggested that it was a kind of metastatic mucinous carcinoma. Immunohistochemical (IHC) results indicated that this carcinoma may be lesion of upper digestive tract because of suspicious cells being CK (+), CK7 (+), CK20 (-), Villin (+), CEA (+), LCA (-), PSA (-) and AB-PSA (+) (**Figure 2A-C**).

In order to determine the cause of this case, further examinations were performed. Enlargement of lymph nodes were always presented in mediastinum, interstice between liver and stomach, retroperitoneal space and surrounding pancreas by Computer Tomographic (CT). Lymphadenopathy and higher sugar metabolism in systemic skeleton PET/CT was also showed. Gastroscope observed that gastric bulgy lesions were frequently associated with

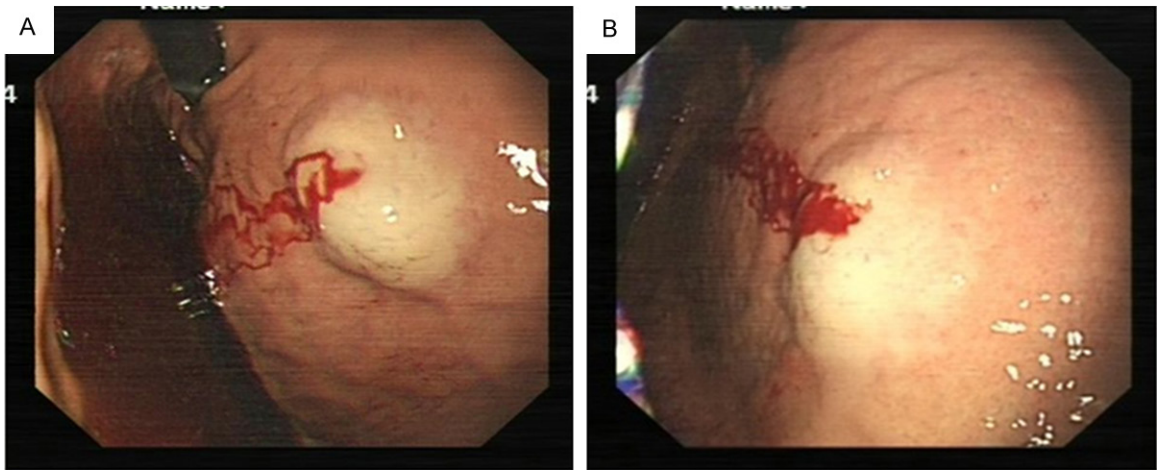


**Figure 3.** Detecting the lesion of swollen stomach by gastroscope and bleeding always present these areas. A. One elevated lesion in antrum of stomach, active bleeding was obvious. B. Another elevated lesion in antrum of stomach, active bleeding was obvious.

bleeding and gastric carcinoma was detected (**Figure 3A**, **3B**).

In view of these examinations, the patient was diagnosed as a case of gastric cancer with BMN chronic DIC.

A supportive therapy was planned and it was decided that a haematopoietic support would be provided to the patient by the means of blood transfusion, with the administration of red cell, platelet, fresh plasma transfusions, fibrinogen injection and tegafur gimeracil oteracil potassium capsule oral chemotherapy. However, the treatment efficacy was poor. Then this patient was discharged automatically.

## Discussion

There are various reasons to cause BMN. After comprehensive investigation of many reports since 1994, BMN was found most commonly in malignant blood diseases, especially in acute leukemia, followed by bone marrow metastasis cancer, severe infection, sickle cell anemia, DIC, drugs, hyperparathyroidism, antiophospholipid antibody syndrome and so on [10]. Until recently, the mechanism about BMN was still unclear, which may include the following factors: (1) Proliferation of large number of leukemia cells or bone marrow microcirculation dysfunction by embolism of bone marrow blood capillary and blood sinus with malignant tumors [11]; (2) Local compression of the bone marrow microvessels or tumor cells infiltration or obstruction and destruction by leukemia cells; (3) Damage of cells in bone marrow regions by enzymes released by tumor cells; (4) Cell apoptosis or immune factors; (5) the bone marrow injuries by poison, toxins from various microbial infection toxins or TNF-α or chemotherapy drugs; (6) Extremely proliferation of bone marrow endothelial cells and oppression of the bone marrow blood sinus that resulted in the blood sinus distortion, rupture, blood supply reduction. Among all of these factors, the main character was obstacle in bone marrow microcirculation. In this case report, BMN may be associated with embolism of bone marrow blood capillary and blood sinus in the bone marrow metastasis of advanced gastric cancer, which lead to bone marrow microcirculation disturbance, tumor cells infiltration and destruction in bone marrow microvessel.

The clinical symptoms of BMN include bone pain, fever, blood cell diminish, liver, spleen and superficial lymph node enlargement and so on. This patient had abdominal pain, fever, and systemic bone pain and blood reduction. Gastroscope and biopsy confirmed he was gastric cancer patient. Laboratory tests showed that hemoglobin and platelet was decreased. Bone marrow re-examination further confirmed he suffered from BMN. All these symptoms were consistent with previous reports.

Kiraly reported that bone pain occurred mainly in the active site of hematopoietic tissues, such as ribs, sternum and spine and so on, with usu-

ally multiple sites of persistent pain [5-7]. Fever can be detected in almost all patients, and the reason may be caused by heat source which released from infection or necrotic tissues. The diagnosis of BMN was depended on multiple bone marrow aspiration smear and pathological biopsy. In the second aspiration, the bone marrow fluid was dark red that suggested BMN. According to literature reports, the incidence of BMN was in the range of 0.37%-6.5% [12-14]. Dunn et al. had reported that the incidence of BMN was 0.15% in patients with bone marrow aspiration or biopsy [15]. All patients had poor prognosis and bad survival less than 6 months [15].

BMN and normal bone marrow always presented in multiple sites and its necrosis degree was related to necrosis area. The appearance of bone marrow fluids can be red, dark red, light yellow or translucent with odor. The smear can be found large necrosis area of hematopoietic and matrix organization in bone marrow. Hyperplasia degree of bone marrow was various and it can be ranged from lower proliferation to active proliferation. BMN was very rare in clinic, and its survival period was not only dependent on the degree and area of BMN, but also on the diagnosis and treatment in early stages [4, 16]. The basic measurement to prolong the survival of BMN patient is to actively cure the original disease, and with adjuvant therapy by blood transfusion, anti-infection, bleeding and other symptomatic treatments.

## Disclosure of conflict of interest

None.

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