

A Case of Occult Colon Cancer with Sepsis as the Primary Manifestation Identified by Bone Marrow Puncture

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Case report

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Abstract

Background: Bone marrow metastasis is common in liver cancer and lung cancer, but there are few reports in colon cancer. To date, there are no research reports from mainland China; in particular, reports of bone marrow metastasis combined with septic shock as the main manifestation are even rarer. We hope that this case report can raise clinical awareness of the insidiousness of colon cancer and the possibility of metastasis to the bone marrow, especially for patients with progressive thrombocytopenia that is difficult to correct, should be treated differently from sepsis.

Case presentation: A 71-year-old elderly woman presented with sepsis as the first symptom, which mainly manifested as high fever, low blood pressure, high inflammatory indicators, etc. CT examination revealed mild inflammation of the lungs and no obvious abnormalities in the abdomen. Blood culture suggested *Escherichia coli* and *Aeromonas hydrophila/caviae*. After anti-infective treatment, the patient's sepsis symptoms improved significantly, but after repeated platelet transfusion, her hypothermia had still not been corrected. Finally, a large number of malignant cells were identified through a bone marrow puncture smear, and further PET-CT examination confirmed that a malignant tumor in the ascending colon accompanied by multiple metastases, such as in the liver and bones. This patient was ultimately confirmed to have colon adenocarcinoma by autopsy.

Conclusions: Colon cancer can have bone marrow metastasis, and it can be accompanied by intractable thrombocytopenia. Bone marrow aspiration may help distinguish between transient thrombocytopenia associated with sepsis.

Background

Bone marrow metastasis of colon cancer is quite rare in clinical practice, and there are few reports worldwide [1]. The incidence is currently lack of accurate investigation reports, but it is generally believed that once bone marrow metastasis occurs, it is more common in advanced tumors, and most patients often have hematological systems abnormalities, especially platelet abnormalities, have a poor prognosis [2], but there are also reports of successful treatment [3]. Colon cancer often lacks symptoms in the early stage, and is found to be mostly in the late stage of the tumor, so the prognosis is often poor. If bone marrow metastasis occurs, progressive bone marrow puncture smear can be performed to assist diagnosis and treatment.

Case Presentation

The patient was a 71-year-old female who suffered from hypertension for 3 years. She took 80 mg of Lisinartan capsule orally daily to control blood pressure, and her blood pressure was controlled. The patient developed fever 3 hours prior to admission, with a peak temperature of 39°C, accompanied by chills, no cough, expectoration, pharyngeal pain, abdominal pain, diarrhea, increased urination frequency, increased urination urgency, perianal pain and other symptoms. Routine blood examination revealed the

following: white blood cell count $13.2 \times 10^9/L$, neutrophil percentage 88.5%, hemoglobin 66 g/L, platelet count $11 \times 10^9/L$, and blood glucose 33 mmol/L. Chest and abdominal CT findings were as follows: 1. mild inflammation in both lungs; and 2. bilateral pleural thickening. The suspected diagnoses upon admission were as follows: 1. fever of undetermined origin (potentially indicating severe sepsis); 2. pneumonia; and 3. hypertension. After admission, intravenous meropenem 0.5 micropump (Q6h) was administered as anti-inflammatory therapy, 5 g of intravenous human immunoglobulin (QD) was administered to improve immunity, 4 units of erythrocyte suspension was administered to correct anemia, and 10 units of platelets was administered to correct low platelets. In addition, insulin micropumps were continuously used to control blood glucose. The next day, the patient was cold and shivering, the temperature reached 40°C , and the blood pressure dropped to 85/53 mmHg. The report from the microbiology department indicated *Escherichia coli* and *Aeromonas hydrophila/caviae* in the blood culture. The patient was transferred to the ICU, and a meropenem 0.5 micropump (Q6h) combined with 50 mg of intravenous tegloctin (Q12h) was used to fight the infection; fluid resuscitation and vasoactive drugs were also administered to maintain blood pressure stability. Recombinant human granulocyte colony-stimulating factor was used to elevate the white blood cell count, and recombinant human platelet growth factor was used to promote platelet production. In addition, erythrocyte suspensions, platelets, and other supportive treatments were administered. One week after the anti-infection treatment, the patient's infection was controlled, her blood pressure and body temperature returned to normal, and her blood culture was negative, but the platelet count was difficult to maintain (Fig. 1). A bone marrow biopsy was performed, and the bone marrow smear revealed many malignant cells (Fig. 2). Due to suspicion that the cancer had spread to the bone marrow, further whole-body ^{18}F -FDG PET/CT examination was performed, and the results revealed high metabolic signals in the ascending colon (Fig. 3). A malignant tumor in the ascending colon was suspected. Because the patient suffered from thrombocytopenia as a result of bone marrow metastasis, surgery and endoscopy were contraindicated; eventually, the tumor progressed, and the patient died 3 weeks later. The final autopsy and pathological results of the patient after death showed colon adenocarcinoma (Fig. 4).

Discussion

Carcinoma metastasis to the bone marrow is a result of the migration of medullary tumor cells to the bone marrow through blood or body fluids. Bone marrow metastasis can occur with almost any malignant tumor; lung cancer, breast cancer and prostate cancer are the most prone to metastasize to the bone marrow, while colon cancer is relatively unlikely to lead to bone marrow metastasis [1–4]. In addition to the clinical symptoms of primary tumors, bone marrow metastasis is generally characterized by abnormalities in the circulatory system, which mainly manifest as myelosuppression, including decreased counts of platelets, hemoglobin levels and white blood cell counts, or myeloproliferative manifestations [5, 6]. When the patient in this case was admitted to the hospital, she exhibited no obvious other clinical symptoms, the tumor markers were normal, and no special abnormalities were found on chest and abdomen CT imaging; this lack of symptoms is consistent with early-stage colon cancer. In this case, severe sepsis was the primary manifestation, including high fever, shock, and the detection of

Escherichia coli and *Aeromonas hydrophila/caviae* in blood culture. The patient may have developed sepsis due to the destruction of the mucosal barrier of the intestinal wall by the tumor, which allowed the intestinal flora to enter the bloodstream; such a manifestation has rarely been reported in previous cases. Whether trilineage decreases in blood cells are a direct result of hematological disease or secondary to bone marrow suppression caused by severe sepsis is often difficult to determine at first, which can easily result in missed diagnoses or misdiagnoses. Thrombocytopenia caused by sepsis is generally related to bone marrow suppression and increased osteolysis. Once the infection is controlled, the platelet count gradually returns to normal within 6 days, especially after the application of thrombopoietin[7]. However, in this case, when the patient's infection was controlled and the blood culture was negative, the platelet count was still difficult to maintain, even after repeated platelet transfusions. Therefore, it was necessary to look for other causes, such as blood system diseases or tumor-related thrombocytopenia. A bone marrow puncture was further performed, and the bone marrow smear revealed a large number of malignant cells, which further confirmed the diagnosis of colon cancer suggested by ¹⁸F-FDG PET/CT examination. The incidence of thrombocytopenia associated with solid tumors is increasing year over year, and its mechanism is complex, involving multiple factors that are both immune-related and non-immune-related. Bone marrow metastases damage the living microenvironment of hematopoietic stem cells and bone marrow stromal cells and interfere with the normal proliferation, differentiation and physiological functions of blood cells, making them an important factor in tumor-related thrombocytopenia. Therefore, bone marrow smears have important auxiliary value for the diagnosis of some occult tumors. Studies have shown that 41% of patients with malignant tumors have bone marrow metastasis, and evaluation of bone marrow smears to identify cancer cells is important for the diagnosis of bone marrow metastases. Detecting cancer cells on bone marrow smears or in biopsy samples can not only aid in the diagnosis of tumors but also help to identify the primary tumor origin[8, 9]. It is worth noting that not all metastatic cancers can be identified by a single bone marrow biopsy, and staining the sediment of the puncture or bone marrow biopsy samples is necessary to improve the positive diagnosis rate [10]. The diagnosis of bone marrow metastasis can assist the diagnosis of primary tumors and prognostic predictions, suggesting that it is a useful auxiliary method for the diagnosis of tumors.

Conclusions

Colon cancer with sepsis as the first manifestation is very rare. When a progressive reduction in platelets is observed and difficult to correct, bone marrow metastasis should be considered once sepsis is controlled. Bone marrow aspiration or biopsy and PET-CT can help confirm the diagnosis of occult colon cancer.

Declarations

Ethical approval and consent to participate:

All procedures performed in studies involving human participants were performed in accordance with the ethical standards of the Ethics Committee of Ningbo Yinzhou People's Hospital and the 1964 Declaration

of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from the patient.

Consent for publication:

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent form is available for review by the Editor-in-Chief of this journal.

Availability of data and materials:

All data have been presented within the manuscript and in the form of images.

Competing Interests:

We declare that there are no competing interests to declare.

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Authors' Contributions:

GC was responsible for preparing the paper and providing final approval. CZ was responsible for the acquisition, analysis, and interpretation of data and revised the paper critically for important intellectual content. FY and YLN were responsible for editing the English translation. All authors have read and approved the manuscript.

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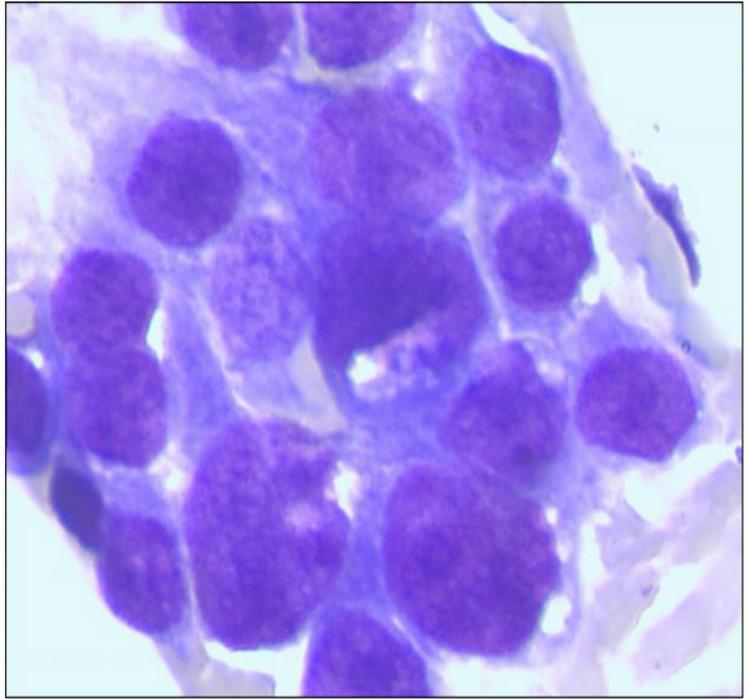
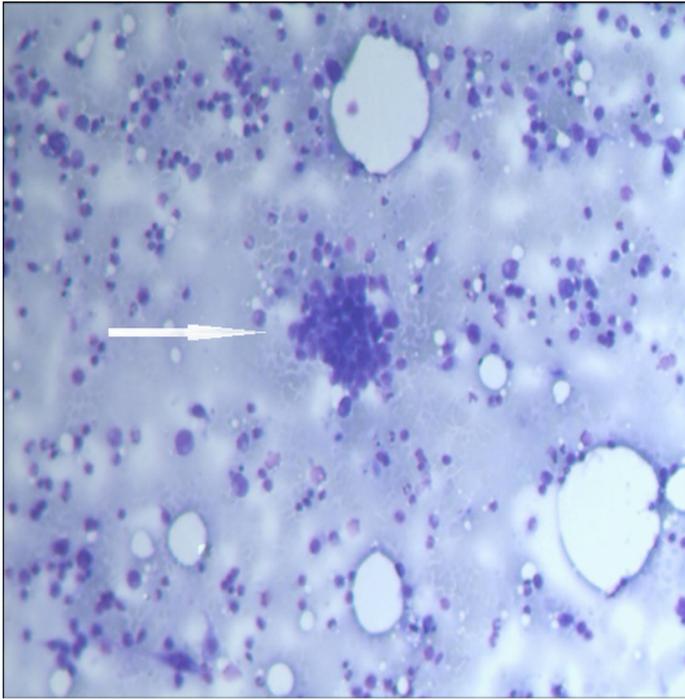
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Figures



A

B

Figure 2

The bone marrow smear stained with Wright-Giemsa showed a class of abnormal cells (arrow points $\times 10$). Clumps of cohesive cells, uneven in size, with abundant cytoplasm, irregular margins, and rough chromatin were visible with 1-3 faint nucleoli ($\times 100$).

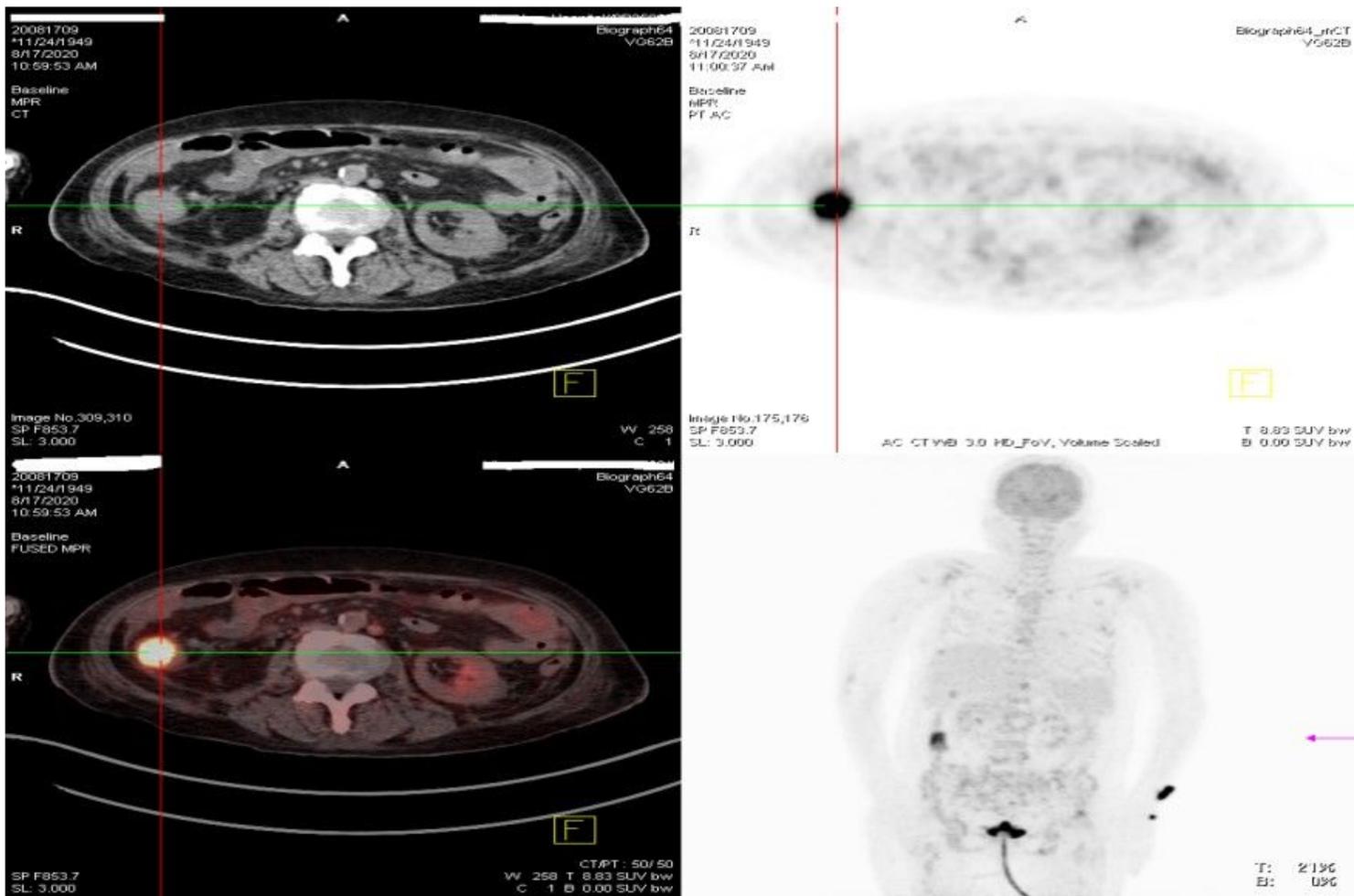


Figure 3

18F-FDG PET/CT showed abnormally high signals in the ascending colon and left radius.

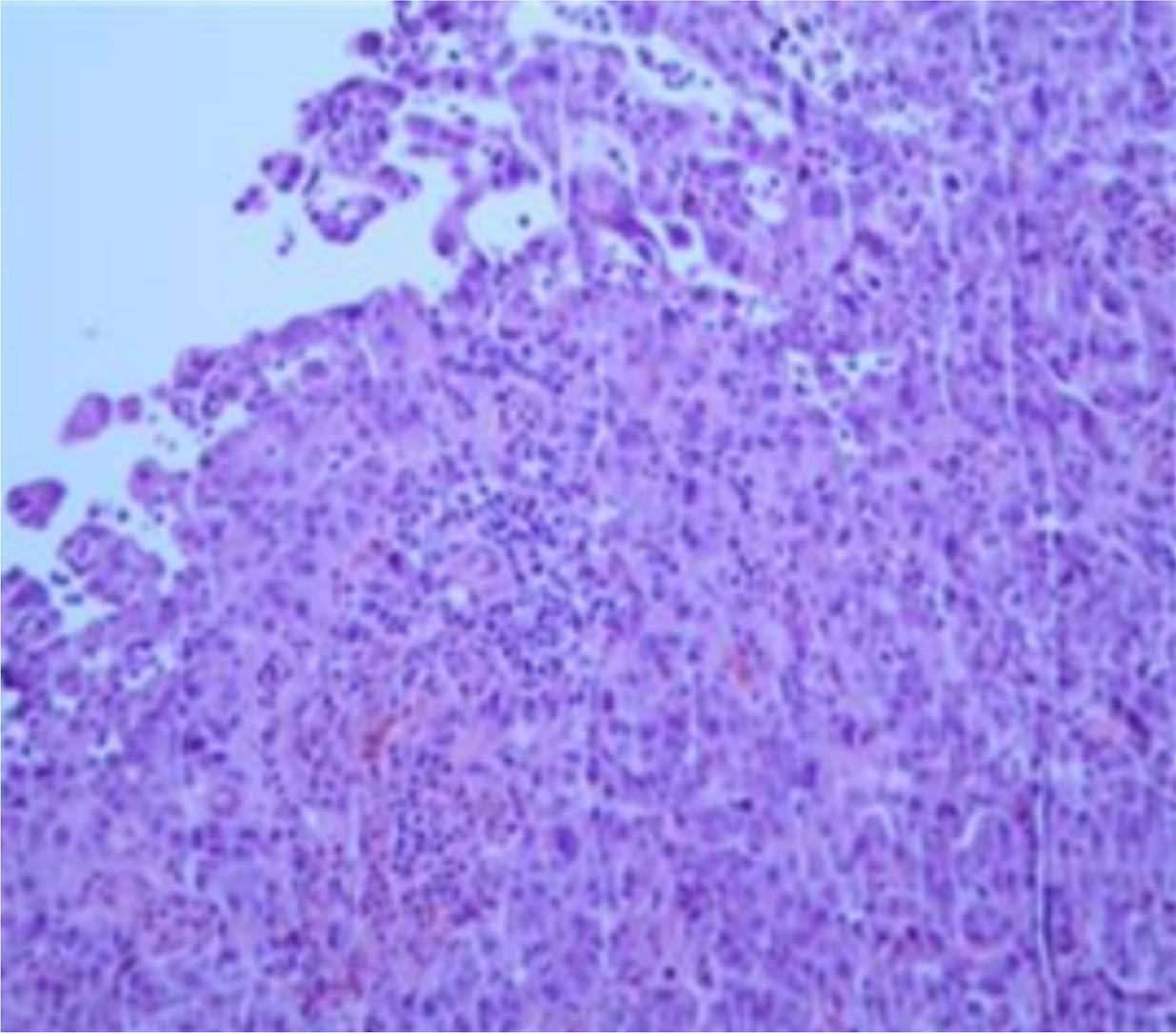


Figure 4

The patient's autopsy and pathological results revealed colon adenocarcinoma.