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Case Report

Colon Cancer with Bone Marrow Metastasis as the Initial Presentation: A Case Report

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Abstract:

Colorectal carcinoma still represents a global health burden despite the advances in its management. The most common sites of distant metastasis from colorectal carcinoma are hepatic and pulmonary metastases while metastases are rarely reported to affect the bone marrow. We report a 59-year-old male patient who presented with progressively worsening pain in the right scapular region and pancytopenia. He was diagnosed by a bone marrow biopsy as a case of metastatic descending colon cancer. The patient had pancytopenia. CT and bone marrow puncture examinations indicated the presence of bone marrow metastasis of colon tumor. Though being rare, bone marrow metastasis should be suspected in colorectal carcinoma cases with abnormalities in peripheral blood count.

Key words: colon cancer; bone marrow metastasis; reduced-dose chemotherapy

Introduction

According to the 2020 global cancer statistics, colorectal cancer accounts for approximately one-tenth of all new cancer cases, ranking second only to female breast cancer and lung cancer in incidence, and second in cancer-related mortality [1]. The most common sites of distant metastasis in colorectal cancer are the liver (up to 70%) and lungs (up to 30%), while bone marrow metastasis is exceedingly rare[2,3] . In cases of malignant tumors with bone marrow metastasis, the primary clinical manifestations include reduced blood cell counts and coagulation abnormalities, with occasional occurrences of disseminated intravascular coagulation (DIC) or thrombotic thrombocytopenic purpura (TTP). For DIC induced by malignant tumors, supportive therapy targeting coagulation abnormalities alone is insufficient, and appropriate chemotherapy targeting the tumor is necessary to improve coagulation dysfunction [4–6]. Currently, there is no standardized chemotherapy regimen specifically for bone marrow metastasis, and the prognosis for most patients is poor. Globally, cases of colorectal cancer with bone marrow metastasis are extremely rare, with only 18 reported cases presenting with bone marrow suppression as the initial symptom. To date, no such cases have been reported in China. Existing literature indicates that patients with this condition often present with poor general health and concurrent metastases to other organs (e.g., liver, lymph nodes, and lungs), with survival typically not exceeding 10 months [7–10]. This study presents the first reported case of colon cancer with bone marrow metastasis as the initial manifestation in mainland China. This rare case provides valuable insights into the diagnosis and research of atypical metastatic patterns in colorectal cancer.

Case Presentation

I. General Information

A 59-year-old male patient presented with "progressively worsening pain in the right scapular region and pancytopenia." The patient had no history of chronic diseases such as hypertension, diabetes, coronary artery disease, or stroke, denied unhealthy lifestyle habits, and reported no family history of tumors.

II. Laboratory and Imaging Findings

Admission laboratory results: White blood cells (WBC) 3.22 × 10^9/L, red blood cells (RBC) 2.3 × 10^12/L, hemoglobin (Hb) 68 g/L, platelets (PLT) 24 × 10^9/L. Tumor markers: Carcinoembryonic antigen (CEA) 24.8 ng/mL, ferritin 5993 mg/mL, CA199 66.62 U/mL. Lactate dehydrogenase (LDH) 2887 U/L. Plasma D-dimer 40.003 μg/mL, fibrinogen degradation products (FDP) 251.02 μg/mL (Source: Laboratory test records, Hangzhou Bay Hospital, Zhejiang Province, China reported on April 24, 2024).

Bone marrow biopsy pathology: Adenocarcinoma metastasis, likely of gastrointestinal origin. Immunohistochemistry: Ki67 (15%), MLH1 (+), PMS2 (+), MSH2 (+), MSH6 (+), CK20 (partial cells +), PD-L1 22C3 (−). Genetic testing: No mutations in BRAF, ERBB2, KRAS, NRAS, or POLE; mutations in APC and TP53 exons; MYC gene amplification.

Colonoscopy: A large nodular protrusion with fresh blood was observed in the descending colon, accompanied by luminal stenosis.

Abdominal CT scan (Figure 1): Irregular thickening of the descending colon wall with blurred surrounding mesenteric fat, and multiple enlarged lymph nodes in the iliac vessels, pelvic cavity, and retroperitoneum.

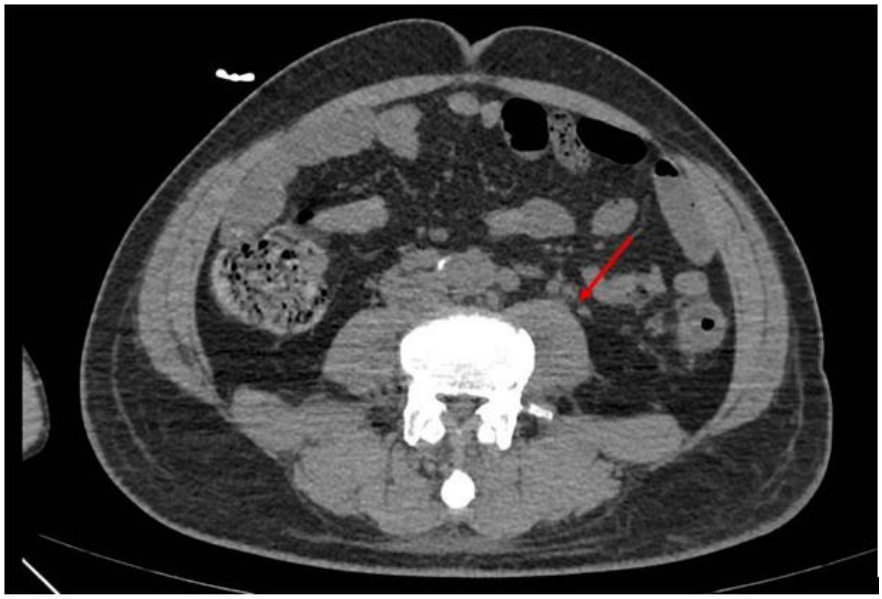

Figure 1: Abdominal CT scan

Bone scintigraphy (Figure 2) and PET/CT: Multiple areas of tracer uptake were observed in the cervical, thoracic, and lumbar vertebrae, right scapula, bilateral ribs, bilateral ilium, and left proximal femur, indicating extensive bone metastases.

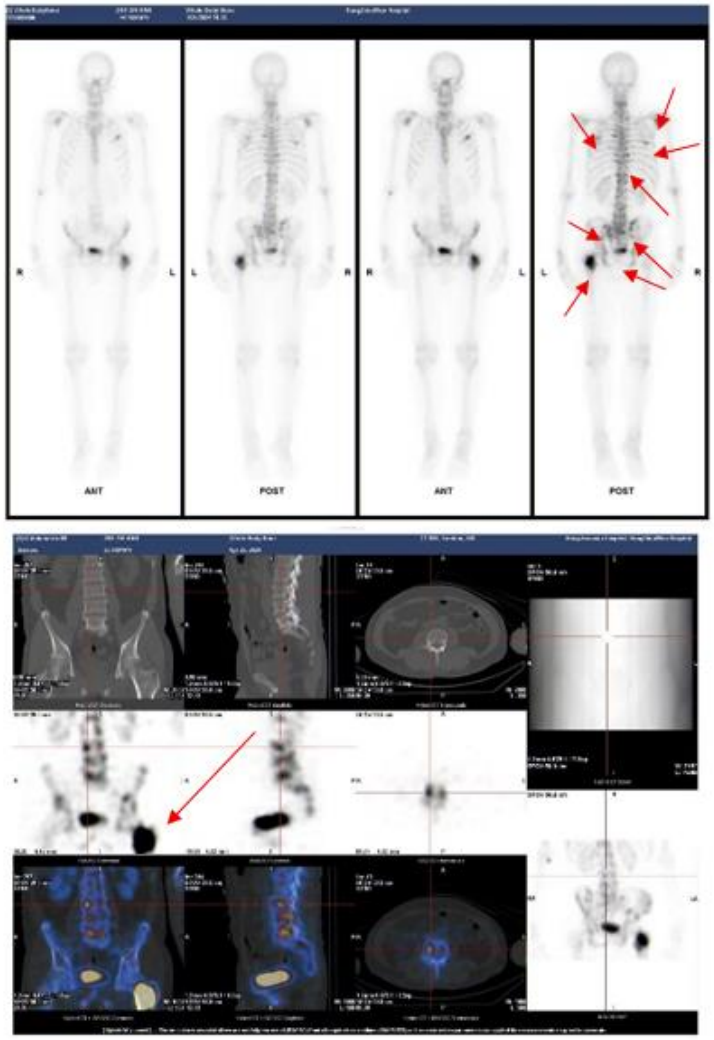

Figure 2: Bone scintigraphy

III. Diagnosis and Differential Diagnosis

Diagnosis:

The diagnosis was made by comprehensively analyzing the clinical laboratory test results of the patients: Colon adenocarcinoma (T4NXM1b, stage IVB) with bone marrow metastasis.

Differential diagnoses:

Colorectal cancer (CRC) requires systematic distinction from the following benign and malignant conditions, integrating endoscopic, radiographic, and histopathologic findings. Benign Lesions include adenomatous polyps, inflammatory bowel disease, infectious colitis, diverticulitis, ischemic colitis and non-neoplastic polyps. Malignant Mimics include gastrointestinal stromal tumors, lymphomas, neuroendocrine tumors and metastatic malignancies (NCCN Guidelines for Colon Cancer, Version 2.2024). In this case, we still need to make a special differentiation from primary bone marrow malignancies and bone metastasis from colon cancer. Primary bone marrow malignancies don't have primary lesions outside the bone marrow and the diagnosis is confirmed by pathology and immunohistochemistry. Bone metastasis from colon cancer lacks severe bone marrow suppression, usually involves single metastatic foci, and rarely presents with bone metastasis as the initial symptom.

IV. Treatment

Supportive Therapy Upon admission, the patient exhibited fulminant bone marrow suppression with severe pancytopenia, particularly thrombocytopenia. Coagulation tests showed markedly elevated D-dimer and FDP levels, suggesting DIC. Before initiating chemotherapy, the patient received supportive therapy for DIC, including blood component transfusions. Due to bone marrow suppression, the patient developed a high fever (39°C) on May 12, which was treated with levofloxacin and meropenem. Pathological tests confirmed respiratory cytomegalovirus infection, prompting the addition of ganciclovir. The fever subsided after antiviral treatment, and the infection was controlled. However, as the disease progressed, the patient developed refractory Pneumocystis pneumonia. Recurrent infections and high fever caused significant distress, highlighting the challenges in managing terminal infections in patients with severe bone marrow suppression.

Chemotherapy

After the infection was controlled, chemotherapy was initiated on May 23 due to worsening pancytopenia. A reduced-dose regimen of capecitabine and cetuximab (50% dose) was administered every three weeks. After one cycle, laboratory tests showed WBC 4.32 × 10^9/L, RBC 2.59 × 10^12/L, PLT 44 × 10^9/L, and LDH 673 U/L, indicating a favorable response. After two cycles, WBC normalized, PLT stabilized at 40 × 10^9/L, Hb at 80 g/L, and LDH decreased to 810 U/L. However, on July 9, 2024, the patient's condition deteriorated abruptly, with a sharp rise in LDH (Chart 1) and PLT dropping to 12 × 10^9/L (Chart 2). To better control the tumor, irinotecan (50% dose) was added in the third cycle.

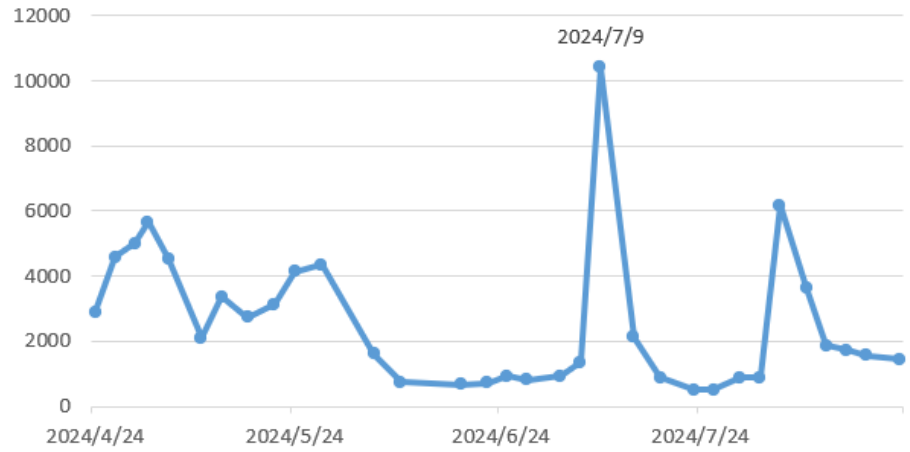

Chart 1: Trend chart of LDH changes

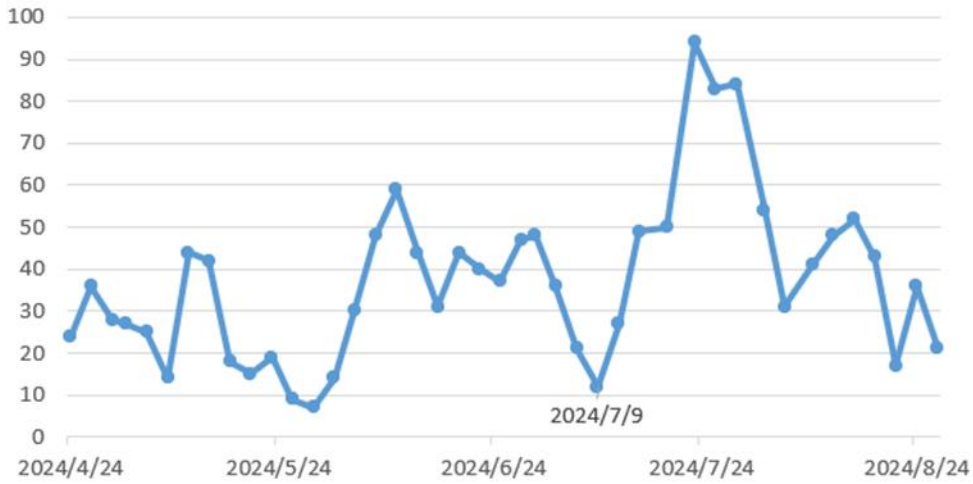

Chart 2: Trend chart of PLT changes

V. Treatment Outcome, Follow-up, and Prognosis

After supportive therapy for DIC, the patient received first-line chemotherapy with capecitabine and cetuximab, followed by the addition of irinotecan in the third cycle. The patient discontinued treatment after the third cycle and passed away on September 2, 2024, with an overall survival of 132 days.

Discussion

Colorectal cancer is one of the most common malignancies globally and a leading cause of cancer-related mortality. Like most malignancies, colon cancer has distinct metastatic patterns. Due to blood flow dynamics, over 70% of patients present with liver involvement as the most common initial metastatic site. The lungs are the second most common site, accounting for 20–30% of cases[2]. Bone metastasis is rare, typically occurring in advanced-stage patients and often accompanied by metastases to other organs. Isolated bone metastasis is even rarer, with an incidence of only 1–2% (11). Bone marrow metastasis is exceedingly rare, usually occurring in late-stage patients after surgery or chemotherapy [12,13]. Globally, fewer than 20 cases have been reported with bone marrow metastasis as the initial symptom (Chart 3), and no such cases have been reported in China.

We summarizes all retrievable cases of colon cancer presenting with bone marrow metastasis as the initial symptom. Most reported cases are from East Asia, predominantly male patients aged 60–70 years, with survival times ranging from 7 to 330 days. Treatment regimens vary, with no consensus, though most involve FOLFOX or modified FOLFOX regimens. The survival time of this case was four months, not the longest reported, underscoring the need for further research into drug selection and dosing (Chart 3).

NO.	COUTRY	GENDER	AGE	SYMPTOM	THERAPY	SURVIVAL TIME
1(7)	Egypt	Female	33	Fever, back and pelvic bone pain	Unknown	1 week
2(8)	USA	Male	56	Fever, back pain, abdominal distension, jaundice	FOLFOX	6 months
3(8)	USA	Male	55	Severe low back pain, anorexia, weight loss	FOLFOX	4 months
4(9)	Japan	Male	60	Low back pain, anorexia, difficulty defecating	mFOLFOX6(3 cycles); CapeOX (5 cycles); Irinotecan + Panitumumab (8 cycles); Trifluridine (3rd-line therapy)	10 months
5(10)	Japan	Male	62	Low back pain; hematuria; epistaxis; skin petechiae	Unknown	11 days
6(27)	South Korea	Male	67	Low back pain; mild abdominal pain; night fever; weight loss	mFOLFOX4	>4.5 months
7(28)	Japan	Male	51	Back pain	Unknown	25 days
8(29)	Japan	Male	45	Low back pain	mFOLFOX6	Unknown
9(30)	Japan	Male	66	Back pain; fever	mFOLFOX6	6 months
10(31)	USA	Male	70	Persistent back pain	Unknown	Unknown
11(32)	Germany	Female	65	Bleeding tendency; acute renal failure	FOLFOX; Cetuximab added in the 2nd cycle	7 months
12(19)	Japan	Male	61	Back pain	CapeOX+Brentuximab vedotin; Denosumab every 2 months	>100 days
13(33)	Japan	Male	65	Low back pain; melena	Tumor resection; mFOLFOX6 (started on day 5 post-op); Bevacizumab added in the 5th cycle	128 days
14(34)	Japan	Male	66	Cough; respiratory failure	mFOLFOX6 + Pegfilgrastim; Panitumumab added on day 170	330 days
15(35)	Netherlands	Female	65	Headache; spontaneous head hematoma; rectal bleeding	CapeOx (11 cycles); Later switched to FOLFIRI	8 months
16(36)	Japan	Male	68	Low back pain	mFOLFOX4; Bevacizumab added after 2 cycles	>6 months
17(37)	USA	Male	80	Conjunctival pallor	FOLFOX + Radiation therapy	Lost to follow-up (31 days)
18(38)	Australia	Male	61	Back pain; weight loss; anorexia; night sweats	Hartmann's procedure	9 days

Chart 3: Summary of colon cancer cases with myelosuppression symptoms as the initial symptom.

Note: In the survival time, ">" indicates that the patient was still alive at the time of reporting.

Isolated bone metastasis is commonly associated with breast, lung, and prostate cancers [14]. In the gastrointestinal tract, most bone marrow metastases originate from gastric cancer (over 90%), while colon cancer rarely metastasizes to bone (<10%) and even less frequently to bone marrow (<1%)[15]. This highlights the distinct clinical and biological behaviors of tumors in terms of metastatic pathways, involving not only blood and lymphatic flow but also molecular signaling and organ-specific interactions. Studies suggest that successful colonization of distant organs

by colon cancer cells is mediated by specific adhesive interactions between these cells and the host organ's microvasculature. In rats injected with colon cancer cells of varying metastatic potential, each organ exhibited unique microenvironments that influenced tumor cell behavior through intrinsic molecular pathways, affecting the likelihood of tumor spread and implantation[2]. The rarity of colon cancer bone marrow metastasis may be attributed to: [1] the requirement for specific steps in tumor-microenvironment crosstalk to initiate secondary tumors, with most metastatic cancer cells remaining dormant in the bone marrow[16]; [2] deposited cancer cells in the bone and marrow may never progress to clinical metastasis or require prolonged latency[17]; (3) the bone marrow, rich in immune cells[18], is rarely an isolated site for malignant metastasis, and early bone marrow metastasis is challenging to detect, making colon cancer with bone marrow metastasis as the initial presentation exceptionally rare.

Bone marrow metastasis is associated with three primary symptoms: anemia, back pain, and bleeding tendency. Hematological and biochemical tests typically reveal severe anemia, leukoerythroblastosis, and elevated alkaline phosphatase and LDH levels. Additionally, due to diffuse marrow infiltration, the condition is often complicated by DIC, with metastases presenting as diffuse infiltration rather than nodular lesions[19].

Colon cancer with bone marrow metastasis often presents with severe pancytopenia due to marrow suppression, complicating treatment. Most reported cases were treated with FOLFOX or modified FOLFOX regimens (Chart 3). Although neurotoxicity is the primary side effect of oxaliplatin, myelosuppression with thrombocytopenia is also clinically significant[20]. Thus, oxaliplatin was avoided in this case. Capecitabine has been used to treat myeloid-derived suppressor cells in other malignancies[21,22]. Cetuximab, an EGFR antibody, is approved for colorectal and head-and-neck cancers[23], particularly as a third-line treatment for metastatic colon cancer when combined with irinotecan[24]. However, EGFR is also expressed on bone marrow stromal cells[23], and cetuximab may exacerbate marrow suppression in patients with severe pancytopenia. Clinical trials have shown that cetuximab does not significantly improve outcomes in RAS wild-type patients, especially those with right-sided colon cancer [25,26]. In this case, chemotherapy delayed disease progression but did not achieve significant tumor control, underscoring the ongoing controversy and need for further research into treatment regimens for colon cancer with bone marrow metastasis.

Conclusion

Due to the extreme rarity of colon cancer with bone marrow metastasis, its mechanisms remain poorly understood, and optimal treatment strategies and dosing require further investigation. A deeper understanding of the natural history of these rare metastases may reveal distinct clinical and biological patterns in primary colon cancer. We strongly advocate for advanced molecular and genetic studies in such patients to identify specific tumor expression profiles, enabling early diagnosis and improved survival. This represents a shared challenge for gastroenterologists and hematologists, warranting greater attention and exploration.

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