

The Adverse Outcomes and Progressive Nature of Early-Onset Colorectal Cancer

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Case Report

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Abstract

Early-onset colorectal cancer (EOCRC), also known as young colorectal cancer, is already increasing in incidence each year, approximately 2% each current year. The current report already described the uncommon type of progression of this cancer based on the age group. In the clinical setting, the patients usually presented emergency cases of colorectal cancer, such as large bowel obstruction and perforation, which led to emergency operation with the increased incidence of postoperative morbidity and lower chance of curative operation in these cases. Multimodality treatment has already been administered in these cases, but in most of the cases, we have limitations in predicting and treating the progression of both locoregional and distant metastasis, although adjuvant therapy has already been given following the curative resection of the tumor.

Introduction

Colorectal cancer is the third most common cancer worldwide and the second leading cause of death globally. In Asian populations, there is a tendency for an increase in incidence and mortality rates, with an estimated 1,698,000 new CRC cases in 2040.¹ Early-onset CRC is CRC that occurs in individuals under the age of 50.² According to GLOBOCAN, there were 188,069 new cases of early-onset CRC.³ Although there is a downward trend in CRC incidence in the total population of developed countries, the incidence rate of early-onset CRC is increasing in both developed and developing countries.⁴ The causes of the increasing trend in the incidence of early-onset CRC are inseparable from the influence of genetic predisposition, environmental exposure, and lifestyle-related factors.^{5,6,7}

Adenocarcinoma is the most common subtype.⁸ The genetic profile of CRC is highly complex, involving various molecular pathways related to tumor growth and metastasis.⁹ There are several advanced treatment modalities such as surgery, chemotherapy, radiotherapy, and targeted therapy.¹⁰ Immunotherapy can enhance the immune response but is limited to certain groups of patients. Targeted therapy aims to inhibit specific mutations but is limited to individuals with certain genetic alterations and may experience secondary resistance. Overall, existing treatment strategies do not fully meet clinical needs, as treatment outcomes remain suboptimal, with high recurrence rates and a significant impact on patient survival and quality of life.^{6,8,9}

Case Description

Case 1. 22-year-old male

A 22-year-old male presented to hospital with intermittent abdominal pain and recurrent nausea, predominantly during chemotherapy follow-up. He had been previously diagnosed with rectal/colonic adenocarcinoma following colonoscopy at another institution and underwent serial chemotherapy at the digestive surgery outpatient clinic from February to December 2025. The chemotherapy regimen consisted of 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX regimen)

A significant 10kg decreasing in the last 3 months. The patient was hospitalized again due to recurrent abdominal pain without diarrhea. Serial laboratory assessments demonstrated progressive anemia, increasing leukocytosis, relative thrombocytosis, elevated liver transaminases, and electrolyte disturbances, while renal function remained preserved. These findings were consistent with progressive systemic inflammation and hepatic involvement.

Chest X-Ray (Fig. 1) identified nodular pulmonary lesions suggestive of metastases, recommendation for contrast-enhanced MSCT. The patient received supportive inpatient care and was discharged for outpatient palliative management and continuation of chemotherapy.

The patient re-presented with progressive dyspnea. He presented chief complaint shortness of breath for several days as he was under hospitalization. Contrast-enhanced MSCT of the thorax and abdomen (Fig. 2) performed on 8 January 2026 confirmed nodular and pneumonic-type pulmonary metastases with multiple hepatic metastatic lesions. He presented chief complaint shortness of breath and dyspnea.

Case 2. 39-year-old male

A 39-year-old male patient was referred to outpatient clinic with complaints of left lower abdominal pain and intermittent bloody stool. Colonoscopic biopsy revealed an adenoma with moderate dysplasia, while CT scan demonstrated a rectal mass with multiple lymphadenopathies and blastic bone metastases involving the bilateral iliac bones and right femoral head, as well as liver metastasis.

Based on the AJCC 8th edition (2017), the patient was diagnosed with stage IVB rectal cancer (T4bN2bM1b). The patient underwent laparotomy with low anterior resection (LAR) and Hartmann's procedure. Intraoperative findings revealed a mass measuring 5 × 4 cm in the middle third of the rectum, with tumor infiltration into the urinary bladder and surrounding lymph nodes. Histopathological examination showed a well-differentiated adenocarcinoma with perineural invasion, without lymphovascular invasion, and a low tumor-infiltrating lymphocyte (TIL) level (5%). The patient was planned for chemotherapy using fluorouracil and leucovorin combined with radiotherapy.

After the first cycle, the patient was hospitalized due to bowel obstruction, presenting with nausea, vomiting, absence of stoma output, and typical radiological findings as seen in Fig. 3. CT scan confirmed a 7.3 cm intraluminal rectal mass infiltrating the small bowel as the cause of obstruction. After decompression, stabilization, and the second chemotherapy cycle.

Although an initial response to chemotherapy was observed, 18 months after the first chemotherapy the patient developed an ileorectal fistula, requiring laparotomy and ileostomy. Follow-up CT scans revealed new nodular lung metastases.

Case 3. 35-year-old male

A 35-year-old male with a history of rectal adenocarcinoma was followed from 2024. He had previously undergone surgical resection with stoma formation, followed by adjuvant chemotherapy and radiotherapy. Disease progression later included central nervous system metastases.

In June 2024, the patient was admitted with chronic peristomal abdominal pain and stoma bleeding. He was moderately ill, fully conscious, and hemodynamically stable. Clinical evaluation confirmed rectal adenocarcinoma status post ileostomy and adjuvant therapy. He received supportive care, tranexamic acid, and analgesics, and was discharged after clinical improvement.

In 2025, the patient developed progressive headaches, right-sided weakness, nausea, vomiting, and reduced functional capacity. Neurological assessment and imaging revealed left parieto-temporal brain metastasis. He underwent whole-brain radiotherapy in April 2025 (30 Gy in 10 fractions) with corticosteroids and symptomatic treatment. Subsequent follow-up showed fluctuating neurological symptoms with preserved consciousness. In July 2025, right-sided proptosis and chemosis were noted and managed conservatively. Palliative chemotherapy with 5-fluorouracil and leucovorin was continued.

In late August 2025, the patient presented decreased of consciousness, unresponsive to medical treatment and supportive care, 4 days after supportive treatment, the patient has passed away.

Discussion

Early-onset colorectal cancer (EOCRC), defined as colorectal cancer diagnosed before the age of 50 years, has emerged as a distinct and increasingly important clinical entity. Over the past two decades, multiple population-based studies have demonstrated a consistent rise in EOCRC incidence worldwide, contrasting with the declining or stable trends observed in older populations, largely attributed to effective screening programs.^{2,4} The three cases presented in this report reflect this trend, with all patients diagnosed at a notably young age and presenting with advanced or metastatic disease.

Younger patients often present at more advanced stages, with higher rates of nodal involvement and distant metastases at diagnosis compared with average-onset CRC.^{4,5} This delay in diagnosis is commonly attributed to low clinical suspicion, overlapping symptoms with benign gastrointestinal conditions, and the absence of routine screening in younger populations. In the present cases, all patients demonstrated rapid disease progression.

Several studies have suggested that EOCRC may possess distinct molecular and immunological characteristics, including altered tumor microenvironment, reduced tumor-infiltrating lymphocytes, and unique genomic profiles, which may contribute to its aggressive behavior and resistance to therapy.^{6,7} In Case 2, the presence of perineural invasion and low tumor-infiltrating lymphocyte levels is consistent with previously reported adverse prognostic markers associated with poorer outcomes in EOCRC.⁸

Metastatic patterns in EOCRC can be highly heterogeneous and unpredictable. While the liver and lungs remain the most common metastatic sites, younger patients appear more prone to developing metastases at less typical locations, including bone and central nervous system involvement.^{9,10} In this case series, pulmonary metastases were observed in two patients, while one patient

developed brain metastases, a relatively rare but devastating complication of colorectal cancer. Brain metastases from CRC are associated with poor prognosis and limited therapeutic options, underscoring the aggressive nature of advanced EOCRC and the need for vigilant neurological assessment when symptoms arise.^{7, 10}

Management of EOCRC, particularly in advanced stages, requires a multimodality approach involving surgery, systemic chemotherapy, radiotherapy, and supportive care.^{4,7} Systemic chemotherapy, typically fluoropyrimidine-based regimens combined with oxaliplatin or irinotecan, remains the backbone of treatment for advanced disease and has been shown to improve survival and quality of life.¹⁰ Radiotherapy plays an important role in local control and palliation, particularly for rectal tumors and brain metastases.

Despite aggressive multimodal therapy, outcomes in advanced EOCRC remain suboptimal. While some large cohort studies suggest that younger patients may tolerate intensive treatment better and achieve survival outcomes comparable to or slightly better than older patients, this potential advantage is often offset by advanced stage at diagnosis and aggressive tumor behavior.^{4, 5}

As shown in Table 1, a characteristic of patients with early-onset colorectal cancer is the uncontrolled progression of the disease, even after adjuvant treatment has been administered.

Although multimodality treatment remains essential, outcomes in advanced disease are often poor. Early recognition, timely diagnosis, multidisciplinary management, and proactive integration of palliative care are crucial to optimizing both survival and quality of life in this young and vulnerable patient population.

Declarations

CRedit authorship contribution statement

Conceptualization and design: Budhi Ida Bagus

Administrative support: Budhi Ida Bagus

Provision of study materials or patients: Budhi Ida Bagus, Gibraltar Kasyiful Haqi, Meidita Putri Hendrianti

Collection and assembly of data: Gibraltar Kasyiful Haqi, Meidita Putri Hendrianti

Data analysis and interpretation: Gibraltar Kasyiful Haqi, Meidita Putri Hendrianti

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

Declaration of generative AI in scientific writing

During the preparation of this manuscript, ChatGPT was used to improve the clarity of this manuscript. The authors reviewed and edited the text and take full responsibility for the final content.

Ethical Approval

This study has already been reviewed and approved by Health Research Ethic Committee of Moewardi General Hospital, Surakarta, Indonesia. Ethical clearance number: 126 / IV / HREC / 2025.

Both patients have been hospitalised in the Department of Surgery at Moewardi General Hospital, Surakarta, Central Java, Indonesia.

Data Availability : All datasets are already included in the paper and could be available for the reader.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The patient was informed about the nature and purpose of the publication and provided consent for the use of clinical information and relevant

images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon reasonable request.

Funding Declaration

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Conflict of interest

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

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Informed consent

All participants were informed about the objectives of this trial and consented to the use of their clinical information, including operative findings, imaging results, and follow-up data, for research and publication purposes. Written informed consent was obtained from each participant for the use of their data and relevant clinical images in this study.

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Table

Table 1 Summary of the characteristics and disease progression of patients with early onset colorectal cancer (EOCRC)

Case No.	Age (years)	Gender	Presenting Symptom	Staging (TNM)	Site	Histopathology	Metastasis Site	Management	Survival
1	22	Male	Recurrent abdominal pain and vomiting	Stadium IV	Ascending Colon	Pleural effusion in the right lung, may support colorectal adenocarcinoma metastasis	Lung	Colonoscopy with biopsy, chemotherapy, radiotherapy	Still alive
2	39	Male	Lower left abdominal pain and bloody stool	Stadium IVB	Rectum	Well differentiated adenocarcinoma	Bone, liver, lung	Colonoscopy with biopsy, LAR and Hartmann's procedure, laparotomy ileostomy chemotherapy, radiotherapy	26 months
3	35	Male	Progressive headache	Stadium IV	Rectum	-	Brain	Colonoscopy with biopsy, chemotherapy, radiotherapy	12 months

Figures

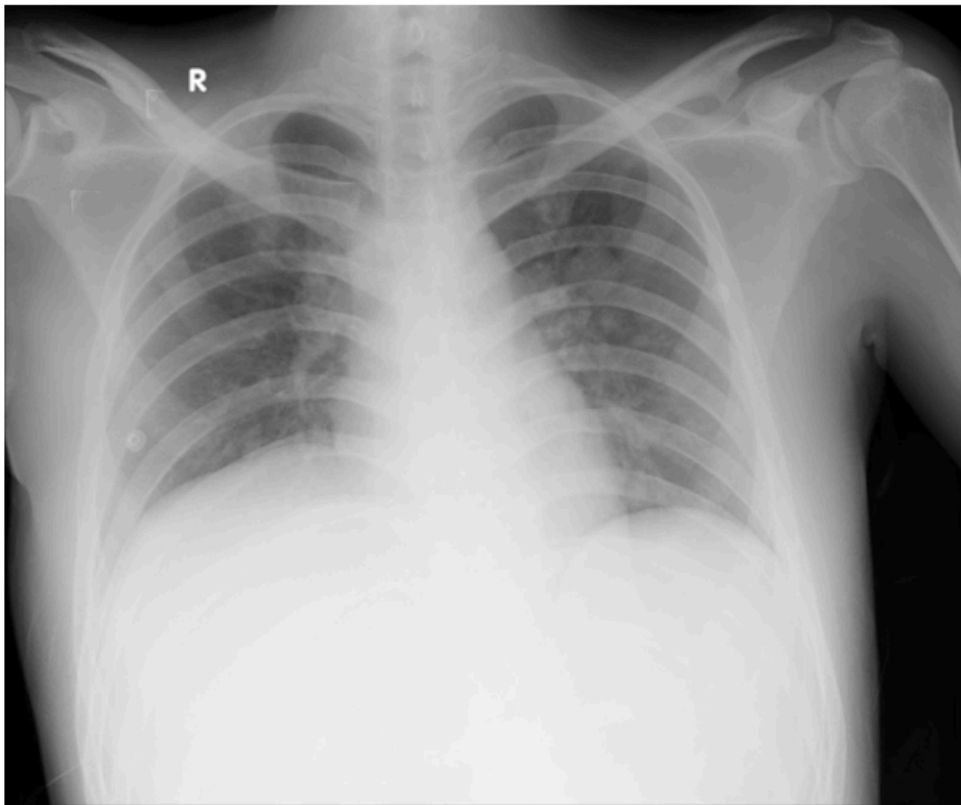


Figure 1

CXR shows multiple bilateral pulmonary nodules are nodular type pulmonary metastases

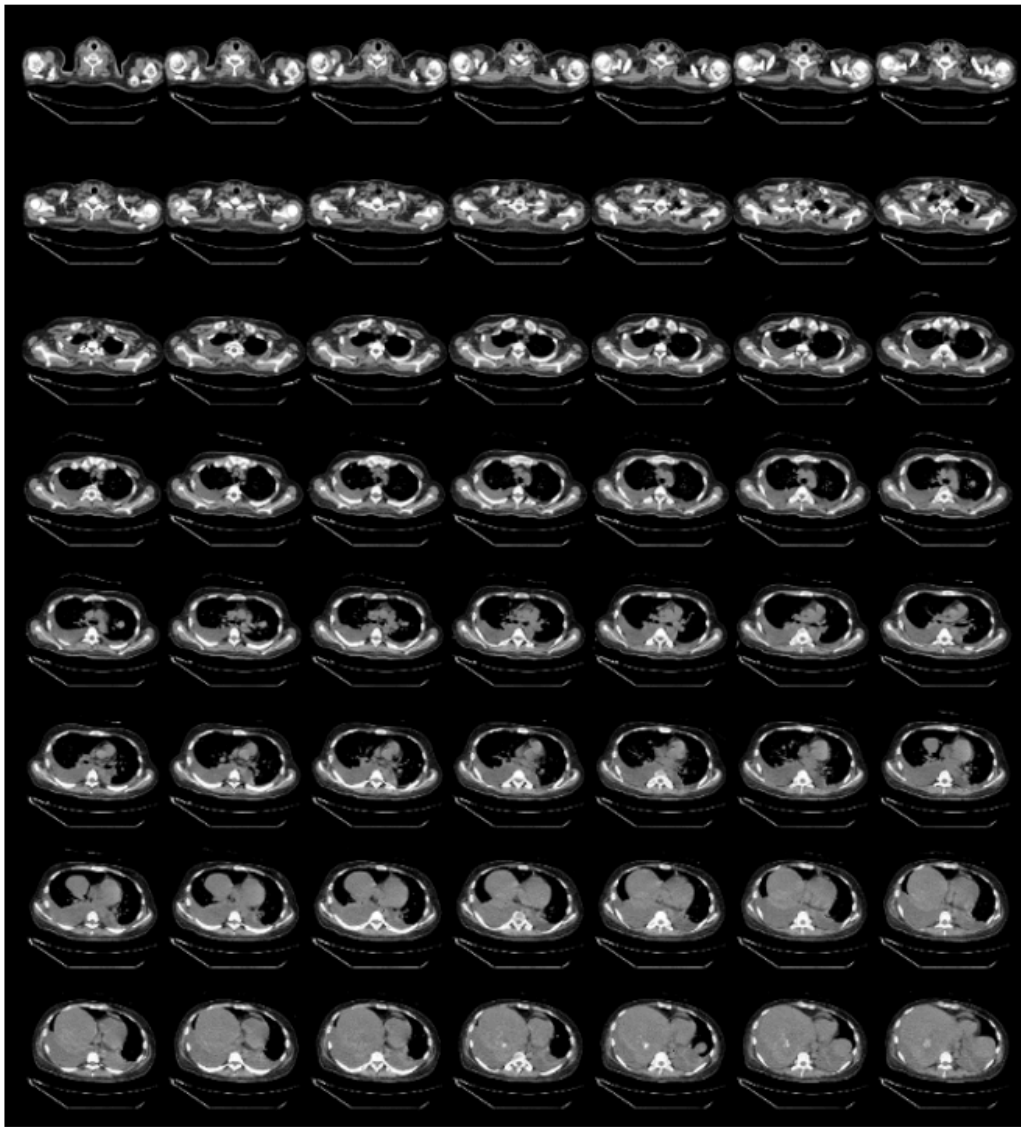


Figure 2

Thoracoabdominal MSCT shows multiple bilateral pulmonary metastases, demonstrating both nodular and pneumonic-type patterns, consistent with metastatic pulmonary involvement. Multiple hepatic metastases involving both lobes of the liver.

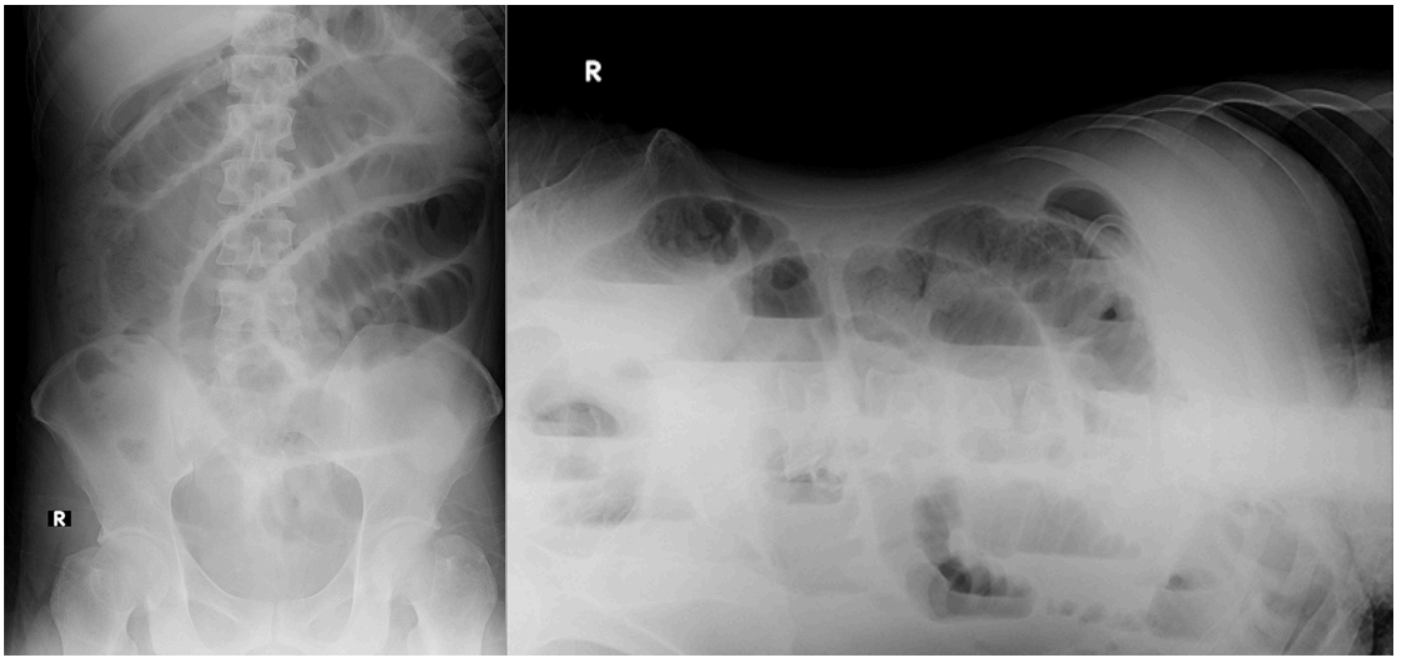


Figure 3

Abdominal X-ray showing typical signs of bowel obstruction in the second patient