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Case report

Asymptomatic intestinal tuberculosis of the terminal ileum diagnosed on colonoscopy: a case report and literature review

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Abstract

Objective: Colonoscopy is useful in diagnosing intestinal tuberculosis. However, the terminal ileum is generally not examined during routine colonoscopy. Therefore, even with colonoscopy, the diagnosis can be missed in patients with lesions confined to the terminal ileum. Herein, we report the case of an asymptomatic patient with intestinal tuberculosis, in whom a colonoscope insertion into the terminal ileum led to the diagnosis.

Patient: An asymptomatic 71-year-old man visited our hospital for a colonoscopy after a positive fecal occult blood test.

Results: Colonoscopy revealed diffuse edematous and erosive mucosa in the terminal ileum. *Mycobacterium tuberculosis* was detected by polymerase chain reaction and culture of biopsy specimens from the erosions, leading to the diagnosis of intestinal tuberculosis. The patient was treated with antitubercular agents for 6 months, and a follow-up colonoscopy revealed healing of the lesions.

Conclusion: Asymptomatic intestinal tuberculosis may occasionally be detected on colonoscopy following a positive fecal occult blood test and is sometimes confined to the terminal ileum. Therefore, clinicians should consider intestinal tuberculosis in the differential diagnosis of the causes of positive fecal occult blood test results and perform colonoscopies, including observation of the terminal ileum.

Key words: colonoscopy, fecal occult blood test, intestinal tuberculosis

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Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* and is the thirteenth leading cause of death worldwide[1]. Despite a steady decline in the worldwide incidence of tuberculosis, its prevalence remains high, especially in developing countries. One-quarter of the global population is estimated to have latent tuberculosis[1]. In addition, the World Health Organization reported that 10.6 million individuals worldwide were diagnosed with tuberculosis in 2021, of whom 1.6 million died from the disease[2]. Tuberculosis is a major infectious disease worldwide.

Tuberculosis is primarily a lung infection but can affect other body organs. Extrapulmonary tuberculosis accounts for approximately 20% of tuberculosis cases, and intestinal tuberculosis accounts for about 10% of extrapulmonary tuberculosis cases[1]. A resurgence of intestinal tuberculosis occurred in the last decade following an increase in immigrants to Western countries[3]. Patients with intestinal tuberculosis commonly present with nonspecific clinical manifestations such as fever, abdominal pain, diarrhea, weight loss, and fatigue[4, 5]. However, asymptomatic cases of intestinal tuberculosis are occasionally observed[5–9], and the lack of typical manifestations may delay diagnosis[5, 8]. Confirming intestinal tuberculosis in asymptomatic individuals is challenging and may lead to incorrect or missed diagnosis[1, 5].

Colonoscopy is useful in diagnosing intestinal tuberculosis[5], and the terminal ileum and cecum are the most fre-

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quently affected[8]. However, the terminal ileum is generally unexamined during routine colonoscopy[5, 9]. Therefore, even with colonoscopy, the diagnosis can be missed in patients with lesions confined to the terminal ileum. Herein, we report a case of an asymptomatic patient with intestinal tuberculosis in whom a colonoscope insertion into the terminal ileum led to the diagnosis. We also discuss the key points in diagnosing asymptomatic intestinal tuberculosis based on a review of the relevant literature.

Case Presentation

An asymptomatic 71-year-old man visited our hospital for a colonoscopy after obtaining a positive fecal occult blood test (FOBT) during a routine medical checkup. The colonoscopy revealed diffuse edematous mucosa and multiple erosions with scars in the terminal ileum (Figure 1a). Biopsy specimens of these erosions showed epithelioid granulomas without caseating necrosis (Figure 2a and 2b). Ziehl–Neelsen staining for acid-fast bacilli yielded a negative result. However, *Mycobacterium tuberculosis* was detected in biopsy samples using polymerase chain reaction (PCR), and a tuberculosis-specific interferon-γ release assay (IGRA) (T-SPOT.TB) was positive (Table 1). In addition, cultures of biopsy specimens taken from these erosions revealed the presence of *Mycobacterium tuberculosis* after 2 weeks. Based on these findings, the patient was diagnosed with intestinal tuberculosis. He had a history of pulmonary tuberculosis. Chest computed tomography revealed inflammatory nodules and pleural thickening in the pulmonary apex regions (Figure 3a and 3b), consistent with the previous pulmonary tuberculosis. To exclude active pulmonary tuberculosis, spu-

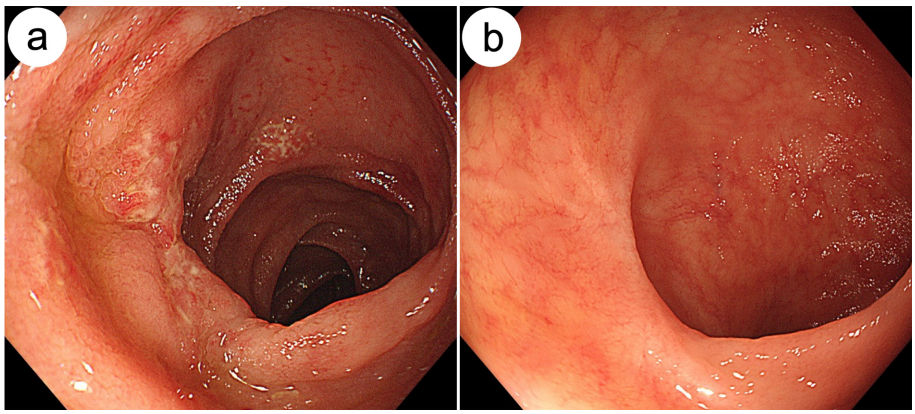

Figure 1 Endoscopic findings of the terminal ileum before (a) and after (b) the antitubercular treatment. (a) Colonoscopy showing edema, indicated by the lack of visible vascular pattern and mucosal erosions with scars in the terminal ileum. (b) Colonoscopy after completion of antitubercular treatment showing a lack of lesions in the terminal ileum.

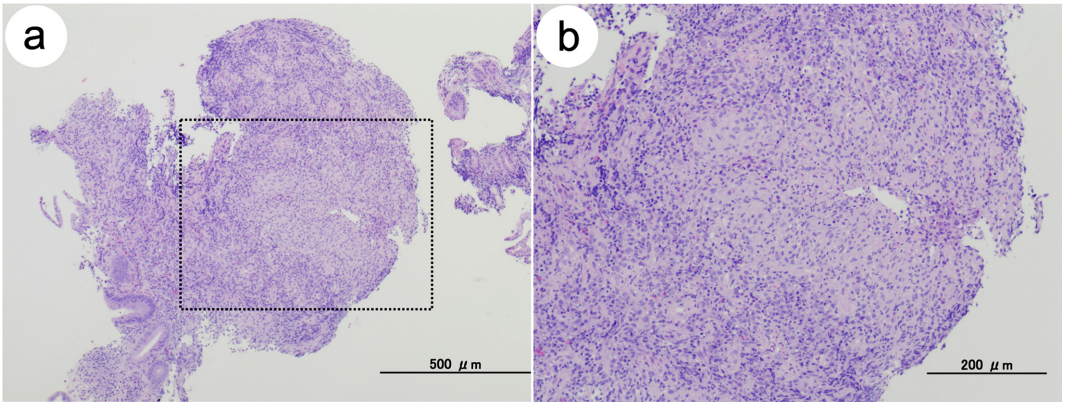

Figure 2 Pathological findings before the initiation of antitubercular treatment. (a) Hematoxylin and eosin staining of the biopsy specimen showing granulation tissue formation, consistent with an epithelioid granuloma. Caseating necrosis is absent. Scale bar, 500 μm. (b) An enlarged image of the regions enclosed within the dotted line shown in (a). Scale bar, 200 μm.

Table 1 Laboratory data at the time of diagnosis of intestinal tuberculosis

Parameter	Data	N.R.	Parameter	Data	N.R.
WBC (cells/μL)	7,290	3,300–8,600	Na (mmol/L)	135	138–145
Neut (%)	54.0	38–74	K (mmol/L)	4.5	3.6–4.8
Lym (%)	25.8	16.5–49.5	Cl (mmol/L)	103	101–108
RBC ($\times10^6$/μL)	4.63	4.35–5.55	T.Bil (mg/dL)	0.5	0.4–1.5
Hb (g/dL)	14.2	13.7–16.8	AST (U/L)	30	13–30
Ht (%)	40.7	40.7–50.1	ALT (U/L)	28	10–42
Plt ($\times10^3$/μL)	194	158–348	ALP (U/L)	265	106–322
PT (%)	100	70–130	γ-GTP (U/L)	49	13–64
TP (g/dL)	7.9	6.6–8.1	ChE (IU/L)	282	240–486
Alb (g/dL)	4.2	4.1–5.1	Amy (U/L)	83	44–132
TC (mg/dL)	156	142–248	CRP (mg/dL)	1.07[a]	<0.14
HDL-C (mg/dL)	40	38–90	ESR 30 min (mm)	5	2–10
LDL-C (mg/dL)	88	65–163	60 min (mm)	28[a]	2–10
TG (mg/dL)	139	40–243	CEA (ng/mL)	3.0	<5.0
FBS (mg/dL)	83	73–109	CA19-9 (U/mL)	14.5	<37.0
HbA1c (%)	5.0	4.9–6.0	T-SPOT.TB	(+)	(–)
UN (mg/dL)	11.9	8.0–20.0	HBs-Ag	(–)	(–)
Cr (mg/dL)	0.93	0.65–1.07	HCV-Ab	(–)	(–)

[a]Increased compared with normal range. Alb: albumin; ALP: alkaline phosphatase; ALT: alanine aminotransferase; Amy: amylase; AST: aspartate aminotransferase; CA19-9: CA19-9 antigen; CEA: carcinoembryonic antigen; ChE: cholinesterase; Cl: chloride; Cr: creatinine; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FBS: fasting blood glucose; γ-GTP: gamma-glutamyl transpeptidase; Hb: hemoglobin; HbA1c: hemoglobin A1c; HBs-Ag: hepatitis B surface antigen; HCV-Ab: hepatitis C virus antibody; HDL-C: high-density lipoprotein cholesterol; Ht: hematocrit; K: potassium; LDL-C: low-density lipoprotein cholesterol; Lym: lymphocyte; Na: sodium; Neut: neutrophil; N.R.: normal range; Plt: platelet; PT: prothrombin; RBC: red blood cell; T.Bil: total bilirubin; TC: total cholesterol; TG: triglyceride; T-SPOT.TB: tuberculosis specific interferon-γ releasing assay; TP: total protein; UN: urea nitrogen; WBC: white blood cell.

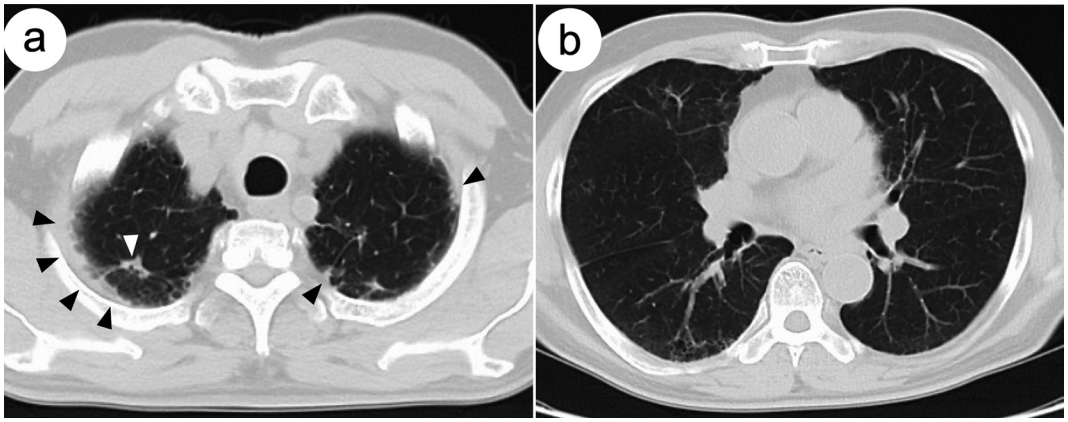

Figure 3 Chest computed tomography images before antitubercular treatment.
Chest CT scan images showing: (a) inflammatory nodules (white arrow) and pleural thickening (black arrows) in the pulmonary apex regions, (a and b) emphysematous changes in the apical and middle lung fields. CT, computed tomography.

tum examinations were performed thrice. Sputum smears and culture tests were negative, and PCR revealed the absence of *Mycobacterium tuberculosis* deoxyribonucleic acid in the sputum specimens. Thus, lesions found in the terminal ileum on colonoscopy were considered secondary intestinal tuberculosis, arising from pulmonary tuberculosis.

The patient was asymptomatic and had no abnormal physical findings, such as anemia or emaciation, at the time of diagnosis (Table 1). Blood examination revealed increased C-reactive protein (CRP) level and erythrocyte sedi-

mentation rate (ESR), suggesting a chronic inflammatory state (Table 1). Therefore, the patient was required to undergo antitubercular treatment according to the international guidelines for tuberculosis[10]. The patient was treated with isoniazid, rifampicin, ethambutol, and pyrazinamide for 2 months, followed by isoniazid and rifampicin for an additional 4 months. During treatment, the patient was followed up every 2 weeks to assess any treatment-related adverse events. Two weeks after initiating antitubercular treatment, small skin eruptions with slight itchiness developed on his extremities and trunk. However, these eruptions improved following oral administration of an antihistamine. The patient completed the treatment regimen without additional adverse events. A follow-up colonoscopy revealed healing of the mucosal edema and erosions in the terminal ileum (Figure 1b). Biopsy specimens obtained from the scars showed fibrosis and slight infiltration of inflammatory cells into the stroma; however, no epithelioid granulomas or caseating necrosis were observed. In addition, a PCR test and a 6-week culture of the biopsy specimens confirmed the absence of *Mycobacterium tuberculosis*. The CRP levels and ESR returned to normal after antitubercular treatment. Intestinal tuberculosis did not recur during the 3 years of follow-up.

Discussion

Individuals with intestinal tuberculosis commonly present with nonspecific clinical manifestations, such as fever, abdominal pain, diarrhea, weight loss, and fatigue[1, 4, 5]; however, symptoms are occasionally absent[1, 5–7]. The diverse and nonspecific clinical presentations of intestinal tuberculosis make it difficult to diagnose[11]. Diagnosing asymptomatic intestinal tuberculosis is particularly challenging, leading to incorrect or missed diagnosis[1, 5]. Untreated intestinal tuberculosis can cause severe morbidity, leading to prolonged hospitalization and surgery[11]. Therefore, understanding the features of asymptomatic intestinal tuberculosis is essential for adequate disease management.

Fifteen asymptomatic intestinal tuberculosis cases, including this case, have been reported since 2004 (Table 2). A colonoscopy was performed on all patients. Twelve of the 15 patients (Cases 1–6 and 9–14) had lesions in the large intestine, and three (Cases 7, 8, and 15), including our patient, had lesions only in the terminal ileum (Table 3). In our patient (Case 15), the lesions were discovered after an incidental colonoscope insertion into the terminal ileum during the initial colonoscopy, leading to the diagnosis of intestinal tuberculosis. The terminal ileum is not routinely examined during colonoscopy[5, 9]; therefore, missed diagnoses may occur in patients with lesions localized to the terminal ileum. In Case 8, the lesions were confined to the terminal ileum and were overlooked during the initial colonoscopy[5]. Considering that the terminal ileum is one of the most frequent sites of intestinal tuberculosis[8, 11], colonoscopy and observation of the terminal ileum are essential for diagnosing intestinal tuberculosis.

A positive FOBT result led to the diagnosis in 10 of the 15 cases of asymptomatic intestinal tuberculosis presented in Table 2. FOBT, particularly immunological FOBT (IFOBT), is widely used for colorectal cancer (CRC) screening because its sensitivity is higher than that of guaiac-based FOBT[12, 13]. IFOBT is specific for human hemoglobin and is more sensitive and specific for detecting occult bleeding from any intestinal lesion[14]. Therefore, IFOBT can show a positive reaction to lesions with occult lower gastrointestinal bleeding, including CRC. A prospective cross-sectional

Table 2 Characteristics of the asymptomatic patients with intestinal tuberculosis (clinical profile)

Author, year	Case no.	Age (years)/sex	Clinical symptoms	Reason for CS	Underlying disease	Refs.
Sato *et al.*, 2004	1	64 F	None	FOBT positive	N/A	5)
Sato *et al.*, 2004	2	55 F	None	FOBT positive	N/A	5)
Sato *et al.*, 2004	3	69 F	None	FOBT positive	N/A	5)
Sato *et al.*, 2004	4	65 F	None	FOBT positive	N/A	5)
Sato *et al.*, 2004	5	58 F	None	FOBT positive	N/A	5)
Sato *et al.*, 2004	6	84 M	None	FOBT positive	N/A	5)
Sato *et al.*, 2004	7	74 M	None	Follow up of colon polyps	N/A	5)
Sato *et al.*, 2004	8	56 M	None	Postoperative surveillance	N/A	5)
Yang *et al.*, 2007	9	38 M	None	Medical checkup	None	6)
Yamane *et al.*, 2013	10	47 M	None	FOBT positive	None	7)
Yamane *et al.*, 2013	11	72 F	None	FOBT positive	None	7)
Inoue *et al.*, 2017	12	62 F	None	FOBT positive	None	8)
Lin *et al.*, 2022	13	N/A	None	Medical checkup	N/A	9)
Lin *et al.*, 2022	14	N/A	None	Medical checkup	N/A	9)
Current study	15	71 M	None	FOBT positive	Hypertension	N/A

CS: colonoscopy; FOBT: fecal occult blood test; F: female; M: male; N/A: not applicable; No.: number; Refs.: references.

Table 3 Characteristics of the asymptomatic patients with intestinal tuberculosis (lesion site and endoscopic findings)

Author, year	Case no.	Lesion site	Endoscopic findings	Refs.
Sato *et al.*, 2004	1	Transverse colon	Annular ulcer with flared surrounding nodules	5)
Sato *et al.*, 2004	2	Ascending colon	Annular ulcer with flared surrounding nodules	5)
Sato *et al.*, 2004	3	Ascending colon	Annular ulcer with flared surrounding nodules	5)
Sato *et al.*, 2004	4	Transverse colon	Small ulcers without surrounding nodules	5)
Sato *et al.*, 2004	5	Ascending colon	Small ulcers without surrounding nodules	5)
Sato *et al.*, 2004	6	Sigmoid colon	Multiple erosions, mucosal edema	5)
Sato *et al.*, 2004	7	Terminal ileum	Aphthous ulcer, erosions	5)
Sato *et al.*, 2004	8	Terminal ileum	Aphthous ulcer, erosions	5)
Yang *et al.*, 2007	9	Cecum	Annular ulcer with flared surrounding nodules	6)
Yamane *et al.*, 2013	10	Terminal ileum–Ascending colon	Annular ulcer, scarring mucosa	7)
Yamane *et al.*, 2013	11	Terminal ileum–Ascending colon	Annular ulcer, multiple erosions	7)
Inoue *et al.*, 2017	12	Cecum–Ascending colon	Annular ulcer with scars	8)
Lin *et al.*, 2022	13	Terminal ileum–Cecum	Small ulcers with irregular fold	9)
Lin *et al.*, 2022	14	Terminal ileum– Cecum	Small ulcers with irregular fold	9)
Current study	15	Terminal ileum	Multiple erosions, mucosal edema	N/A

N/A: not applicable; No.: number; Refs.: references.

Table 4 Characteristics of the asymptomatic patients with intestinal tuberculosis (pathological findings and bacteriological results)

Author, year	Case no.	Caseating granuloma	Non-caseating granuloma	Ziehl–Neelsen staining	Culture of biopsy samples	PCR of biopsy samples	IGRA	Refs.
Sato *et al.*, 2004	1	−	+	−	−	N/A	N/A	5)
Sato *et al.*, 2004	2	−	+	−	+ (*M. tuberculosis*)	N/A	N/A	5)
Sato *et al.*, 2004	3	−	+	−	+ (*M. tuberculosis*)	N/A	N/A	5)
Sato *et al.*, 2004	4	−	−	−	+ (*M. tuberculosis*)	N/A	N/A	5)
Sato *et al.*, 2004	5	−	−	−	+ (*M. tuberculosis*)	N/A	N/A	5)
Sato *et al.*, 2004	6	−	−	+	−	N/A	N/A	5)
Sato *et al.*, 2004	7	+	−	−	−	N/A	N/A	5)
Sato *et al.*, 2004	8	−	+	−	+ (*M. tuberculosis*)	N/A	N/A	5)
Yang *et al.*, 2007	9	+	−	−	+ (*M. tuberculosis*)	+	N/A	6)
Yamane *et al.*, 2013	10	−	+	−	−	−	+	7)
Yamane *et al.*, 2013	11	−	−	−	−	−	+	7)
Inoue *et al.*, 2017	12	−	−	−	−	−	+	8)
Lin *et al.*, 2022	13	−	+	+	−	N/A	N/A	9)
Lin *et al.*, 2022	14	−	−	−	−	N/A	+	9)
Current study	15	−	+	−	+ (*M. tuberculosis*)	+	+	N/A

IGRA: Interferon gamma release assay; N/A: not applicable; No.: number; Refs.: references.

study involving 200 asymptomatic subjects in Bangladesh confirmed positive IFOBT results in 90 patients. Eighty of them underwent colonoscopy, and intestinal tuberculosis was identified in five patients (6%)[14]. This indicates that a positive FOBT result can lead to a diagnosis of intestinal tuberculosis in asymptomatic individuals, although the prevalence of intestinal tuberculosis differs by country and region[11]. Therefore, clinicians should consider intestinal tuberculosis in the differential diagnosis of patients with positive FOBT results without gastrointestinal symptoms.

Several diagnostic modalities, including pathological examination, acid-fast bacilli staining, culture, PCR of biopsy specimens, and IGRA, have been used to diagnose intestinal tuberculosis. The sensitivity and specificity of each modality have been reported to be 68% and 77.1% for pathological examination[15], 17.3%–31% and 100% for acid-fast staining[1], 9.3% and 100% for culture[1], 42% and 97% for PCR[16], and 74%–88% and 74%–87% for IGRA[17–20]. Except for IGRA, the sensitivity of these modalities is relatively low, and the risk of obtaining false-negative results is high. Therefore, a combination of diagnostic modalities is required for diagnose[21]. Several diagnostic modalities were used in all asymptomatic intestinal tuberculosis cases, as shown in Table 4, and a combination of these modalities helped diagnose intestinal tuberculosis in 14 of 15 cases (Cases 2–15). Case 1 had nonspecific findings on pathologi-

cal or bacteriological tests for intestinal tuberculosis screening (Table 4). However, the patient was suspected to have the disease based on typical endoscopic findings (Table 3). Our patient also had nonspecific findings on pathological examination and acid-fast bacilli staining (Ziehl–Neelsen staining). However, the results of both culture and PCR of biopsy specimens facilitated the diagnosis of intestinal tuberculosis (Table 4). A recent report demonstrated that a combination of history-taking, physical examination, and several diagnostic modalities can improve diagnosis accuracy and prevent underdiagnosis[1]. Thus, clinicians should use a combination of diagnostic modalities for suspected intestinal tuberculosis.

The primary treatment for intestinal tuberculosis is oral administration of antitubercular agents, including isoniazid, rifampin, ethambutol, and pyrazinamide[10]. International guidelines recommend 6 months of therapy with standard regimens for pulmonary tuberculosis[10], which is sufficient to achieve a response. Prolonged treatment for more than 6 months showed no additional benefit[22]. A small proportion of patients may require surgery due to complications, such as intestinal strictures, despite the administration of oral antitubercular agents[23, 24]. None of the asymptomatic intestinal tuberculosis cases identified in the literature review required surgery. All patients were cured after receiving oral antitubercular agents, although the details of each treatment regimen and period were not fully reported for all patients[5–9]. Thus, the oral administration of antitubercular agents effectively treats asymptomatic intestinal tuberculosis.

Conclusion

This study describes a case of asymptomatic intestinal tuberculosis in which a colonoscope insertion into the terminal ileum was critical for diagnosis. Asymptomatic intestinal tuberculosis can occasionally be discovered by colonoscopy after a positive FOBT result, and the lesions are sometimes present only in the terminal ileum. Therefore, clinicians need to consider intestinal tuberculosis in the differential diagnosis of the causes of positive FOBT results and perform colonoscopies, including observation of the terminal ileum.

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Consent for publication: Written informed consent was provided by the patient for the publication of this study.

Data availability statement: The anonymized patient data used in this study are all included in the text.

Author contributions: HS and MS contributed to the study conception and design. HS, HI, JT, MK, TI, and YS performed the case study and acquired the data and images. HS analyzed and interpreted the data and wrote the manuscript. HS, TI, YS, and MS revised the manuscript. MS supervised manuscript preparation. All the authors have read and approved the final version of the manuscript.

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