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CASE REPORT

Submucosal tumor-like lesion originating from colon tuberculosis: a case report and review of the literature

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Abstract A 76-year-old male had a solitary submucosal tumor-like lesion in the sigmoid colon originating from tuberculosis. The lesion, up to 1 cm in diameter, was found incidentally during a routine colonoscopy, which revealed a protuberant submucosal growth with a shallow depression of the overlying mucosa in the center of the tumor. Histologically, the endoscopic biopsy revealed caseating granulomas and infiltration of Langhans giant cells and epithelioid cells, consistent with tuberculosis, were also observed. Five reports of similar lesions from colon tuberculosis were found in a literature review, including the present case. In all cases, the submucosal tumor-like lesions which originated from tuberculosis were small and in an active stage of tuberculosis. Five cases of submucosal tumor-like lesions from gastric tuberculosis were also reported, with characteristics very similar to those of the lesions from colon tuberculosis. Therefore, we propose that lesions originating from tuberculosis should be included in the differential diagnosis of submucosal tumor-like lesions in the colon and stomach.

Keywords Colon · Tuberculosis · Submucosal tumor-like lesions · Colonoscopy

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Introduction

Endoscopic diagnosis of active colon tuberculosis is not difficult because of many fairly specific endoscopic findings, such as ulcerative hyperplastic lesions [1]. Findings regarding submucosal tumor-like lesions have not been included in the differential diagnosis of submucosal tumor lesions, although there have been some recent reports about submucosal tumor-like lesions originated from colon tuberculosis. Here, we present a case of a submucosal tumor-like lesion in the sigmoid colon formed during the course of tuberculosis.

Case report

A 76-year-old male, admitted to our hospital in May 2014 to start hemodialysis, also presented with severe anemia and general fatigue. He had no history of pulmonary tuberculosis or diabetes mellitus. His family history was unremarkable. Findings on admission were height 160 cm, weight 50 kg, body temperature 37.3 °C, respiration rate 12 breaths/min, blood pressure 163/100 mmHg, pulse rate (regular) 100/min. A humming systolic murmur and normal respiratory sound were audible. There was low-grade pitting edema in the lower legs but no swelling of surface lymph nodes. On admission, he was in the terminal stage of chronic renal failure based on levels of blood urea nitrogen (181 mg/dl), creatinine (10.97 mg/dl), electrolyte disturbance (Na 123 mEq/L, K 6.4 mEq/L, Cl 89 mEq/L), increase of CRP (9.74 mg/dl), and soluble IL-2 receptor (3,380 U/ml) (Table 1). Other serological parameters and tumor markers were within normal limits. In addition to chronic renal failure, gastrointestinal (GI) tract malignancy, tuberculosis, and malignant lymphoma were selected for

Table 1 Laboratory data on admission

Hematology		*Blood chemistry*		Fe	91 μg/dl
WBC	5,300 /μl	T. Bil	0.3 mg/dl	Ferritin	226 mg/dl
neut.	89.5 %	AST	20 IU/L	*Serology*	
lymph.	3.9 %	ALT	14 IU/L	CRP	9.74 mg/dl
mono.	6.6 %	LDH	194 IU/L	TPLA	(−)
eo.	0 %	ALP	291 IU/L	HBsAg	(−)
baso.	0 %	γ-GTP	38 IU/L	HCVAb	(−)
RBC	347 × 10^4 /μl	BUN	181 mg/dl	*Tumor markers*	
Hb	9.5 g/dl	Cre	10.97 mg/dl	CEA	4.4 ng/ml
Ht	29.3 %	Na	123 mEq/L	CA19-9	15.5 U/ml
Plt	14.2 × 10^4 /μl	K	6.4 mEq/L	AFP	1.3 ng/ml
Coagulation and fibrinolysis		Cl	89 mEq/L	PIVKA-II	12 mAU/ml
PT	66 %	Ca	6.2 mEq/L	s-IL2-R	3380 U/ml
PT (INR)	1.27	T-chol	162 mg/dl		
APTT	37.9 sec	TG	116 mg/dl	SpO_2 (room air)	97 %
Fibrinogen	335.3 mg/dl	T.P.	6.4 g/dl		
FDP	16.9 μg/ml	Alb	2.5 g/dl		
D-dimer	9.4 μg/ml	FBS	135 mg/dl		
AT-3	64 %	HbA1c (NGSP)	5.8 %		

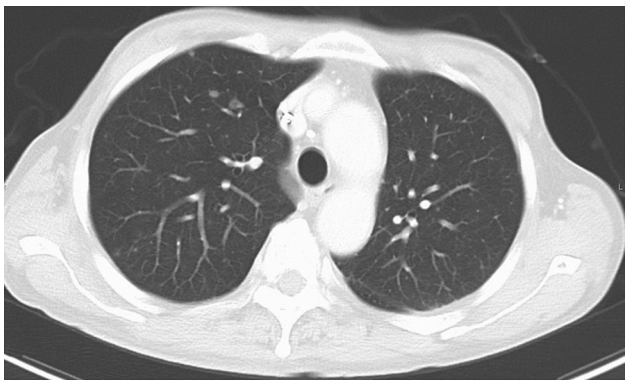

Fig. 1 Chest CT on 18th hospital day revealed diffuse small multiple nodular lesions, which suggested miliary tuberculosis

differential diagnosis. Abdominal computed tomography (CT), echography, and endoscopy were performed.

Abdominal echography revealed multiple small (several mm in diameter), low-echo level hepatic lesions. Tumors (up to 5 cm in diameter) were observed bilaterally on the abdominal aorta.

Chest and abdominal plain radiographs and chest CT on admission revealed no abnormal findings. However, on the 18th hospital day, chest CT revealed multiple small, nodular lesions, suggesting miliary tuberculosis (Fig. 1).

Abdominal CT on admission revealed multiple small cystic lesions and borderless low-CT level lesions in the liver, a nodular lesion in the left adrenal gland, multiple swollen lymph nodes surrounding the abdominal aorta, and bilateral kidney atrophy. There was no remarkable lesion in the sigmoid colon. Thus, malignant lymphoma and metastatic lesions of a GI tract malignancy were suggested. We performed a gastroscopy on the 13th hospital day, which revealed esophageal hiatal hernia, Barrett's epithelial cells, and atrophic gastritis.

A colonoscopy on the 31st hospital day revealed a solitary protuberant submucosal tumor-like lesion with a shallow central depression of the overlying mucosa in the sigmoid colon, 28 cm from the anus. The tumor was up to 1 cm in diameter, and the surface was slightly yellowish on magnifying endoscopy (Fig. 2a). A shallow central depression of the submucosal tumor-lesion was revealed by indigo carmine staining (Fig. 2b). Narrow band imaging (NBI) revealed vessel networks on the tumor surface. During colonoscopic biopsy of the submucosal tumor-lesion, we observed white liquid-like pus (Fig. 2c). There were no remarkable findings in the ileocecal region.

Histologic endoscopic biopsy revealed caseating necrosis and epithelioid cell infiltration in the colon mucosa to the submucosal layer (Fig. 3a). Caseating granulomas and liquefactive necrosis were observed in the submucosal layer (Fig. 3b). At high magnification, epithelioid and Langhans giant cell infiltration was recognized (Fig. 3c). Several acid-fast bacteria were identified in necrotic tissues by Ziehl−Neelsen staining (Fig. 3d). Therefore, a submucosal tumor-like lesion was suspected to have been formed from the inflammatory granuloma and liquefactive necrosis due to tuberculosis.

Peripheral blood T-spot-Tb test (estimation of γ-interferon from activated T cells specific for antigens of *Mycobacterium tuberculosis*) was positive. Gastric juice and bacterial cultured sputa and gastric juice were positive for

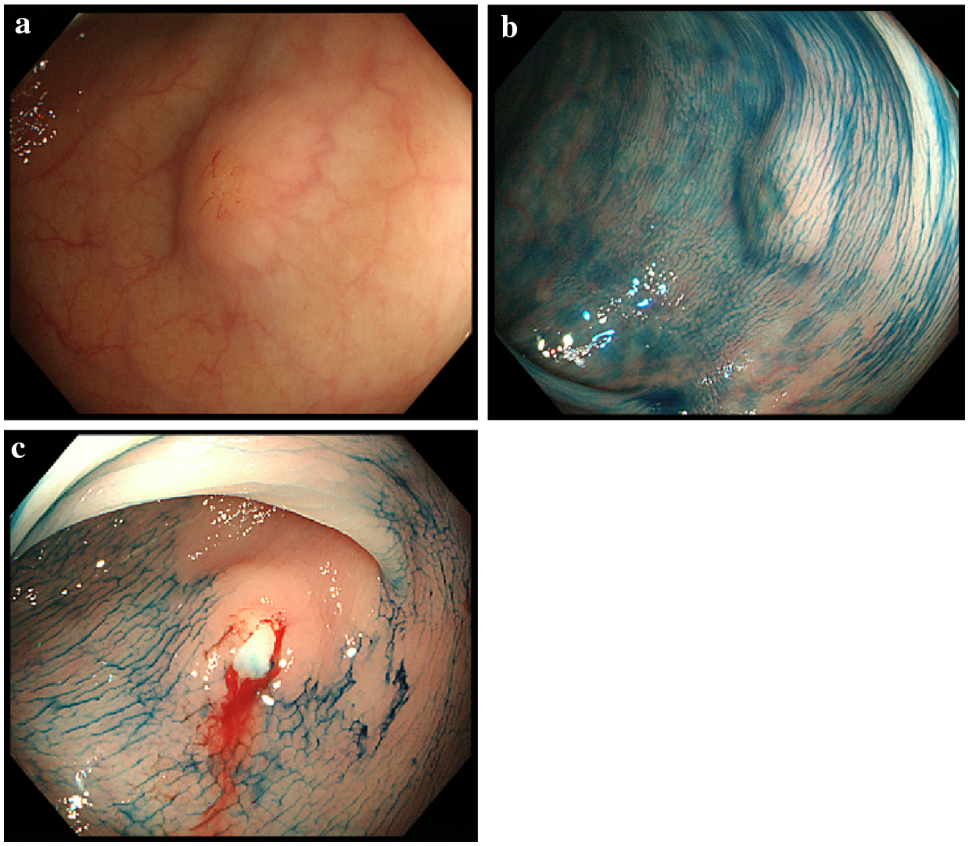

Fig. 2 **a** Colonoscopy on 31st hospital day revealed solitary protuberant submucosal tumor-like lesion with a shallow central depression of the overlying mucosa in sigmoid colon, 28 cm from the anus.(**a**) The tumor was approximately 1 cm in diameter and the surface of tumor showed vessel networks. The color of the tumor surface was slightly yellowish on magnifying endoscopy.(**b**)A shallow central depression of submucosal tumor-lesion was revealed by indigo carmine staining.(**c**)When a colonoscopic biopsy of the submucosal tumor lesion was performed, white liquid-like pus leaked

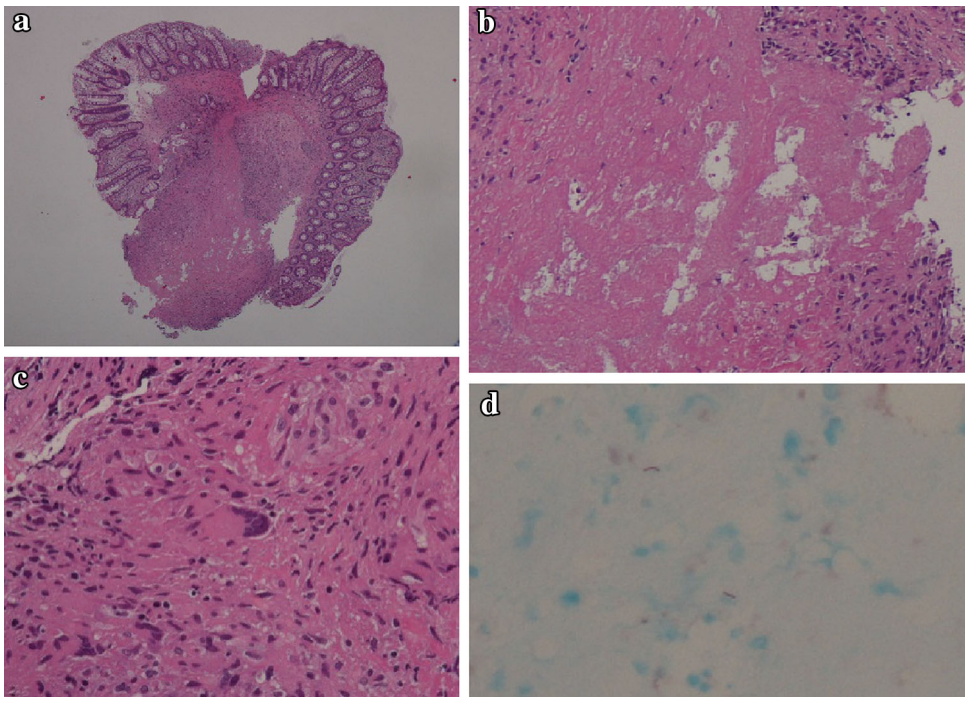

Fig. 3 Pathohistological examination of the endoscopic biopsy specimen. Histologically, the endoscopic biopsy revealed caseating necrosis and infiltration of epithelioid cells in the colon mucosa to the submucosal layer (**a,** H&E × 40). Caseating granuloma and liquefactive necrosis were observed in the submucosal layer (**b,** H&E × 200**).** In high magnification, infiltration of epithelioid cells and Langhans giant cells were recognized **(c,** H&E × 400**)**. Several acid-fast bacteria were identified in necrotic tissues by Ziehl−Neelsen staining **(d,** Z–N, × 400**)**

acid-fast bacteria. *M. tuberculosis* complex (*M. tuberculosis, bovis,* and *africanum*) was positive by polymerase chain reaction (PCR) in gastric juice and sputa.

From these findings and clinical course, tuberculosis of the lung, colon, and abdominal adrenal and lymph nodes was diagnosed. We decided to administer isoniazid (INH)

Table 2 Case reports showing submucosal tumor-like lesion due to colon tuberculosis

No.	Age (years)	Sex	Localization	Size	Endoscopic findings	References
1	66	Female	Ileocecal	Approx. 1 cm	Multiple small ulcers Deformity of ileocecal valve Stenoasis, ulcer and inflammatory polyps	Tachikawa et al. [10]
2	55	Male	Rectum	2 cm	Shallow central depression	Yanagida et al. [11]
3	57	Male	Ascending–descending	No size	Multiple small open ulcers Multiple mucosal nodules predominantly	Yoshino et al. [12]
4	37	Male	Rectum	1 cm	Presence of a rectal mass	Choudhury et al. [13]
5	76	Male	Sigmoid	Approx. 1 cm	Shallow central depression Color of surface was slightly yellowish Leaking white liquid-like pus	Present case

We searched PubMed using 'colon tuberculosis' and 'submucosal tumor and found four case reports; these four cases and the present case are summarized

(300 mg/day), rifampicin (RFP) (450 mg/day), and ethambutol (EB) (750 mg/day). However, we did not administer pyrazinamide, because liver dysfunction was observed in the patient before treatment. After administration of INH, RFP, and EB was initiated on the 39th hospital day, fever improved, and CT on the 66th hospital day, revealed that the size of lung lesions was drastically reduced. CT on the 215th hospital day revealed no lung lesions and a reduction in lymph nodes surrounding the abdominal aorta. The diagnosis of tuberculosis of the lung, colon, and adrenal and lymph nodes was confirmed with the effects of INH, RFP, and EB.

Discussion

In the present case, the findings of a submucosal tumor-like lesion, normal tumor surface mucosa, the cushion sign, and the tenting sign were typical of submucosal tumors [2, 3]. According to the criteria of Paustian et al. [4] at least one of the following specific findings must be obtained for a conclusive diagnosis of intestinal tuberculosis—caseating granulomas, acid-fast bacilli, or positive bacterial cultures. The absence of reliable evidence often makes a diagnosis of tuberculosis difficult. Pathophysiological findings, identification of acid-fast bacilli (*M. tuberculosis*) in the lesion, PCR-positivity for *M. tuberculosis* complex in sputa and gastric juice, and the effect of anti-tuberculous chemotherapy confirmed that submucosal tumor-like lesions were formed from *M. tuberculosis* infection in this case.

Typical intestinal tuberculosis has recently become rare since the advent of effective anti-tuberculous chemotherapy [5]. However, *M. tuberculosis* infection remains prevalent globally, especially in developing countries. Even in Japan, total mortality due to *M. tuberculosis* infection amounts to approximately 20,000 per year [6]. The aging society and prevalence of HIV, [7] diabetes, chronic renal failure, and the increasing use of immunosuppressants, including anti-TNFα antibody, [8] may lead to increasing tuberculosis infection. In turn, submucosal tumor-like lesions due to tuberculosis may also increase. Such findings will become more important for rapid diagnosis in the early stages of colon tuberculosis, when submucosal tumor-lesions are observed. In that regard, tuberculosis infection should be included in the differential diagnosis of submucosal tumor lesions.

Intestinal tuberculosis usually presents with mucosal ulceration typically occurring as skip lesions developing circumferentially. Bowel wall deformity, such as clover-like pseudo-diverticulosis, follows ulcer healing. The endoscopic findings for colon tuberculosis including ulceration, inflammatory polyps, sclerotic lesions [9], and deformation of the Bauhin valve are well known, but submucosal tumor-like lesions are rare in colon tuberculosis. We searched PubMed using 'colon tuberculosis' and 'submucosal tumor' as keywords and found four case reports. These four cases and the present case are summarized in Table 2 [10–13]. Male patients were predominant. Localization of submucosal tumor-like lesion originated from tuberculosis, ileocecal, ascending–descending, sigmoid and rectum, are not fixed. Tumor diameter was <2 cm in all cases and <1 cm in three cases.

The mechanism by which submucosal tumors form is speculative; as these lesions are very small, submucosal tumor-like lesions would be formed during the early and active stage of tuberculosis. Granuloma formation and liquefactive necrosis of caseating lesions are candidates as causes of tumor formation in tuberculosis. In our case, leaking of white liquid-like pus from the biopsied lesion was first observed. Accumulation of seminar cases are needed to confirm that submucosal tumor-like lesions form

partially from tuberculosis abscesses. During granuloma formation with tuberculosis, a cold abscess would form through liquefactive caseating necrosis during the inflammation against bacilli, as lung cavity formation occurs through liquefaction of caseating lesions. Lung tuberculoma is a tumor-like lesion consisting of granuloma enclosed by collagenous tissue. The tubercle may damage surrounding tissue, leading to necrosis and granulomatous reaction. Since the tubercle usually grows non-expansively, damage to the surrounding tissue seems unlikely. Moreover, the oil-drop appearance of the granuloma cannot be explained by this process. Oil from the suppositories may have been the foreign body described by Yanagida et al. [11]. Tuberculosis infection would have been only the first step in granuloma formation, followed by a secondary foreign-body reaction to the oil suppository.

We searched PubMed again using 'gastric tuberculosis' and 'submucosal tumor as keywords and found five case reports [14–18]. Male patients were predominant. Tumor sized ranged from 2.5−5 cm. Since submucosal tumor-like lesions were observed in both gastric and colon tuberculosis, they should be recognized as common finding of GI tuberculosis.

Submucosal tumors of the colon are relatively uncommon. Tumors of smooth muscle and lymphoid tissue, vascular hamartomas, lipomatous and neurogenic tumors, and other miscellaneous neoplastic tumors arise as nonepithelial tumors of the colon. In our search, we found five cases showing submucosal tumor-like lesions originated from tuberculosis, suggestive of tuberculoma (granuloma formation), in the colon.

In conclusion, we propose that colon tuberculosis should be included in the differential diagnosis of submucosal tumor-like lesions.

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Disclosures

Conflict of Interest: All authors report no conflict of interest.

Human/Animal Rights: Please confirm that this study has been approved by the appropriate ethics committee and that there will be no problem to publish the statement below. If this study does not contain any data about human or animal subjects, edit the text in the space below.

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