

## Investigation of Undetected Small Bowel Tumors on Capsule Endoscopy

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### ABSTRACT

**AIM:** The rate of undetected small bowel tumors when performing capsule endoscopy (CE) has been reported to be 44.1% to 83.3%. The aim of this study was to review the CE findings in patients with small bowel tumors and analyze the cases in which CE failed to detect tumors.

**METHODS:** Twenty-one cases (18 males, 3 females) with small bowel tumors underwent CE and double-balloon enteroscopy at the Dokkyo Medical University Hospital and the Nikko Medical Center from February 2003 to March 2015. CE findings in the 21 patients were retrospectively reviewed on the basis of the lesion shape and location.

**RESULTS:** Of the 21 patients, CE accurately diagnosed tumors in 12 patients (57.1%). However, tumors were not detected in 9 patients because of a poor endoscopic view due to visual obstruction caused by blood, bowel residue, or feces ( $n=5$ ; 23.8%), the presence of ulcerated lesions ( $n=3$ ; 14.3%), or angioectasia ( $n=1$ ; 4.8%). The sources of bleeding were considered to be ulcerated lesions or angioectasia. Of the 9 patients, 7 patients had tumors in the duodenum or the proximal jejunum.

**CONCLUSION:** On CE, small bowel tumors showed atypical features, including a smooth submucosal bulge and the presence of ulcerated lesions and of blood, bowel residue, or feces, probably due to regional transit abnormalities related to the tumor. In such cases, it may be necessary to perform computed tomography, positron emission tomography/computed tomography, other examinations, or repeat CE after performing colonic irrigation to remove bowel residue.

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**Key words:** Capsule endoscopy; Small bowel tumor; Ulcerated lesions; Undetected small bowel tumor; Regional transit abnormalities; Small bowel GIST with an extraluminal growth pattern

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### List of abbreviations

CE: capsule endoscopy; CT: computed tomography; DBE: double-balloon enteroscopy; GI: gastrointestinal; GIST: gastrointestinal stromal tumor; OGIB: obscure gastrointestinal bleeding; RAPID: Reporting and Processing of Images and Date; RTA: regional transit abnormalities; SMT: submucosal tumor; PET: positron emission tomography; PET/CT: positron emission tomography/computed tomography; M: Male; F: Female

### INTRODUCTION

Capsule endoscopy (CE) can be used for imaging of the small and large intestines. This simple and non-invasive endoscopy technique has many potential uses; however, the possibility of undetected

lesions is a major issue, with the failure to detect neoplastic lesions having a major impact on prognosis. According to the literature, the rate of undetected neoplastic lesions in small-bowel CE is high (44.1% to 83.3%)<sup>[1-4]</sup>. Therefore, the aim of this study was to review CE findings in patients with small bowel tumors and analyze cases in which CE failed to detect tumors.

## METHODS

### Patients

Among the 404 patients who underwent CE at the Dokkyo Medical University Hospital and the Nikko Medical Center between February 2003 and March 2015, the presence of small bowel tumors was confirmed by double-balloon endoscopy (DBE) or surgery in 21 patients (mean age, 60.9±14.9 years; 18 males; 3 females). Indications for CE in the 404 patients included gastrointestinal bleeding and anemia (66.0%), diarrhea (12.4%), abdominal pain (8.4%), screening for tumors (3.7%), and others (9.5%).

CE findings in the 21 patients were reviewed retrospectively. The items to analyze were as follows: (1) the detection rates of the small bowel tumors by CE; (2) the analysis of CE findings based on the lesion shape and location identified by DBE and surgery, when the tumor was not found by CE.

### CE procedure

Either the Pillcam SB or the Pillcam SB2 (Given Imaging, Yoqneam, Israel) devices was used for CE. The analysis was conducted using Reporting and Processing Images and Data (RAPID) v6.5. Patients were maintained on a nil per oral (NPO) status for 8 h prior to the examination. Immediately before ingesting the CE capsule, the patients were administered 40 mg in 4 ml of dimethicone solution. Fluid intake and food intake were allowed for 2 h and 4 h, respectively, after the ingestion of the CE capsule. Eight to 15 hours after ingestion, the recorder was recovered, and RAPID software was used to analyze the data.

**Table 1** Cases diagnosed with tumors by capsule endoscopy.

Age (Years)	Sex	Location	Lesion
57	M	Duodenum	GIST
83	M	Proximal jejunum	GIST
62	F	Proximal jejunum	GIST
56	M	Proximal jejunum	Malignant lymphoma
49	M	Jejunum	Small bowel leiomyoma
38	M	Ileum	Ectopic pancreas
36	M	Ileum	Ectopic pancreas
66	F	Ileum	Cavernous hemangioma
46	M	Ileum	Small bowel cancer
64	M	Terminal ileum	Small bowel cancer
67	M	Terminal ileum	Small bowel cancer
82	M	Terminal ileum	Metastatic small bowel tumor

**Table 2** Cases of undetected small bowel tumor on capsule endoscopy.

Cause	Case	Age	Sex	Location	Lesion
Poor view caused by blood or bowel residue	1	71	M	Terminal ileum	GIST with extraluminal growth pattern
	2	78	M	Duodenum (Near the pyloric ring)	Duodenal cancer
	3	73	F	Duodenum	Carcinoid
	4	60	M	Proximal jejunum (near of ligament of Treitz)	Metastatic small bowel tumor
	5	27	M	Proximal jejunum (near of ligament of Treitz)	Metastatic small bowel tumor
Presence of angiectasia and poor view caused by blood and foam	6	62	M	Proximal jejunum (near of ligament of Treitz)	Metastatic small bowel tumor
Presence of ulcerated lesions	7	75	M	Proximal jejunum	Small bowel cancer
	8	62	M	Duodenum (Post-gastric resection anastomosis site)	Metastatic small bowel tumor
	9	64	M	Jejunum - ileum	Enteropathy-associated T-cell Lymphoma

## RESULTS

CE identified tumors in 12 of the 21 patients (57.1%) but failed to detect tumors in 9 patients (Table 1). Tumors were not detected in 9 patients for the following reasons: poor observation due to blood, bowel residue, or feces ( $n=5$ ; 23.8%); the presence of ulcerated lesions ( $n=3$ ; 14.3%); and the presence of angiectasia (the source of bleeding was considered to be angiectasia because of poor observation due to blood and foam.) ( $n=1$ ; 4.8%) (Table 2). The tumors were found in 3 of the 9 patients in the duodenum and 4 of the 9 patients in the proximal jejunum. We present all the 9 cases below.

### Case 1

A 71-year-old male with schizophrenia, chronic renal failure, and asthma had previously undergone upper and lower gastrointestinal (GI) endoscopy due to chronic anemia, but the source of bleeding was unclear. He underwent CE for chronic anemia. Over three years, CE had been performed three times, with negative findings on each occasion caused by residue in the terminal ileum. Computed tomography (CT) demonstrated a neoplastic lesion with a diameter of 7 cm in the terminal ileum, however, DBE indicated a small protruding lesion. The final diagnosis was gastrointestinal stromal tumor (GIST) with an extraluminal growth pattern after surgical resection (Figure 1).

### Case 2

A 78-year-old male with chronic renal failure was referred to our hospital because of obscure GI bleeding (OGIB). CE showed duodenal bleeding and a blood clot. Upper GI endoscopy revealed circumscribed irregular ulcerative lesions (duodenal cancer at biopsy). The final diagnosis was duodenal cancer after surgical resection.

### Case 3

A 73-year-old female was hospitalized for melena. CE showed duodenal bleeding and a blood clot. DBE revealed a well-defined smooth submucosal tumor (SMT). The final diagnosis after surgical resection was carcinoid tumor.

### Case 4

A 60-year-old male was hospitalized for melena. The upper and lower GI endoscopy were normal. He underwent CE for OGIB. The CE showed feces, bowel residue, and a blood clot; however, DBE revealed small bowel tumors. Chest CT indicated lung cancer. The final diagnosis on biopsy was metastatic small bowel tumors (lung cancer).

### Case 5

A 27-year-old male with mesotheliomas was referred to our hospital for melena (OGIB). CE showed bowel residue and a blood clot;

however, DBE revealed small bowel tumors. The final diagnosis on biopsy was metastatic small bowel tumors (mesothelioma).

**Case 6**

A 62-year-old male was hospitalized for melena (OGIB). CE showed angioectasia with bleeding and foam; however, DBE indicated angioectasia and small bowel tumors. Chest CT demonstrated lung cancer. The final diagnosis was metastatic small bowel tumors (lung cancer) at biopsy.

**Case 7**

A 75-year-old male with arteriosclerosis obliterans was hospitalized for melena. The upper and lower GI endoscopy was unremarkable. CE revealed focal irregular upper jejunal ulceration; however, the CE could not differentiate an ulcerated lesion from a small bowel tumor. DBE indicated irregular elevated and ulcerative lesions. The final diagnosis was small bowel tumor after surgical resection (Figure 2).

**Case 8**

A 62-year-old male after surgery (total gastrectomy) of gastric cancer was hospitalized for melena. CE showed blood clots and irregular ulcerated lesions. DBE revealed irregular ulcerated lesions at the site of post-gastric resection anastomosis. The final diagnosis was metastatic small bowel tumors (gastric cancer) after surgical resection.

**Case 9**

A 64-year-old male was admitted to our hospital for chronic abdominal pain and diarrhea. CT showed an isolated dilation and wall thickening of the small intestine. CE revealed diffuse infiltration, ulcerative lesions and atrophic villous in the jejunum and ileum. The final diagnosis was enteropathy-associated T-cell lymphoma at biopsy.

**DISCUSSION**

Small bowel tumors account for only 1% to 6% GI tumors<sup>[5,6]</sup>. However, the introduction of CE and DBE has led to increased detection rates of small bowel tumors, which are identified in 7% to 17.4% patients with OGIB<sup>[7-10]</sup>. According to the report, small bowel tumors included GIST (28.6% to 32.1%), adenocarcinomas (20.5% to 25%), neuroendocrine tumor (14.3% to 15.2%), malignant lymphomas (10.7% to 14.3%), adipose tumors (8.9%), metastatic tumors (10.7%), and Kaposi sarcoma (3.6%)<sup>[11,12]</sup>. Furthermore, the types of malignant small bowel tumor included adenocarcinoma (47%), carcinoid (28%), leiomyosarcoma (13%), and lymphoma (12%)<sup>[13]</sup>.

Approximately one half of these small bowel tumors could be diagnosed by CE; however, the other tumors were not detected. The reasons attributed are follows: (1) the presence of ulcerated lesions; (2) the presence of blood, bowel residue, or feces that may be caused by regional transit abnormalities (RTAs) related to the tumor; (3) submucosal tumors (SMTs); (4) undetected tumor.

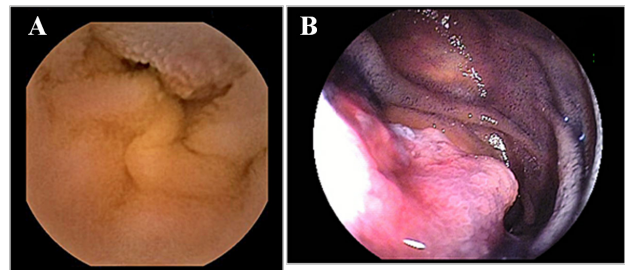


Figure 2 Capsule endoscopy findings in the proximal jejunum. B. Double-balloon endoscopy findings in the proximal jejunum.

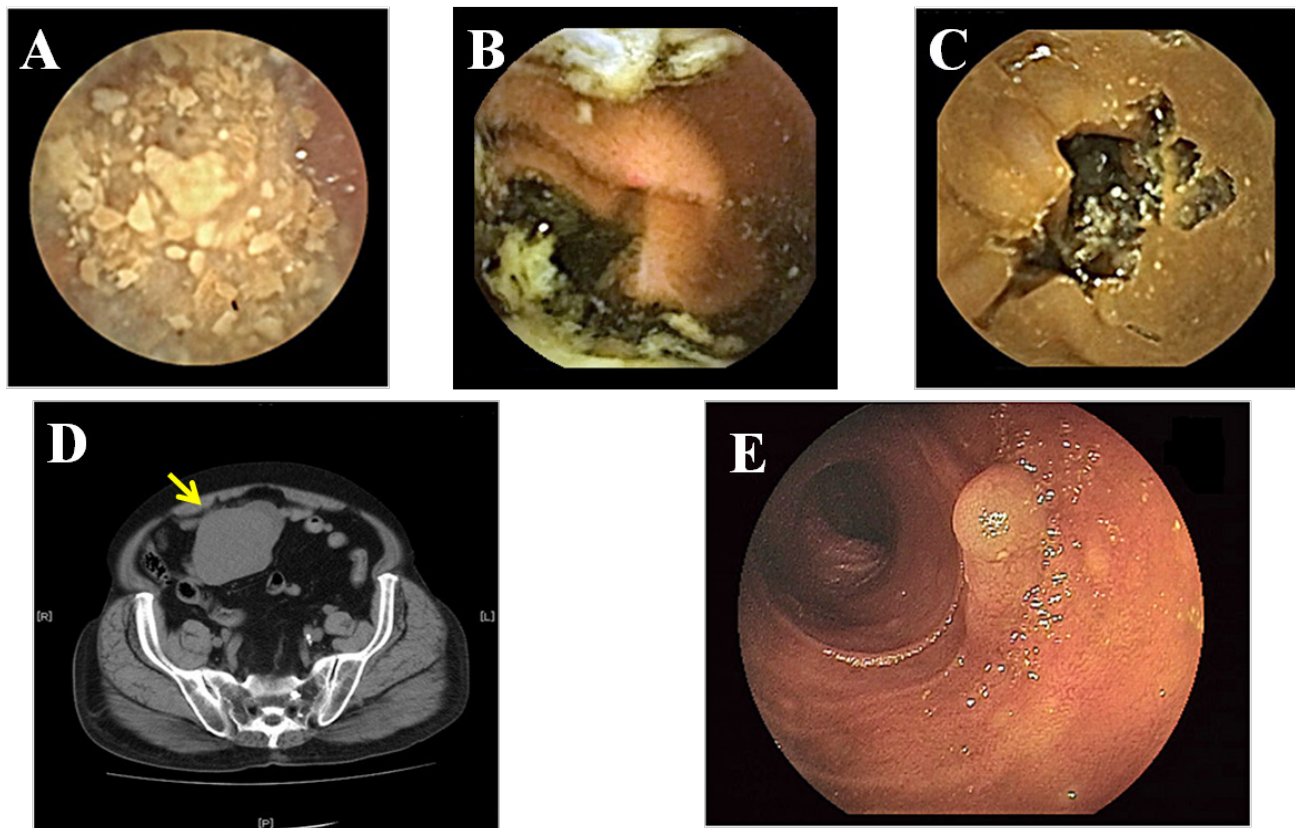


Figure 1 Case 1. Capsule endoscopy findings in the terminal ileum. A. Initial examination. B. One year later. C. Three years later. D. Abdominal computed tomography showed the tumor (arrow). E. Double-balloon endoscopy findings in the terminal ileum.



### (1) The presence of ulcerated lesions

According to the literature, malignant small bowel tumors are reported to appear as irregular ulcers and ulcerated lesions on CE<sup>[6]</sup>. Hence, ulcerated lesions should be considered as tumors.

### (2) The presence of blood, bowel residue, or feces

Regional transit abnormalities (RTAs) were defined as delayed transit within a segment of small bowel, with or without visualization of a mucosal abnormality<sup>[14,15]</sup>. RTAs can detect the presence of tumor besides actual visualization of tumor on CE<sup>[14]</sup>. In general, the intestinal transit abnormalities increase bowel residues because of a GI congestion. Therefore, the presence of GI congestion such as blood, bowel residue, or feces should also be considered as a sign of the presence of tumors.

### (3) Submucosal tumor (SMT)

Approximately 70% of small bowel tumors are SMTs<sup>[11]</sup>. Because endoscopic imaging of SMT reveals smooth submucosal bulge with normal overlying mucosa, it is difficult to distinguish an SMT bulge from those caused by GI tract bending, peristalsis, or external pressure. Caution is necessary that CE finding is a smooth submucosal bulge with or without central umbilication (Delle).

Furthermore, the most common SMTs are GISTs, which can be divided into intraluminal growth pattern, intramural growth pattern, extraluminal growth pattern, and mixed type. The small bowel GISTs with extraluminal growth pattern type are likely to be difficult to diagnose by either DBE or CE, because these do not show up clearly inside the lumen<sup>[16,17]</sup>.

In addition, common symptoms of GIST include GI bleeding (28%) and abdominal symptoms (14%)<sup>[18]</sup>; however, they are uncommon and show an extraluminal growth pattern, resulting in a delay in detection. There are few reported cases of small bowel GIST with extraluminal growth pattern, such as Case 1. In this case, the use of positron emission tomography (PET) and CT together with CE or DBE may be necessary<sup>[19]</sup>.

### (4) Undetected tumor

The rate of undetected neoplastic lesions during small bowel CE is reported to be 44.1% to 83.3%<sup>[1-4]</sup>. For the colon, the colonoscopy has been reported to have a failure rate of 22.8% to 26.0% for detecting lesions<sup>[20,21]</sup> compared with 16% to 33.4% for colonic CE<sup>[22,23]</sup>. According to these reports, the reasons for detection failure on colonoscopy and CE of the colon include the following: the lesion being hidden by the folds of the large intestine, bowel residue, or feces; technical issues, such as the probe being pulled out suddenly and preventing complete observation; or missing the lesion.

For the small intestine, the most common reason for failure to detect a lesion was the lesion being hidden by blood, bowel residue, or feces. The measures to prevent this may include the use of colonic cleansers to secure the field of vision. In 7 of the 9 cases (33.3%), CE failed to detect a tumor that was located in the duodenum to the proximal jejunum. It has been reported that undetected tumor by CE located in the proximal jejunum<sup>[2,4,24]</sup>. This may be because CE travels very quickly through this region<sup>[25]</sup>, and the imaging frame rate is fixed at 2 frames/s when CE is performed with the PillCam<sup>®</sup> SB2 and RAPID<sup>®</sup> Access 6.5 software. This may result in the lesion being insufficiently imaged. However, this issue should be improved when using PillCam<sup>®</sup> SB3 and RAPID<sup>®</sup> Access 8 software because adaptive frame rate technology allows the frame rate to alternate from 2 to 6 frames/s automatically and in accordance with the speed of travel through the GI tract.

In our study, eight of the 9 cases that were not identified as the neoplastic lesions by CE underwent DBE or treatment due to the presence of bleeding, and one of the 9 cases had been followed up. Taking into account cases that are completely overlooked with the total number of cases that underwent CE during the study period (404 cases), the rate for completely missing tumors was approximately 0.24%. Although there have been few similar studies, Baichi *et al* reported 2 cases in which tumors were detected by CT or surgery after no abnormalities were noted on CE<sup>[2]</sup>, and the rate for completely overlooking tumors was 0.66% (2/300). Therefore, when performing CE, physicians should keep in mind that a small bowel tumor may be overlooked in approximately 0.2% to 0.6%.

In conclusion, CE findings of the small bowel tumors had showed atypical features including a smooth submucosal bulge, ulcerated lesions, and the presence of blood, bowel residue, or feces. In the cases of such CE findings, it may be necessary to perform CT, PET/CT, or repeat CE after performing colonic irrigation to remove bowel residue.

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## CONFLICT OF INTERESTS

The Authors state that they have no conflict of interest (COI).

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