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IM - REVIEW

Sporadic small bowel tumors detected by capsule endoscopy in patients with occult gastrointestinal bleeding

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Abstract Intestinal tumors represent less than 6 % of digestive tumors, and, because of the limitations of intestinal investigations, these tumors are difficult to diagnose. In this context, capsule endoscopy has proven effective, especially in patients with obscure digestive bleeding. In a large series of patients undergoing capsule endoscopy, small bowel tumors are found in 2.4–8.9 % of cases. The aim of this retrospective, single-center study, based on prospective database, is to evaluate the frequency of small bowel tumors detected by capsule endoscopy in patients with occult gastrointestinal bleeding. During 2004–2014, 849 consecutive patients underwent CE at our Department for occult gastrointestinal bleeding. Following capsule endoscopy, the medical records of the study population were reviewed. Results of double-balloon enteroscopy or surgery performed after capsule endoscopy were retrieved. Capsule endoscopy identified 55 small bowel tumors (6.5 %), of which 28 malignancies (51 %) and 27 benign neoplasms (49 %) underwent surgery or endoscopic treatment. Malignancies included adenocarcinoma (18.7 %), gastrointestinal stromal tumors (GIST) (12 %) and lymphoma (6.7 %). Benign neoplasms included dysplastic adenomatous polyps (36 %) and hyperplastic polyps (25.3 %). Non-neoplastic masses included one inflammatory polyp. Capsule retention occurred in four patients (5.3 %) and the retained capsule was retrieved during surgery. In our experience neoplasms of small bowel are found in 6.5 % of patients with occult gastrointestinal bleeding. Of these malignancies, small bowel neoplasms are found in 3.3 % of cases. Capsule endoscopy is an effective and sensitive diagnostic tool, and plays an important role in the algorithm for the diagnostic workup of suspected small bowel tumors.

Keywords Capsule endoscopy · Small bowel tumors · Occult gastrointestinal bleeding

Introduction

The small bowel (SB) represents almost 75 % of the gastrointestinal tract extension and nearly 90 % of its mucosal surface, but it is considered a rare site for tumors. SB tumors, either benign or malignant, account for 3–6 % of all digestive neoplasms, although the accuracy of these estimates is uncertain because the traditional methodologies for examining small bowel have been proved inadequate [1]. Most SB tumors are malignant, but they represent only 1.1–2.4 % of gastrointestinal malignancies [2]. SB tumors are the source of bleeding in some patients with obscure gastrointestinal bleeding (OGIB), particularly younger patients. In large series of patients undergoing CE, SB tumors are found in 2.4 % [3], 8.9 % [4, 5], 6.3 % [6], and 4.3 % [7] of cases. Malignant tumors are found in 4.2, 4, and 2.7 % of patients, respectively. In a multicenter Belgian study, the percentage of malignant tumors is 2.5 % [8].

Capsule endoscopy (CE) has become a first-line diagnostic tool in OGIB when the SB is a suspected source. Compared with push enteroscopy (PE), which is performed to establish the source of bleeding, CE detects more than twice as many clinically significant abnormalities (56 vs.

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26 %), whereas any abnormalities are detected in 63 % with CE vs. 28 % with PE [9]. Balloon-assisted enteroscopy (BAE), most often double-balloon enteroscopy (DBE), is performed following both a negative CE or as a complementary procedure guided by the CE findings. Initial studies suggest that CE and DBE have a comparable diagnostic yield in patients with suspected SB disease, including OGIB, when the whole SB is visualized [10].

We performed a retrospective, single-center study, based on prospective database, to characterize frequency, clinical and laboratory signs, endoscopic findings related to SB tumors detected in patients who underwent CE.

Materials and methods

Patients' selection

Patients, who presented with evidence of GI bleeding at the clinic or emergency department between January 2004 and October 2014, were enrolled in the present study after at least one negative upper gastrointestinal endoscopy and colonoscopy. Patients with OGIB were classified into two categories: (a) overt bleeding, and (b) obscure occult bleeding, i.e., anemia associated with positive fecal occult blood without overt bleeding.

CE procedure

The GIVEN Video Capsule system (Given Imaging, Yoqneam, Israel) was used with M2A-SB capsules in 839 patients and MiroCam (IntroMedic Co. Ltd, Seoul, Korea) in 10 patients. In our experience, and according to the literature to date, there are no significant differences in sensitivity and specificity between the two devices [11].

The preparation for CE included fasting from lunchtime onwards, and ingesting 4 l of glycol polyethylene the day before the examination. The capsule was swallowed by the patients with 200 ml water after a sensor array was applied to their abdomen and connected to the data recorder, which they wore on a belt. Patients were allowed to drink clear liquids 3 h after swallowing the capsule. All equipment was disconnected after 8 h, and the images were downloaded and reviewed by two experienced reviewers. The location of the lesions in the small bowel was determined by the time ratio, which was calculated by the transit time from the pylorus to the lesion divided by the transit time from the pylorus to the caecum. Capsule retention was defined as a capsule remaining in the digestive tract for a minimum of 2 weeks, or a capsule remaining in the bowel lumen that required endoscopic or surgical intervention. All the capsule endoscopy examinations were read by the same gastroenterologist (CC).

In a standard evaluation, CE findings were further classified as negative or positive. Positive findings were also classified in two ways: clinically significant or non-significant lesions; in other words, clinically significant lesions were defined as following: (a) tumors or polyps $\geq$10 mm, (b) active bleeding, (c) blood clots, and (d) mucosal breaks.

As CE allows for only an approximate estimation of polyp size, a cutoff polyp diameter of 10 mm was used.

We carefully reviewed results of double or single-balloon, intraoperative enteroscopy performed following CE, and eventually the surgery that was carried out.

Results

Between January 2004 and October 2014, 849 (442 men; mean age 58.3 $\pm$ 20.2 years) consecutive patients underwent CE for OGIB. The characteristics and findings of the study population are summarized in Table 1. All patients swallowed the capsule without difficulty, and the procedure was well tolerated without adverse events.

SB tumors were detected in 75 patients (46 men; mean age 63.7 $\pm$ 17.9 years) (8.8 %). The most frequent tumors are adenocarcinomas ($n = 14$; 18.7 %), gastrointestinal stromal tumors (GIST) ($n = 9$; 12 %), and lymphoma ($n = 5$; 6.7 %) (Table 2) (Fig. 1). Benign neoplasms include dysplastic adenomatous polyps ($n = 27$; 36 %). Non-neoplastic lesion include an inflammatory polyp ($n = 1$) and hyperplastic polyps ($n = 19$; 25.3 %).

The OGIB was occult in 69 patients (92 %) and overt in 6 (8 %). Mean hemoglobin level at presentation was

Table 1 Characteristics and results of the study population ($n = 849$)

	n (%)
Mean age (SD), years	58.3 (±8.2)
Gender (M/F)	442/407
Overt gastrointestinal bleeding	28 (3.3 %)
Occult gastrointestinal bleeding	821 (96.7 %)
Significant findings	
Vascular lesions	163 (19.2 %)
Mucosal breaks	181 (21.3 %)
Tumor or polyp ≥10 mm	75 (8.8 %)
Active bleeding with no visible origin	12 (1.4 %)
Insignificant findings	
Erythema or red spots	162 (19.1 %)
White spots	60 (7.1 %)
Other	10 (1.2 %)
Normal	160 (18.8 %)
Non-diagnostic	26 (3.1 %)

Table 2 Characteristics of patients with malignancy detected on capsule endoscopy

No.	Age (years)	Sex	Bleeding on CE	Location	Capsule retention	Surgery/BE results	Outcome
1	83	M	Yes	Jejunum	No	Adenocarcinoma	Surgery
2	82	M	No	Jejunum	No	Adenocarcinoma	Surgery
3	68	F	No	Jejunum	No	Adenocarcinoma	Surgery
4	79	F	Yes	Ileum	Yes	Adenocarcinoma	Surgery
5	43	M	No	Ileum	No	Adenocarcinoma	Surgery
6	47	M	No	Jejunum	Yes	Adenocarcinoma	Surgery
7	80	M	No	Ileum	No	Adenocarcinoma	Surgery
8	45	M	No	Ileum	Yes	Adenocarcinoma	Surgery
9	81	M	No	Ileum	No	Adenocarcinoma	Surgery
10	72	F	No	Jejunum	Yes	Adenocarcinoma	Surgery
11	78	F	No	Jejunum	No	Adenocarcinoma	Surgery
12	50	M	No	Jejunum	No	Adenocarcinoma	Surgery
13	85	M	No	Jejunum	No	Adenocarcinoma	Surgery
14	51	F	No	Jejunum	No	Adenocarcinoma	Surgery
15	31	M	No	Ileum	No	GIST	Surgery
16	70	M	No	Ileum	No	GIST	Surgery
17	25	F	No	Ileum	No	GIST	Surgery
18	72	F	No	Jejunum	No	GIST	Surgery
19	46	M	Yes	Jejunum	No	GIST	Surgery
20	77	F	Yes	Jejunum	No	GIST	Surgery
21	69	M	No	Ileum	No	GIST	Surgery
22	76	F	No	Ileum	No	GIST	Surgery
23	46	M	No	Ileum	No	GIST	Surgery
24	71	M	Yes	Jejunum	No	Lymphoma	Surgery
25	85	M	Yes	Ileum	No	Lymphoma	Surgery
26	69	M	No	Ileum	No	Lymphoma	Chemotherapy
27	81	M	No	Ileum	No	Lymphoma	Chemotherapy
28	55	F	No	Ileum	No	Lymphoma	Chemotherapy

CE capsule endoscopy, *BE* balloon enteroscopy, *GIST* gastrointestinal stromal tumor

9.4 ± 2.6 g/dl. The capsule reached the colon in 70 (93.3 %) examinations.

Capsule retention occurred in four patients (5.3 %) of the overall population. In particular, all these patients had an adenocarcinoma-related stenosis, and in these patients the retained capsule was retrieved during surgery.

In addition, in 50 patients (66.7 %), the final diagnosis of lymphoma (3 patients), adenomatous (27 patients), hyperplastic polyps (19 patients) and inflammatory polyp (1 patient) was reached using double or single-balloon enteroscopy with biopsies. Surgery was carried out in all patients with adenocarcinoma and GIST, and two of five of lymphomas. Three patients with lymphoma underwent chemotherapy.

In two patients CE showed active bleeding without clear mucosal alteration. For the persisting anemia and overt bleeding they underwent surgery, and the resected pathological specimens revealed a lymphangioma in one case and a bleeding lipoma in the other one.

CE showed no lesions in one patient. This patient underwent single-balloon endoscopy for persisting anemia, and positive fecal occult blood examination that showed a middle ileal ulcerated lymphoma without active bleeding at that moment.

In summary, CE detected SB tumors in 75/78 patients (70.5 %) and identified only active bleeding in two patients (2.6 %). CE failed to find any lesion in only 1 patient (1.3 %).

Discussion

Capsule endoscopy allows trouble-free endoscopic imaging of the entire small bowel, and several studies reveal its diagnostic superiority over other modalities in detecting small bowel lesions [9]. Fukumoto et al. report that CE and DBE are nearly equal in their ability to detect small bowel lesions if the entire small bowel is examined [12]. Arakawa

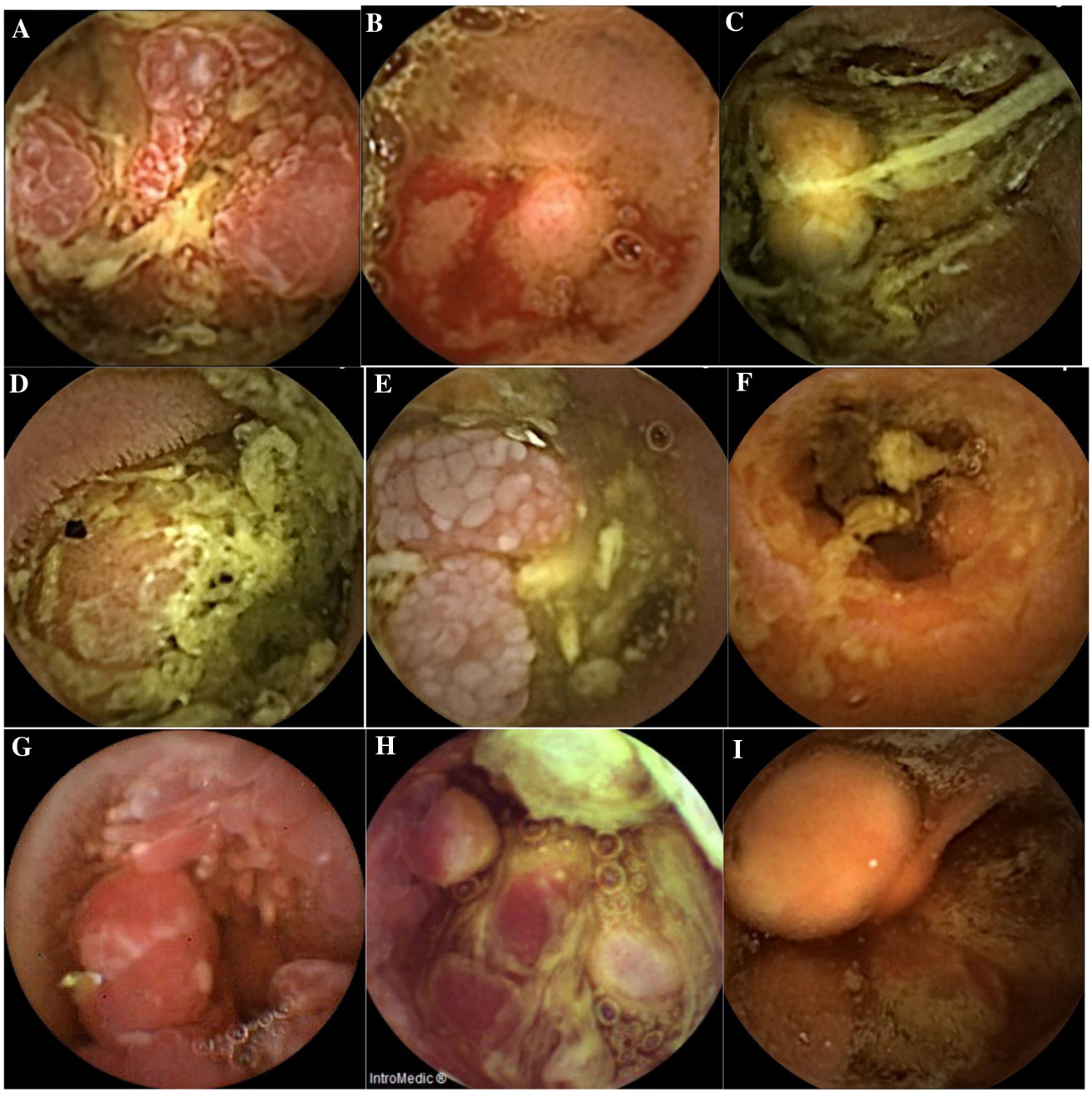

Fig. 1 Malignancy lesions finding at capsule endoscopy. **a–c** Adenocarcinomas, **d–f** lymphoma, **g–i** gastrointestinal stromal tumor

et al. and Pasha et al. report similar results [10, 13]. Nevertheless, CE lacks the ability to obtain biopsy specimens and perform therapeutic procedures.

In our study, the percentage of tumors found is 6.5 %, higher than in other CE series, which may be explained by a well-defined diagnostic criteria used in our center to select patients who undergo CE [2–8]. Our results may be used to create an optimal management of these patients, and to help allocate the economic resources of our national health care system.

There are several differences among the published series, the most important being the number of CE examinations performed, which may explain the significant differences of reported prevalence. Thus, when the relationship between the frequency of tumors detected and the number of CEs performed is examined, there is an inverse relationship, suggesting that the high number of CEs carried out might be related to the low prevalence of tumors detected [3]. In the largest database so far published of SB tumors detected by CE (124 tumors with

5129 capsule procedures performed), Rondonotti et al. report a 2.4 % prevalence of SB tumors, and Pasha et al., in a study including 1000 CE examinations, report a 1.6 % prevalence of SB tumors [3, 10]. There is no clear explanation for these significant differences in the prevalence of SB tumors between studies with high and low number of CE examinations performed. It has been suggested that the studies with fewer CEs carried out adopt stricter criteria for patient selection [13]. In our opinion, other issues are also important, i.e., the lack of pathological examination in some studies, the different indications for CE, and the lack of distinction between malignant and benign tumors.

Our criteria for patient's selection may be more suitable for others when applied in clinical practice [14]. In fact, the endoscopic appearance of SB tumors at CE has been reported only in a few studies, due to the absence of generally accepted terminology. In the majority of cases in which the CE identified abnormalities, those were confirmed pathologically by enteroscopy or surgery.

In conclusion, in our study the prevalence of SB tumors found by CE in only OGIB patients is 6.5 %, and is similar to those studies that include a population with the same clinical characteristics. Capsule endoscopy should be used as the first choice for diagnostic investigation in patients suspected to have SB tumor, and, if necessary, should be followed by double or single-balloon enteroscopy, for histopathological confirmation of the diagnosis and endoscopic or surgery therapy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the author.

Informed consent Informed consent was obtained from all individual participants included in the study.

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