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Case report

Five years missed small jejunal stromal tumor (GIST) causing recurrent episodes of bleeding: Successful diagnosis by capsule endoscopy

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ABSTRACT

A case of obscure gastrointestinal bleeding of a 65-year old woman is presented in a way that illustrates the increasing importance of capsule endoscopy in the field of small bowel stromal tumors. The successful use of capsule endoscopy in this specific clinical context helps to portray an emerging role for capsule endoscopy as part of a new aggressive management strategy of small intestinal GISTs without the pitfalls of overdiagnosis or overtreatment.

Key words: gastrointestinal stromal tumour (GIST), capsule endoscopy, small intestine

INTRODUCTION

Small bowel tumors are the most common cause of obscure gastrointestinal bleeding in patients younger than the age of 50 years.[1] Capsule endoscopy has a high miss rate for neoplastic lesions (18.9%), but most studies underline the clear benefit in clinical outcome compared to vascular lesions since surgery usually equals cure.[2] Despite the frequent recognition of subepithelial neoplastic masses during routine endoscopy, confusion still exists concerning their correct management. Gastrointestinal stromal tumors (GISTs) represent the largest part of these neoplasms according to most recent studies.[3] Small intestine is the second most frequent site for GISTs (25%). Small bowel GISTs have a less favorable prognosis[4]. Furthermore even small tumors (<2 cm) of low mitotic activity can display metastatic potential.[5]The use of capsule endoscopy has revolutionized the investigation of tumors of the small intestine. Accumulating evidence proves its efficacy in diagnosing lymphomas[6], neuroendocrine tumors[7], and metastatic melanomas[8]. The rising incidence and importance of GISTs represents an interesting challenge for capsule endoscopy considering the particular characteristics of these neoplasms. The herein described case provides additional input, as part of a general effort to delineate its exact future role.

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Case Description

A 65 year-old female patient was referred to our department for further evaluation of gastrointestinal bleeding of unknown origin. The patient had repeated hospitalizations in various institutions over the last five years for either overt bleeding, usually melena, or anemia requiring occasional blood transfusions. The patient never showed signs of hemodynamic instability and bleeding episodes stopped spontaneously at all times. Routine laboratory examinations, celiac disease antibodies, and tumor markers were inconclusive. The patient had been submitted to a large number of diagnostic modalities including bidirectional endoscopy, small bowel follow through and conventional abdominal computed tomography. Nevertheless no single intervention had disclosed the source of bleeding. Capsule endoscopy was performed in a time interval close to a sudden drop of the patients' hematocrit. It was complete to the ileocecal valve and disclosed a protruding lesion in the proximal jejunum 54.5 min after capsule

ingestion (pylorus passage at 31 min). At close examination the mass appeared to have a small ulceration and caused partial stenosis without however delaying capsule passage (Fig. 1A, 1B). The endoscopic appearance of the mass (normal overlying mucosa with umbilical ulceration) was strongly suggestive of a submucosal tumor. Since the tumor was clearly symptomatic (bleeding) and resectable, no further diagnostic evaluation was deemed necessary because it would not significantly affect final management. The patient had an unremarkable otherwise medical history, and agreed to have this mass surgically removed. The resected mass proved indeed to be a mesenchymal tumor expressing strong positivity for CD117 antigen (Fig. 2A, 2B). Mitotic index (5 mitoses per 50 high power fields) and tumor size (largest diameter 2.4 cm) helped characterize it as a low risk gastrointestinal stromal tumor. The patients' recovery was uneventful and she is showing no signs of recurrence 1 year after the operation. Regular 6monthly CT scans are scheduled as part of her follow up despite the 'benign' nature of the tumor.

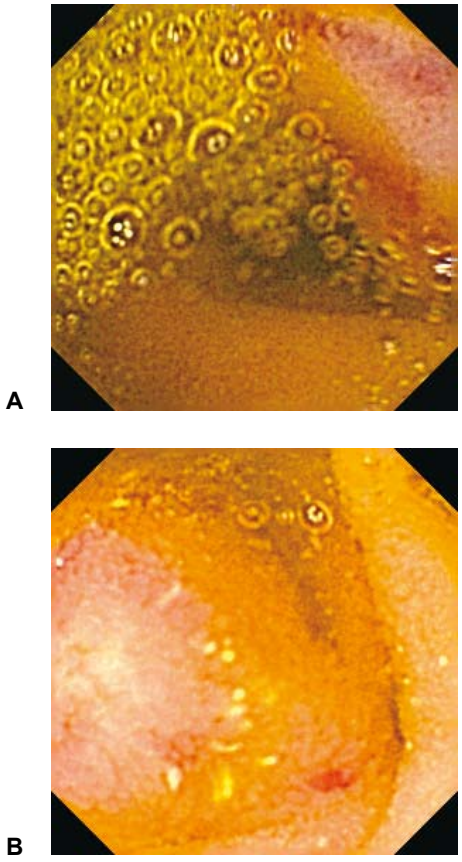

Figure 1A, 1B. Two views of capsule endoscopy showing a submucosal tumor of jejunum with a small central ulceration causing partial stenosis.

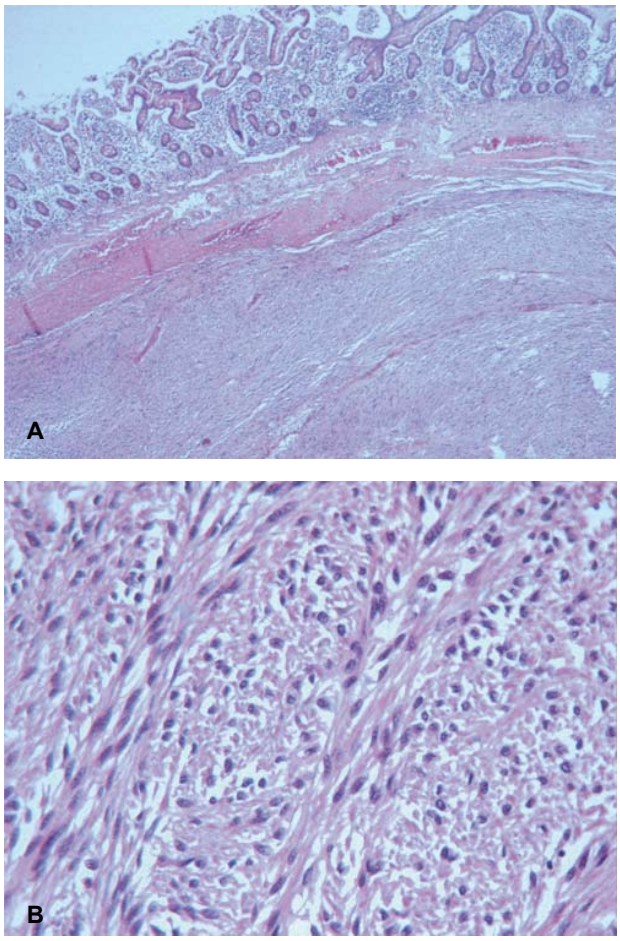

Figure 2A. Histological picture of the specimen showing the relation between the tumor and the jejunal mucosa (H&E stain, original magnification, 2.5X).

2B. Gastrointestinal stromal tumor (GIST) comprised predominantly of spindle cells (H&E stain, original magnification, 20X)

DISCUSSION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract. Recent population based studies estimate their annual incidence at about 10-20 per million per year, much higher than once thought.[9]Experts suggest that their actual incidence can be almost tripled if we include incidentalomas, meaning small tumors incidentally discovered during GI endoscopy performed for other reasons[10]. Although epidemiological data from therapeutic clinical trials show that not all GISTs will grow to be malignant, there is presently no way to accurately predict their biologic behavior, especially in the small bowel.

The ability of capsule endoscopy to detect small

bowel tumors was probably overestimated by previous studies.[11]A recent European multicenter study involving more than 5,000 patients resulted in a 2% frequency. Interestingly GISTs were the most commonly discovered tumors in this study.[12]

The endoscopic features of gastrointestinal stromal tumors are those of submucosal tumors: a mass with normal appearance of the overlying mucosa bulging into the lumen, with no signs of peristalsis and evident bridging of surrounding folds. The characteristic central ulceration is not always present, but it should be sought for, especially when bleeding is present.[13]Although the tumor in this case displayed those endoscopic signs, it was only visible in two images thus highlighting once again the high level of concentration and vigilance required.

Bleeding is the most frequent clinical manifestation of GISTs resulting from the tumor expanding and erupting into the mucosa. It is usually overt with only rare reports of fatal events.[14] It should be rather viewed by the clinician as an opportunity to diagnose an otherwise indolent tumor. Five years of unexplained gastrointestinal bleeding are not acceptable in the era of small bowel endoscopy. Some even go as far as proposing provoked anticoagulation during the procedure in order to facilitate the diagnosis.[15] Pooled epidemiological data provide us with an incentive to strive for early diagnosis in small intestinal stromal tumors since they carry a worse prognosis. This holds true even in the era of targeted therapy of GIST. Intestinal stromal tumors harbor exon 9 mutations almost exclusively and are considered more resistant to standard doses of imatinib treatment.[5] Capsule endoscopy cannot reliably distinguish benign from malignant tumors by consensus[16]. Performing biopsy on GISTs yields poor results because the tissue obtained is usually insufficient to confirm the diagnosis or classify risk of malignancy.[17] In addition biopsy of highly vascular tumors like GISTs entails the risks of bleeding and seeding and is best avoided in cases of potentially resectable disease[18, 19]. Endoscopic ultrasonography can provide additional help in other sites (stomach, esophagus, and rectum). Special probes of endoscopic ultrasonography have been successfully used during double or single balloon enteroscopy in case of small bowel GISTs[20]. Double balloon enteroscopy is particularly useful in the preoperative localization of lesions[21]. The caveats associated with biopsies of submucosal masses and the relatively accurate information on location and nature provided by this specific capsule endoscopy examination discouraged us from using it in this case. Of course as expertise increases double or single balloon enteroscopy will be more widely accepted and utilized in similar clinical circumstances. Magnetic Resonance Imaging enteroclysis seemed to offer no additional information to capsule endoscopy in this patient and there is no available published experience so far.

A trial concerning neuroendocrine tumors demonstrated superiority of capsule endoscopy compared to all other diagnostic modalities except for penreotide nuclear scintigraphy.[7] Because GISTs and neuroendocrine tumors have similar endoscopic features, respectively high sensitivity of capsule endoscopy in detecting GISTs could be expected. Future studies should establish the role of capsule endoscopy in detecting small GISTs as implied by numerous scattered case reports.[22] Patients with a high probability of harboring GISTs (Carneys triad, neurofibromatosis type 1) could serve as initial candidates for trials urgently needed in this direction. This would allow us to adopt an approach similar to that followed in colorectal or gastric tumors where abdominal imaging is used after endoscopy to stage the disease.

In conclusion, capsule endoscopy of the small intestine seems promising in the investigation of small intestinal stromal tumors. It has the potential of shortening the diagnostic work up, especially in cases of obscure gastrointestinal bleeding, provided that it is implemented early on. Gastrointestinal stromal tumors have been the focus of attention by oncologists in recent years. Our patients' case shows that the ability to recognize small intestinal GISTs (by capsule endoscopy and double balloon enteroscopy) and probably affect their natural history should help gastroenterogists be more actively involved in managing a so far unrecognized spectrum of the disease.

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