INTRODUCTION

Obscure gastrointestinal bleeding (OGIB) is due to small-bowel lesions such as neuroendocrine tumours (NETs), gastrointestinal stromal tumours (GISTs) or lymphomas up to 10% of cases. Jejunoileal NETs are often multifocal (up to 40% of cases) with a risk of regional lymph nodes involvement increasing with sizes more than 2 cm in diameter. The diagnosis is usually made by contrast-enhancement computed tomography (CT) scan, positron emission tomography (PET) scan, dosage of blood values (such as chromogranin A), gallium scintigraphy and balloon-assisted enteroscopy (BAE). The diagnosis and treatment of OGIB are a challenge for gastroenterologists and surgeons due to the difficulties in characterising and finding these lesions, especially if multifocal.

The development of laparoscopic surgery has changed the way to manage such conditions. In particular, laparoscopy may be associated with intraoperative balloon-assisted enteroscopy to detect and resect the intestinal bleeding tract.

Keywords: Capsule endoscopy, intraoperative balloon-assisted enteroscopy, lesions missed by capsule endoscopy, minimally invasive surgery, multiple neuroendocrine tumours, obscure gastrointestinal bleeding

Address for correspondence: Dr. Damiano Bisogni, Department of Oncology and Robotic Surgery, Careggi University Hospital, Largo Brambilla 3, Florence 50134, Italy.
E-mail: bisognifelice@libero.it
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Abstract

Jejunoileal neuroendocrine tumours (NETs) are frequently multifocal and represent a consistent source of obscure gastrointestinal bleeding (OGIB). We report the real-life case of a female presenting to our attention for severe episodes of haematochezia caused by multiple localisation of jejunoileal NETs. A discrepancy between pre-operative total body contrast-enhancement computed tomography scan and capsule endoscopy (CE) emerged, in terms of numbers of lesions, so that, as completeness, an intraoperative balloon-assisted enteroscopy (BAE) was carried out, leading to the detection of the multiple lesions missed during CE. In case of obscure gastrointestinal bleeding sources missed by capsule endoscopy, laparoscopic-assisted balloon enteroscopy plays an essential role, allowing both to assess a precise diagnosis and to resect the intestinal bleeding tract.
have three different roles: to validate the pathophysiologic diagnosis (diagnostic laparoscopy), to facilitate and guide a subsequent laparotomy (laparoscopic-assisted open approach) or finally to entirely treat the disease (fully laparoscopic approach).

**CASE REPORT**

A 73-year-old Caucasian female was admitted to our emergency department for severe episodes of haematochezia. The patient complained weakness and dyspnoea for the past month. Her past surgical history was significant for hysterectomy (due to fibromatosis) and right breast quadrantectomy for carcinoma. On the emergency department, she presented haemodynamic stability with the following values: arterial pressure – 107/70 mmHg, cardiac frequency – 101 bpm, rate blood oxygen – 90% and haemoglobin concentration – 5.1 g/dL.

As soon after a blood cell transfusion with 4 units of packed red blood corpuscles was done, an esophagogastroduodenoscopy and complete colonoscopy were performed without revealing any active source of bleeding. In the following days, she underwent a small-bowel study through a capsule endoscopy (CE) showing only an ileal polyp of about 1 cm in diameter with superficial ulceration: this was considered the most likely source of bleeding [Figure 1a]. Within the first 5 days after the hospital admission, she also underwent a total body contrast-enhancement CT scan, revealing at least nine submucosal lesions of the jejunal and ileal small-bowel tract suggestive either for GISTs or for multiple NETs. Since no further episodes of bleeding occurred, she was discharged scheduling a total-body PET, gallium scintigraphy and dosage of blood neuroendocrine markers values. All these examinations did not reveal any suspicious capitation and also blood dosage of chromogranin was in range (<50 µg/L). Considering the discrepancy between the CE and CT scan findings, the case was exposed to the hospital multidisciplinary team meeting that decided to refer the patient to the surgery.

In the operatory room, a pneumoperitoneum was performed according to open laparoscopic Hasson’s technique, and two other trocars were introduced. First of all, several adhesions between the omentum and the anterior abdominal wall were cut, thus allowing an optimal mobilisation of the small bowel. Once identified the biggest lesion (1 cm in diameter), the small bowel was pulled out of the body throughout a minilaparotomy (7 cm), enabling the operators to touch the whole small bowel. Since only a few of them have been detected through the pre-operative examinations, an intraoperative BAE was accomplished through the insertion the endoscope across an enterotomy of 1 cm in length, very close to the biggest lesion. No finding emerged from the retrograde exploration of the small bowel towards the duodenum, whereas nine small submucosal lesions (with sizes ranging from 5 mm to 12 mm in diameter) were found towards the ileocecal valve; the biggest ones presented superficial ulceration, covered by fibrin, suggesting a possible source of bleeding [Figure 1b]. At the light of these findings, a resection of about 120 cm of the ileum and a side-to-side anastomosis were accomplished. At the opening of the resected specimen, the macroscopic appearance confirmed the presence of multiple submucosal lesions [Figure 2]. A careful control of haemostasis was done, and 19-French Blake tube drainage was placed into the pelvis. On the second post-operative day, she tolerated a soft diet, and on the fifth post-operative day, the drainage was removed. The hospital stay was uneventful, and she was discharged on the sixth post-operative day. The histological examination of the resected specimen revealed a multifocal well-differentiated G2 NET without any sign of deep infiltration. The immunological analysis showed an expression of chromogranin A and synaptophysin [Figure 3], whereas CD-117 resulted negative, thus excluding the stromal origin of the lesions.

In the following months, a control contrast-enhancement CT scan revealed a normal aspect of the anastomosis, without any source of bleeding.

**DISCUSSION**

OGIB is due to small-bowel lesions such as NETs, GISTs or lymphomas up to 10% of cases. As Ma et al. reported, till 2000, the small bowel was considered by gastroenterologists as a ‘black box’, since its exploration was very challenging with the common endoscopic tools. The introduction of CE in 2002 and BAE in 2001, respectively, has represented a cornerstone in the diagnostic and therapeutic field of OGIB. As reported by Hong et al. in 2015, both CE and BAE show similar diagnostic yields for small bowel diseases; in particular, as Sidhu R explains in a large single-centre analysis, BAE can be considered an integration to CE for the detection of small-bowel diseases. To date, there are several articles underlining the role of BAE and CE for the identification of gastrointestinal bleeding source. In 2008, Ross et al. published a well-organised retrospective study, analysing these two techniques: the authors concluded that ‘CE is not the diagnostic gold standard for OGIB due to mass lesions’ founding out as a most likely reason the
Bisogni, et al.: The essential role of laparoscopic-assisted balloon enteroscopy in case of obscure gastrointestinal bleeding

Total-body PET. Most articles show that BAE (especially double-balloon enteroscopy) could increase the detection rate of small-bowel lesions when a previous negative CE occurred. In the light of several articles, the detection of OGIB should be achieved through a combination of these two techniques, rather than performing them singularly. As several articles underline, including the one by Johanssen et al., the certain disadvantage of CE in the diagnosis of NETs could be related, sometimes, to their extra-luminal spreading, so that CE alone, if not combined with CT-scan of BAE, does not seem to be the ideal strategy.

Moreover, the role of laparoscopic exploration seems to be very relevant. In our case, in fact, once identified the biggest lesions, the subsequent laparotomic operation was surely facilitated by laparoscopy, which in fact allowed us to avoid a total xifopubic median incision and a long manual manipulation time. As the use of diagnostic and therapeutic laparoscopy improves post-operative outcomes of the patient as compared to patients submitted to laparotomy, also in our case, the patient was discharged on the 6th post-operative day with a rapid recovery of the bowel function. Besides the reduction of post-operative hospital stay, laparoscopy generally is associated with significant reduction of post-operative analgesia, post-operative cardiac and respiratory complications including pneumonia and significant reduction of post-operative mortality rates. Furthermore, in this case report, once identified of the biggest lesion, laparoscopy enabled a minimal enterotomy of 1 cm in length, necessary for the execution of the BAE, avoiding further sutures of the intestinal bowel that had been increased the morbidity in such a type of operation.

In conclusion, explorative laparoscopy associated to BAE has been demonstrated to be a safe and feasible alternative to directly open surgery since, along with its usual advantages, its role combined to BAE could represent an attractive option in patients with a multifocal jejunoileal NET, especially whenever a discrepancy between imaging examinations (such as total-body CT scan) and CE imaging emerges.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.
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**Conflicts of interest**
There are no conflicts of interest.

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