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Diagnostic and Prognostic Benefits of Intra-Operative Enteroscopy in the Intestinal Epithelioid Angiosarcoma: case report

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ABSTRACT

Intestinal epithelioid angiosarcoma is an uncommon, aggressive and invasive neoplasm of vascular origin. We report a case of a 77-year-old male patient who was hospitalized with severe symptomatic anaemia due to bleeding jejunal ulcers and confirmed epithelioid angiosarcoma. Intraoperative enteroscopy enabled detection of multifocal bleeding lesions of the jejunum.

Keywords: Intestinal angiosarcoma, gastrointestinal bleeding, intraoperative Enteroscopy, intestinal resection, survival.

Key clinical message: Intraoperative enteroscopy is a helpful diagnostic and prognostic approach that detects small intestinal tumours in the early stage. Intraoperative enteroscopy could improve the outcome of intestinal angiosarcomas.

INTRODUCTION

Angiosarcomas are a group of proliferative and aggressive vascular tumours. They can affect any organ, but they occur most commonly in the skin and subcutaneous tissues. The first case of angiosarcoma reported was angiosarcoma of the spleen in 1879 [1-3].

Intestinal epithelioid angiosarcoma is an extremely uncommon type of vascular tumour with an unusual, varied clinical presentation including non-explained severe gastrointestinal bleeding, anaemia and abdominal pain [2,4]. The diagnosis is challenging when the tumour is not accessible endoscopically for a biopsy. It is a very aggressive and locally invasive type of tumour, involving the regional lymph nodes. In some patients, it can cause complications such as severe GI bleeding, small bowel obstruction and intestinal perforations, requiring urgent surgical intervention [5]. Endoscopic interventions have major diagnostic and prognostic roles in cases of intestinal epithelioid angiosarcomas. Both histopathological and immunohistochemical examinations are required for accurate diagnosis [2]. Surgery (intestinal resection with wide lymph nodes excision) is the treatment option in most cases. However, the recurrence rate is high, and the prognosis is very poor.

CASE PRESENTATION

The patient was a 77-year-old gentleman with a significant cardiac past medical history, including myocardial infarction, atrial fibrillation and left-side heart failure. He had been hospitalised several times with recurrent acute symptomatic (dyspnoea with efforts) microcytic iron deficiency anaemia, and he had required several blood transfusions. He denied any history of abdominal pain or gastrointestinal bleeding. He also denied any previous exposure to radiotherapy or industrial chemicals, smoking, or alcohol intake.

The findings of the clinical examination:

The patient was hemodynamic stable, pallor, dyspnoeic. There were no abdominal mass, tenderness or hepatosplenomegaly. The digital rectal exam was satisfactory. Laboratory examination showed microcytic anaemia with haemoglobin at 66 g/l and VGM at 66 FL. The results of a full body computed tomography (CT) scan were normal.

We performed complete endoscopic investigations. Esophagogastroduodenoscopy and colonoscopy did not explain the cause of this presentation. A complementary study with video capsule endoscopy showed the presence of an atypical, suspected nonbleeding ulcerated lesion of the proximal jejunum and other vascular jejunal lesions. Enteroscopy using a duodenoscope, performed under general anaesthesia, confirmed an actively bleeding multiple jejunal ulcer, posing two marking metallic clips and injection with indigo carmine-ink for eventual resection. The urgent surgical intervention involved resection of 10 cm of proximal jejunum and end-to-end anastomosis.

Two months later, the patient presented with shortness of breath, melena and severe anaemia. Urgent laparotomy in the presence of a gastroenterologist, who performed an intraoperative enteroscopy, intraoperative enteroscopy, which detected multifocal bleeding lesions of the jejunum. A 30-cm small intestine was resected with lymph node dissection with latero-lateral anastomosis and jejunostomy of discharge. Histological examinations revealed epithelioid angiosarcoma of the submucosa of the

proximal jejunum. The immunohistochemical stains confirmed the vascular nature of this lesion as the tumour cells were positive for CD 34, CD 31, ERG, and very focused on the CK AE1/AE3. The proliferative index was high (Ki 67 > 45 %).

Follow-up with laboratory examination four months after the last surgery showed stable haemoglobin. The positron emission tomography scan (conducted upon the recommendation of the tumour board) did not show any metabolic activity of the small intestine, and there were no metastatic lesions.

Given the proliferative and aggressive nature of angiosarcoma, our prospective therapeutic strategy focuses directly on close follow-up every 1–2 months to determine the outcome and advantages of our approach (intraoperative enteroscopy) in preventing recurrence and improving the survival rate in patients affected by intestinal epithelioid angiosarcomas.

DISCUSSION

Sarcomas are a group of soft-tissue tumours that vary in prognosis according to subtypes. The most common types are pleomorphic sarcoma, gastrointestinal stromal tumours (GISTs), liposarcoma, and leiomyosarcoma.

Angiosarcoma is a rare subtype, accounting for just 1%–2% of all soft-tissue sarcomas. It is a vascular lesion and originates from the vascular endothelium. Angiosarcoma can affect any organ; the most common organs involved are the subcutaneous and skin tissues, while more than 1% of all angiosarcomas affect the head and neck [2]. Most of the reported cases show at least one of the

following risk factors: 1) more than ten years of radiotherapy exposure [6]; and 2) massive occupational exposure to polyvinyl chloride, vinyl chloride, thorium dioxide, and arsenic [1].

Intestinal epithelioid angiosarcoma is a very rare, aggressive and locally invasive vascular tumour. It mostly affects the proximal jejunum and the ileum. The most common clinical presentation is abdominal pain, obscure or occult gastrointestinal bleeding and anaemia, alongside other nonspecific manifestations such as nausea, vomiting and weight loss. Acute presentation with gastrointestinal bleeding or melena is not an uncommon presentation, and it requires treatment by blood transfusions (the typical presentation of our case).

In some cases, this type of tumour causes serious complications – e.g. small bowel obstruction or intestinal perforation – that necessitate urgent surgical intervention. Intestinal epithelioid angiosarcoma has a very poor prognosis, and the median survival rate is less than one year. The prognostic factors are late diagnosis, misdiagnosis and the proliferative character of the neoplasm [5], [7], [8]).

Many factors make the diagnosis of intestinal epithelioid angiosarcoma challenging. Some of these are the similarities of clinical presentations with other common GI disorders such as angiodysplasia IBD, similarities histopathologic with other tumours like poorly differentiated carcinoma [9],[10] and immunohistochemical overlapping with other vascular and stromal tumours ([11]). However, accurate diagnosis requires both histopathological and immunohistochemical examination of the tumour cells. The immunohistochemistry test is positive for CD31, CD34, vimentin, and factor VIII. Genetic studies are useful in detecting mutations in the vascular endothelial growth factor receptor-2 (VEGFR2, also known as KDR or Flk-1) [11], [12], [9]).

Endoscopic interventions have significant diagnostic and prognostic roles in intestinal epithelioid angiosarcomas [2]. Wireless video capsule endoscopy detects and localises the lesions and gastrointestinal bleeding [13]. The specialist performing the enteroscopy takes biopsies, localises the

lesions, marks the lesions by metallic clips and injects the lesions with indigo carmine stains in preparation for eventual surgery. Endoscopic ultrasound evaluates the local invasions of the tumours and lymph-node involvements [13].

The gold standard in the treatment of intestinal epithelioid angiosarcomas is intestinal resection of the affected part of the small intestine with wide lymph-node dissection [14]. However, the risk of cancer recurrence is very high after the surgery. The risk depends on several factors, one of which is the presence of other small intestinal lesions that could not be visualised by other diagnostic tools [15].

Intraoperative enteroscopy is a safe and promising intervention that allows endoscopists to explore the small intestine using the enteroscope during surgery. This is an integrated procedure that needs a surgeon and a gastroenterologist. This procedure applies in few conditions in patients with gastrointestinal bleeding caused by small intestine lesions, angiodysplasia and for tailoring the extent of surgery in CD patients [16].

Intraoperative enteroscopy is a necessary procedure to evaluate the intraluminal extent of the tumour, to detect intestinal multifocal lesions that are missed by other diagnostic measures and to take biopsies of the lesions discovered [17].

In our case, the patient had two occasions of cancer recurrence, the cause being the presence of multiple intestinal lesions (multifocal involvement) that could not be seen previously by other diagnostic tools. The patient had three surgical interventions that could have been avoided by applying this integrated method. Although there are no recommendations for using intraoperative enteroscopy in patients with intestinal angiosarcomas or other small intestinal lesions, we suggest utilising this approach to avoid further multiple complicated surgeries, eventually improve the outcome.

Further clinical trials in collaboration with other centres around the world are needed to learn more about this integrated approach and its applications, and thus to develop a proper strategy for detecting

and treating the small lesions at an early stage using objective intestinal resection and hopefully improving the survival rate.

In conclusion, Intestinal angiosarcomas are extremely rare locally aggressive tumours that are rarely metastatic. The diagnosis is based on histopathological and immunohistochemical examination. The treatment is always intestinal resection with lymph-node dissection. Intraoperative Enteroscopy is an integrated diagnostic and prognostic method which can be used to detect the small intestinal lesions in the early stage to avoid further multiple complicated surgeries, and eventually improving the outcome.

Authorship:

AA was responsible for all steps pertaining to preparation of this manuscript.

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Conflict of Interest Statement:

The author declare that there is no competing interests.

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