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Colonic angiosarcoma: A case report and review of literature

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ABSTRACT

INTRODUCTION: Angiosarcomas are rare tumours that arise from the vascular endothelium. They can occur anywhere in the body, mostly affecting the head and neck. Their occurrence in the gastrointestinal tract is quite rare with a few reported cases in medical literature.
PRESENTATION OF CASE: A 40-year-old man presented with metastatic sigmoid colon angiosarcoma, for which he was operated due to endoscopically uncontrollable massive tumour bleeding. The patient is presently still alive at 24 months after his first presentation. He is receiving palliative care.
DISCUSSION: This article presents a review of the literature on this rare clinical entity, emphasising the very aggressive behaviour and the poor outcome of this malignancy. We present, briefly, 17 reported cases on primary colonic angiosarcoma since 1949.
CONCLUSION: The role of chemotherapy and radiation is established neither in the adjuvant setting nor in metastatic disease. Surgery is the mainstay to treat localised colorectal angiosarcomas.

1. Introduction

Gastrointestinal angiosarcomas are very rare malignant tumours that arise from the vascular endothelium, constituting far less than 1% of all gastrointestinal tract malignancies and only 1% of all sarcomas.[1,2] In this article, we present a review of the literature on this rare clinical entity, with an emphasis on colorectal angiosarcomas, after reporting the case of a 40-year-old male who presented to our care with worsening lower gastrointestinal bleeding from a sigmoid colonic angiosarcoma that has shown to be metastatic to the bone and muscles upon presentation. The patient underwent a segmental sigmoidectomy to stop rectal bleeding and was referred to the care of the oncologist to receive chemotherapy, radiation and supportive care. Metastases to the bone and muscles have resulted in severe functional disability. Interestingly, the patient is still alive at 24 months after his first presentation despite his metastatic disease.

2. Report of a case

2.1. History

A 40-year-old male presented with a 4-week history of painless, intermittent rectal bleeding and progressively, worsening pain involving the left hip joint and the right thigh, restricting mildly his physical ability. He is an active labourer with no significant past history except for occasional alcohol intake and tobacco smoking. He denied weight loss or any other constitutional symptoms. Physical examination revealed no significant findings except for bright, red blood on rectal examination. Paraclinical studies revealed iron-deficiency anaemia and several areas of translucency involving the right and left femurs and around the left pelvic girdle. The pelvic osteolytic lesions were found on abdominal CT that showed no intra-luminal masses or focal liver lesions. Colonoscopy revealed an ulcerating, friable polyp at 25 cm from the anal verge with the presence of blood and clots (Fig. 1). A biopsy showed the mass to be a glandular epithelioma. CEA and CA19.9 levels were normal. Among others, HIV test was negative. A bone biopsy was free of malignancy contradicting the results of a bone scan that considered the osseous lesions to be highly suggestive of malignancy. The decision to perform a sigmoid colectomy was taken because the patient continued to have severe rectal bleeding that could not be addressed endoscopically.

2.2. Pathology

A sigmoid colectomy was performed with a smooth early postoperative course. Macroscopically, the reddish, ulcerating polyp was 1.5 cm × 1.3 cm × 0.3 cm, having a sessile morphology. Few diverticula were noted in the specimen. Histopathology revealed a malignant, highly vascularised, poorly differentiated tumour invading the submucosa with a vague aspect (epithelial vs. sarcomatous). Positive immunohistochemical staining for CD31 and von Willebrand factor confirmed the endothelial nature of the mass (Fig. 2), to note; however, that a group of juxtatumoral capillaries

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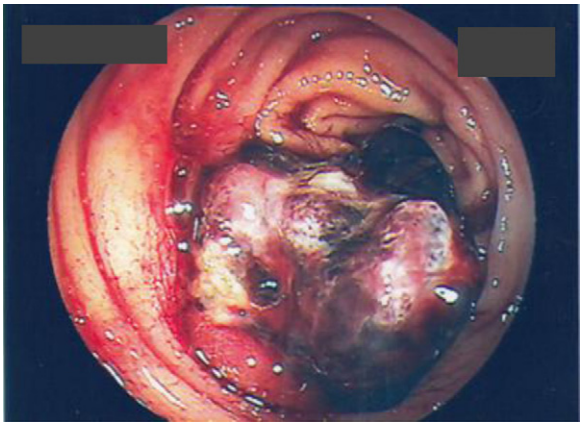

Fig. 1. A colonoscopic view of the sigmoid tumour.

stained positive for CD34, while tumour cells stained negative for this marker. Tumour cells stained positive, with variable intensity, to diverse cytokeratines recognised by the following antibodies: CAM 5.2, AE1/AE3 and MNF116. Final pathology revealed an epitheloid angiosarcoma infiltrating both the mucosa and the submucosa. The specimen had normal margins and was free of any lymphadenopathy.

2.3. Outcome

The early post-operative course was unremarkable. The patient was referred to the oncologist and was started on a taxane-based chemotherapy protocol. Three months later and during chemotherapy, the patient presented with abdominal pain that showed to be secondary to a contained pelvic abscess related to a colonic perforation that was treated supportively (antibiotics and total parenteral nutrition) with good resolution and restoration of oral feeding. Eight weeks later, chemotherapy was resumed. The patient is presently, at 24 months after his presentation, on supportive care being almost continuously bed-ridden secondary to bone and muscle metastases that severely restrict his mobility. He is receiving palliative radiotherapy sessions for his bone metastases.

3. Discussion

Angiosarcomas are a subtype of soft tissue sarcomas and are aggressive, malignant endothelial-cell tumours of vascular or lymphatic origin.[4] They account for less than 1% of all soft tissue sarcomas.[3] About 60% of these lesions occur in the skin and superficial soft tissues of the head and neck.[5] They rarely occur in the gastrointestinal tract and most of these occur in the stomach and small bowel.[6,7] Colorectal angiosarcomas are rare constituting less than 0.001% of all colorectal cancers,[8] with only a few cases reported in medical literature (Table 1). The first description of a colonic angiosarcoma was made by Steiner and Palmer.[9]

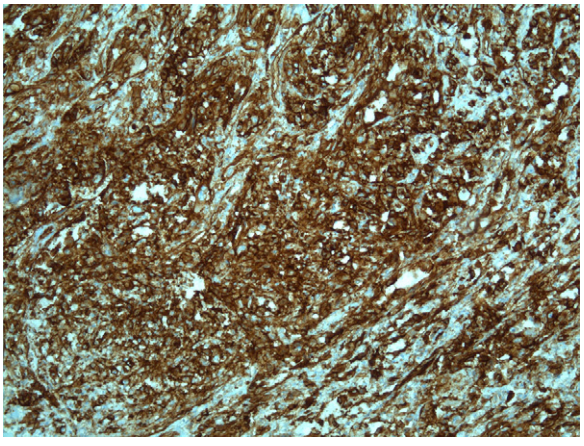

Fig. 2. A photomicrograph illustrating positive CD31 immunohistochemical staining in the specimen (×5).

Angiosarcomas have a similar distribution between both sexes. They can develop at any age, being commoner in older patients.[4]

The usual presentation of colorectal angiosarcomas is abdominal pain associated with a mass and rectal bleeding. This context is usually suggestive of colonic adenocarcinoma in spite of the unusual haemorrhagic endoscopic appearance. Unusual presentations have also been reported including free intraperitoneal bleeding,[10,11] intestinal obstruction[9,32] and chief complaints related to metastatic disease.

Most reported colorectal angiosarcomas have been localised to the sigmoid colon, which is the case of the patient presented herein.

Several predisposing factors for colorectal angiosarcomas have been suggested including radiation, chronic lymphoedema and foreign body implants[11,12] yet no final associations can be made. However, arsenic, thorium dioxide (Thorotrast) and polyvinyl chloride have been associated with hepatic angiosarcomas.[13,14] Most angiosarcomas arise spontaneously, yet there are few reports of malignant transformation within pre-existing benign vascular lesions.[4,15]

Histopathologically, these tumours are highly vascularised with abundance of endothelial cells and areas of solid and spindled cell tumour with an infiltrative and destructive growth pattern typical of angiosarcoma.[3] With better immunohistochemical studies, some atypical sarcomas would now be correctly classified as angiosarcomas.[10] These tumours typically express endothelial markers including von Willebrand factor, CD34, CD31, *Ulex europaeus* agglutinin 1 and vascular endothelial growth factor (VEGF). Immunohistochemistry is; therefore, a mainstay in confirming the diagnosis. In poorly differentiated cases, von Willebrand factor and CD 31 are the most useful markers. Kaposi's sarcoma, which has a similar immunohistochemical staining pattern to conventional angiosarcoma, can be distinguished by its tendency to be multifocal in the intestine and its usual association with HIV infection or other forms of immunosuppression.[3,16]

Tumour size and age at presentation have been suggested as prognostic factors affecting the course after treatment and survival in angiosarcomas. Longer survival has been associated with tumours less than 5 cm; size has shown to be an independent prognostic factor in angiosarcomas.[14] Furthermore, younger age at presentation is associated with better survival, with patients younger than 50 years of age have a significantly better 2-year survival rate compared to older patients.[3,13] However, data regarding better survival in younger patients is sometimes conflicting.[17,21,30] Other obvious factors associated with a poorer outcome include metastatic disease at presentation, poor patient performance status[4,18] and involved margins (R1 or R2) upon resection.

Concerning tumour staging, the International Union Against Cancer and the American Joint Committee on Cancer (UICC/AJCC) staging systems apply. This is based on the TNM (tumour-node-metastasis) staging system with an additional notation for histological grade.[19] By definition, angiosarcomas are high-grade tumours. The tumour size defines the T entity in the TNM system, with tumours less than or equal to 5 cm being T1, larger tumours being T2.

As for treatment, radical surgery with complete (R0) resection is the treatment of choice. Wide margins are recommended because of the invasive and often multifocal nature of angiosarcoma,[4] but this is often difficult to achieve. The role of adjuvant therapy in

Table 1
A summary of 17 reported cases on primary colonic and rectal angiosarcoma since 1949.

Author	Patient Age, Gender	Tumour size (max. diameter in cm.)	Tumour location	Clinical presentation	Treatment	Outcome
Steiner and Palmer[9]	46, Female	3.5	Sigmoid	Abdominal pain, palpable mass and obstruction	Sigmoidectomy	Alive 21 months postoperatively with uterine recurrence
Ormos and Sin[22]	34, Female	7	Cecum	Abdominal pain, palpable mass, weight loss	Right hemicolectomy with adjuvant radiotherapy	Died 23 months postoperatively with liver metastases
Saito et al.[23]	72, Male	10	Descending colon	Abdominal pain, rectal bleeding	Left colectomy	Death from disseminated disease 1 month postoperatively
Taxy and Battifora[24]	57, Female	6	Cecum	N/A	Right hemicolectomy	Death from disseminated disease 6 months postoperatively
Lo et al.[25]	37, Male	2	Rectum	Rectal bleeding	Abdomino-perineal resection	Alive 18 months postoperatively with no recurrence
Smith et al.[26]	16, Female	5.5	Sigmoid	Abdominal pain, palpable mass, rectal bleeding	Sigmoidectomy	Alive and disease-free 36 months postoperatively
Deleaval et al.[27]	74, Female	3	Cecum, transverse colon and rectum	Melaena	Palliative care	Died at about 1 month after diagnosis
Hofman et al.[28]	66, Male	6	Sigmoid	Abdominal pain, rectal bleeding	Sigmoidectomy	Death from disseminated disease 5 months postoperatively
Solheim et al.[29]	75, Female	NA	Cecum	Systemic upset, weight loss	Right hemicolectomy	Death from disseminated disease 4 months postoperatively
Ben-Izhak et al.[12]	70, Female	5	Rectum	Rectal bleeding	Surgical resection and adjuvant radiotherapy	Death from persistent haemorrhage 2 months postoperatively
Watanabe et al.[30]	70, Female	1.7	Sigmoid	Rectal bleeding	Sigmoidectomy	Alive at 2 years follow-up
Rozario and Ravi[31]	55, Male	2.5	Cecum	Abdominal pain, palpable abdominal mass	Right hemicolectomy	Alive 13 months postoperatively with no recurrence
Brown et al.[3]	77, Male	4.5	Sigmoid	Rectal bleeding, abdominal mass, weight loss	Sigmoid colectomy	Died 6 months postoperatively with liver metastases
Komorowski et al.[32]	17, Male	12	Sigmoid	Rectal bleeding, constipation	Sigmoid colectomy	Alive and well 19 months postoperatively
El Chaar and McQuary[11]	60, Female	N/A	Sigmoid	Abdominal pain	Segmental resection	Died 4 months postoperatively with metastases
Pascual et al.[21]	85, Female	2	Cecum	Lower gastrointestinal bleeding, haemorrhagic shock	Right hemicolectomy	Alive 24 months postoperatively with no evidence of recurrence
Lo et al.[10]	21, Female	9	Sigmoid	Abdominal pain and intraperitoneal bleeding	Sigmoid colectomy	Alive 36 months postoperatively with no evidence of recurrence

angiosarcoma is unclear, but there generally seems to be limited, if any, survival benefit with adjuvant chemotherapy in the treatment of sarcomas.[3,13] Limited experience in angiosarcomas has shown disappointing results.[13]

Cytotoxic chemotherapy is the primary treatment option for metastatic angiosarcoma, although the evidence for this is also limited. Anthracyclines, ifosfamide and more recently taxanes are the mainstay of chemotherapy.[4] Furthermore, biological therapies, in particular antiangiogenic therapies, may have a significant role in the treatment of angiosarcomas, either in the adjuvant setting or as a primary option in metastatic disease.[20]

4. Conclusion

Angiosarcoma of the colon and rectum is a rare malignancy. The case presented in this article and the review of literature suggest that colorectal angiosarcomas behave aggressively resulting in poor outcomes. No clear-cut guidelines concerning prognostic factors and treatment options can be made. However, complete (R0) surgical resection is the only treatment that has shown to result in long-term survival. Younger age at presentation and tumours less than 5 cm may be associated with better outcomes, yet the overall survival is generally poor. The role of adjuvant therapy and chemotherapy/radiation in the context of metastatic disease is unclear reflecting the need for further prospective studies to clarify treatment strategies.

Conflict of interest

None.

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None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Dr. Ahmad Tabech, the attending general surgeon, he has operated on the patient and has put the design of the paper and analysed data and approved the final version to be submitted.

Dr. Roberto Algaba, general surgeon and admitted patient for treating his acute bout of sigmoid diverticulitis. He revised the article.

Dr. Christophe Firket, general surgeon and shared in decision-making concerning patient's treatment and overall management. He revised the article.

Dr. Daniel Brenez, the attending medical oncologist, he treated the patient and has put the chemotherapy and palliative care regimens. He revised the article.

Dr. Osama Al Beteddini, general surgery fellow, he has written the article and collected relevant literature.

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