Small intestine bleeding due to multifocal angiosarcoma

Luisa Zacarias Föhrding, Arne Macher, Stefan Braunstein, Wolfram Trudo Knoefel, Stefan Andreas Topp

Abstract
We report a case of an 84-year-old male patient with primary small intestinal angiosarcoma. The patient initially presented with anemia and melena. Consecutive endoscopy revealed no signs of upper or lower active gastrointestinal bleeding. The patient had been diagnosed 3 years previously with an aortic dilation, which was treated with a stent. Computed tomography suggested an aorto-intestinal fistula as the cause of the intestinal bleeding, leading to operative stent explantation and aortic replacement. However, an aorto-intestinal fistula was not found, and the intestinal bleeding did not arrest postoperatively. The constant need for blood transfusions made an exploratory laparotomy imperative, which revealed multiple bleeding sites, predominantly in the jejunal wall. A distal loop jejunostomy was conducted to contain the small intestinal bleeding and a segmental resection for histological evaluation was performed. The histological analysis revealed a less-differentiated tumor with characteristic CD31, cytokeratin, and vimentin expression, which led to the diagnosis of small intestinal angiosarcoma. Consequently, the infiltrated part of the jejunum was successfully resected in a subsequent operation, and adjuvant chemotherapy with paclitaxel was planned. Angiosarcoma of the small intestine is an extremely rare malignant neoplasm that presents with bleeding and high mortality. Early diagnosis and treatment are essential to improve outcome. A small intestinal angiosarcoma is a challenging diagnosis to make because of its rarity, nonspecific symptoms of altered intestinal function, nonspecific abdominal pain, severe melena, and acute abdominal signs. Therefore, a quick clinical and histological diagnosis and decisive measures including surgery and adjuvant chemotherapy should be the aim.

Key words: Gastrointestinal bleeding; Small intestine; Angiosarcoma; Small intestinal neoplasm

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INTRODUCTION
Primary malignant tumors of the small intestine are rare neoplasms, which comprise < 2% of all gastrointestinal tumors[1], including adenocarcinoma, carcinoid, sarcoma, gastrointestinal stromal tumors, and lymphoma. The reason for the poor prognosis of small bowel malignant tumors is partly due to a late diagnosis. The difficulty diagnosing this type of tumor is associated with the nonspecific symptoms, including nausea, vomiting, abdominal pain, constipation, generalized weakness, fatigue,
malaise, weight loss, anemia, diarrhea, ileus, intestinal perforation, or hemorrhage\(^{[3-7]}\), as well as limited diagnostic methods for the small intestine.

Angiosarcoma is a rare mesenchymal tumor that most often arises from skin and subcutaneous tissues\(^{[3-7]}\) but can ultimately arise anywhere in the body. Angiosarcomas have been described in the liver\(^{[8-11]}\), spleen\(^{[12,13]}\), adrenal glands\(^{[14-16]}\), ovaries\(^{[17-19]}\), heart\(^{[20,22]}\), lung\(^{[23,24]}\), breast\(^{[25-27]}\) and, very rarely, in the gastrointestinal tract\(^{[28-32]}\). Consequently, an intestinal angiosarcoma that is located in the small bowel rather than the upper or lower gastrointestinal tract is a very rare medical condition. Angiosarcomas are aggressive tumors with a high rate of lymph node and peripheral metastases. This tumor arises as a de novo primary tumor or secondary to irradiation or chemical exposure. Angiosarcoma of the small intestine presents unique diagnostic challenges and is often discovered late, leading to a very poor prognosis.

Additionally, the histological diagnosis is difficult and can be confused with other neoplasms such as poorly differentiated carcinoma\(^{[13,33,34]}\). Diagnosis is facilitated by immunohistochemical expression analysis of the endothelial markers CD31 and CD34, as well as factor VIII-associated antigens.

Herein, we describe the case of an 84-year-old man with the first episode of gastrointestinal bleeding due to angiosarcoma of the small intestine.

**CASE REPORT**

The patient was transferred to the Department of Internal Medicine of a peripheral hospital with gastrointestinal bleeding, which required a blood transfusion. Three lesions with coagulum and vessels necessitating application of two clips were found by endoscopy of the distal duodenum and upper segment of the jejunum. A colonoscopy revealed old blood, so bleeding in the small intestine was suspected. The patient had been diagnosed with an aortic aneurysm 3 years previously, which was treated with juxtarenal stent-graft prosthesis. A prosthetic-enteric fistula was suspected on the emergency abdominal aortic computed tomography (CT) scan. With this suspected diagnosis, the patient was transferred to the University Hospital Düsseldorf, and emergency vascular surgery was performed. The stent-graft prosthesis was removed and desobliteration of the saccular aortic aneurysm and the renal arteries was implemented, followed by implantation of an aorto-biilacal silver-graft prosthesis. However, a prosthetic-enteric fistula was not revealed intraoperatively. The gastrointestinal bleeding did not arrest postoperatively, and Forrest IIb bleeding in the proximal jejunum was endoscopically diagnosed and treated. The local bleeding was stopped with hemoclips.

An exploratory laparotomy was performed due to persistent gastrointestinal hemorrhage, which showed multiple intra-abdominal hemorrhagic lesions in the intestinal wall of the jejunum (Figure 1). Three segmental resections and a distal loop jejunostomy were performed for a histological evaluation but achieved only temporal arrest of bleeding, which again became visible postoperatively after a loop jejunostomy. As no transanal bleeding was observed, and the histological analysis suggested a malignant angiosarcoma, a small bowel resection proximal to the loop jejunostomy with an end-to-end duodenoileostomy was subsequently performed.

Only approximately 1 m of small intestine could be preserved to achieve bleeding control. Adjuvant therapy was intended with paclitaxel, due to histological evidence of angiosarcoma. Unfortunately, a spontaneous intracranial hemorrhage with ventricular bleeding led to death of the patient, and the cause could not be determined. During hospitalization, the patient had received 75 erythrocyte concentrates, 49 units of fresh frozen plasma, 12 thrombocyte concentrates, and coagulation factors.

**Histopathological findings**

The small bowel showed an epithelium partly ulcerated with hemorrhage and infiltration of a mesenchymal fusiform tumor with parts of high-grade cells and nuclear polymorphism, including several mitoses and apoptosis formation (Figure 2). The tumor cells formed slit-shaped hollows, and they were predominantly grouped together with a solid appearance. The neoplastic cells were multifocal with macronucleoli. Eight mitoses were
identified per 10 high-power fields. The tumor cells stained positive for CD31, cytokeratin, and vimentin and slightly weaker for CD34. The tumor cells were also focally positive for factor VIII. The MIB-1 marker of proliferation was expressed in approximately 40% of nuclei. The Berlin blue reaction indicated siderin deposits and Elastica-van-Gieson staining revealed collagen fibers. In summary, the tumor showed a less differentiated, multifocally growing epithelioid angiosarcoma (degree of malignancy III Coindre) in the submucosa with infiltration of the suberosal fat tissue and extensive lymphatic spread.

**DISCUSSION**

A gastrointestinal hemorrhage is a potentially dangerous condition that warrants a quick diagnosis and decisive treatment. The vast majority of these bleeding events are due to either upper or lower gastrointestinal bleeding, and only 5% cannot be localized endoscopically. These bleeding events typically occur from the small intestine. The most common cause of small intestinal bleeding is a vascular abnormality such as angioectasia, followed by tumors and, more infrequently, small bowel ulcers and aortoenteric fistulas. Angiosarcoma of the small intestine is an extremely rare but potentially life-threatening cause of such bleeding.

Angiosarcomas typically occur in skin and superficial soft tissue, rather than in the gastrointestinal tract, and compromise < 2% of all sarcomas. Consequently, only 33 cases of small intestinal angiosarcoma have been reported in the English literature over the past 42 years (Table 1).

The precise predisposing factors remain unknown. Exposure to vinyl chloride, thorotrast, arsenic, and radiation have been associated with the pathogenesis. Of the 33 cases reported, 14 describe patients developing an angiosarcoma after being treated with radiation for a malignant tumor, including ovarian carcinoma, ovarian dysgerminoma, squamous cell carcinoma of the uterine cervix, endometrial adenocarcinoma of the uterus, and Hodgkin’s disease. The first report of an angiosarcoma of the small intestine after postoperative irradiation was published in 1979. That patient developed an angiosarcoma in the terminal ileum 8 years after irradiation for an ovarian carcinoma. Since then, 13 more angiosarcoma cases following radiation have been published (Table 1). In one case, an angiosarcoma occurred after exposure to irradiation and polyvinyl chloride, but predisposing factors could not be identified in the remaining 19 cases. The patient presented in this report also did not have any known malignancy or exposure to irradiation, vinyl chloride, or other chemicals known to induce angiosarcomas such as thorotrast or arsenic.

Categorization by sex and age does not reveal any clear-cut distribution. The average age of patients with this type of angiosarcoma was 62 years (range, 25–87 years), and 18 patients were male and 15 were female (Table 1).

The clinical manifestations of patients with angiosarcomas of the small intestine include lethargy, weakness, altered intestinal function, nonspecific abdominal pain, severe melena, anemia, acute abdominal signs and/or ileus symptoms, and even nonspecific chest pain (Table 1). In 15 of the 33 cases, the patient had signs of gastrointestinal bleeding, similar to the patient described in this report. This variability in clinical manifestations makes it even more difficult to reach a quick and correct diagnosis. Furthermore, currently available diagnostic modalities, including CT, capsule endoscopy, double-balloon enteroscopy, magnetic resonance imaging, and positron emission tomography-CT all fail to detect the bleeding site, let alone lead to a diagnosis.

Angiosarcomas are classified as well-differentiated, poorly differentiated, and epithelioid tumors. A histological diagnosis can be challenging because angiosarcoma of the small intestine shows high architectural and cytological variability. The epithelioid morphology is typical but can be easily confused with other entities such as a poorly differentiated carcinoma. Immunohistochemical expression analysis for the endothelial markers CD31, CD34, and factor VIII-associated antigen is crucial. The majority of cases listed in Table 1 were positive for these antigens. Other antigens show limited relevance and can...
| Patient [age (yr)/sex] | Tumor manifestation | Histology | Radiation/ pre-disposition | Symptoms | Therapy | Outcome | Ref. |
|------------------------|---------------------|-----------|-----------------------------|----------|---------|---------|------|
| 46/M Duodenum, ileum, and stomach | Epithelioid | None | Abdominal pain, melena | Resection | Died after 6 mo | [50] |
| 65/F Ileum | Well-differentiated tumor | Radiation | Abdominal pain, nausea, vomiting | Resection, chemotherapy | Died after 14 mo | [39] |
| 64/M NA | Epithelioid | None | Gastrointestinal bleeding | Resection | Died after 1 yr | [29] |
| 64/M Small intestine | Epithelioid | NA | Abdominal pain | Resection, chemotherapy, radiation | Died after 4 mo | [40] |
| 65/F Ileocecal valve, small bowel, and mesenteric ileum | Well-differentiated tumor | None | Abdominal pain, nausea, vomiting | Resection, chemotherapy | Died after several days | [30] |
| 76/M Jejunum | Well-differentiated tumor | Radiation | Abdominal pain, poor appetite, fatigue | Resection | Died after 9 d | [59] |
| 74/F Jejunum | Well-differentiated tumor | NA | Melena | Resection | Died due to multiple complications | [60] |
| 75/M NA | Well-differentiated tumor | Radiation | Abdominal pain | Resection, chemotherapy | Died after 5 mo | [48] |
| 60/F Small intestine | Well-differentiated tumor | Radiation | Acute abdomen, and a distal jejunal perforation | Resection | Died after 3 mo | [44] |
| 80/F Small and large bowel | Well-differentiated tumor | Radiation | Altered intestinal function | Resection | Died after 2 wk | [42] |
| 69/F Small and large bowel | Well-differentiated tumor | Radiation | Weight loss, abdominal distention, hematochezia | Resection | Died after 23 d | [42] |
| NA/M Duodenum, stomach | Epithelioid | None | Severe melena | Resection | Died of respiratory failure, metastases were found in various organs, including the lungs, bones, liver, gall-bladder, and lymph nodes | [61] |
| 78/F Small intestine | High-grade tumor | Radiation | Relative bowel obstruction | Resection | Died after 2 yr | [41] |
| 50/F Ileum | Multifocal and infiltrating tumor | Radiation | Repeated symptoms of intestinal obstruction | Resection, chemotherapy | Died after 21 mo | [41] |
| 61/F Ileum | Well-differentiated tumor | Radiation | Fullness, abdominal pain | Resection | Died after 10 mo | [46] |
| 67/M Jejunum, ileum | Epithelioid | None | Weight loss, Intermittent severe abdominal pain, and melena | Resection | Died after 3 mo | [51] |
| 85/M Small intestine | High-grade tumor | None | Weight loss, decreased appetite, generalized weakness, left upper quadrant abdominal pain | Resection, chemotherapy | Survived at least 1 yr | [52] |
| 59/M Ileum | Mixed epithelioid and well-differentiated tumor | None | Gastrointestinal bleeding | Resection | Died after 11 d | [37] |
| 70/M Duodenum | Epithelioid | None | Melena, anemia | Chemotherapy | Died after 4 mo | [49] |
| 70/M Jejunum | Epithelioid | None | Melena, anemia, shortness of breath | Chemotherapy | Died after 17 mo | [49] |
| 47/M Jejunum | Epithelioid | None | Melena, anemia, shortness of breath | NA | Died after 4 mo | [49] |
| 25/M Small intestine | Epithelioid | None | Gastrointestinal bleeding, hemoptysis, anemia | Chemotherapy, radiation | Alive 18 mo after diagnosis, palliative situation | [49] |
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| Age/M | Site | Histology | Staging | Symptoms | Treatment | Outcome |
|-------|------|-----------|---------|----------|-----------|---------|
| 70/M  | Ileum | Mixed, well-differentiated | None | Abdominal pain, vomiting | Resection, chemotherapy | Survived at least 3 yr [53] |
| 68/M  | Ileocecal | High-grade | Radiation, polyvinyl chloride | Gastrointestinal bleeding, melena | Resection, radiation | Died before starting chemotherapy [31] |
| 51/F  | Ileum | Well-differentiated | Radiation | Decreased appetite and vague abdominal pain of several months duration | Resection | Died after 10 mo [47] |
| 87/M  | Duodenum, jejunum | Epithelioid | None | Lethargy, weakness, and nonspecific chest pain | Endoscopy, argon plasma coagulation | Died after 6 wk [62] |
| 73/M  | Duodenum, jejunum | Epithelioid | Radiation | Weakness, dizziness, constipation, and melena | Resection | Died after 4 mo [32] |
| NA/M  | Jejunum | NA | NA | Acute abdominal signs | Resection, chemotherapy | Survived at least 3 yr [2] |
| 25/F  | Small and large bowel | NA | None | Intermittent abdominal pain, weight loss, and progressive abdominal distension, a 7-wk history of shortness of breath, hematemesis, and melena | Resection | Died after 2 wk [63] |

NA: Not available; M: Male; F: Female.

cause confusion with other carcinomas. There is some controversy about the relevance of cytokeratin, which has been reported positive by some authors [32,37,49,51]. However, most authors have reported no such expression by intestinal angiosarcomas [31,41,48,52].

The current therapy for angiosarcoma includes bleeding control and symptomatic therapy to stabilize the patient, followed by radical tumor resection. Six patients in the literature received adjuvant chemotherapy, and three patients were treated with combination chemotherapy and radiation [52,48,53]. Adjuvant therapy with paclitaxel was intended in the present case; however, the patient died before starting chemotherapy. All adjuvant therapy protocols are generally empiric and based on studies of cutaneous angiosarcoma, as randomized clinical studies on gastrointestinal angiosarcomas are lacking due to their rarity. The first case published received combination chemotherapy consisting of doxorubicin, vincristine, dacarbazine, and cyclophosphamide, after operative resection of the terminal ileum. That patient survived 14 mo [39]. Another combination therapy that has been used is doxorubicin and dacarbazine, which led to 5 mo survival after diagnosis [38]. Monotherapy with doxorubicin showed survival of 21 mo, at which time the tumor was widely disseminated [38]. Furthermore, thalidomide therapy was initiated as an experimental measure after operative resection in one case [32]. That patient was still alive 1 year after the initial diagnosis. No recommendation can usually be made, but paclitaxel and/or thalidomide are currently commonly considered [32,45,54]. The newest studies suggest administering doxorubicin and paclitaxel weekly for cutaneous angiosarcoma, which seem to provide longer progression-free survival [16,51].

Despite all efforts, survival of patients with small bowel angiosarcoma is generally poor. Survival usually ranges from several days after surgical intervention to 2 years. The majority of patients die within 6 mo to 1 year after being diagnosed (Table 1). Only two reported patients survived > 2 years after resection and adjuvant (radio-) chemotherapy [2,53].

One major cause of this poor outcome seems to be that the diagnosis is difficult, and many tumors are diagnosed only in the late stages of the disease. Therefore, a quick diagnosis using endoscopy and imaging procedures, as well as fast and decisive surgical intervention and adjuvant chemotherapy are necessary.

REFERENCES

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin 2007; 57: 43-66.
2. Turan M, Karadayi K, Duman M, Ozer H, Arici S, Yildirir C, Koçak O, Sen M. Small bowel tumors in emergency surgery. Ulas Tumur Acil Cerrahi Derg 2010; 16: 327-333.
3. Mendenhall WM, Mendenhall CM, Werning JW, Reith JD, Mendenhall NP. Cutaneous angiosarcoma. Am J Clin Oncol 2006; 29: 524-528.
4. Mobini N. Cutaneous epithelioid angiosarcoma: a neoplasm with potential pitfalls in diagnosis. J Cutan Pathol 2009; 36: 362-369.
5. Vogt T. [Angiosarcoma]. Hautarzt 2008; 59: 237-248; quiz 249-250.
6. Girard C, Johnson WC, Graham JH. Cutaneous angiosarcoma. Cancer 1970; 26: 868-883.
7. Maddox JC, Evans HL. Angiosarcoma of skin and soft tissue: a study of forty-four cases. Cancer 1981; 48: 1907-1921.
8. Locker GY, Doroshow JH, Zwelling LA, Chabner BA. The clinical features of hepatic angiosarcoma: a report of four cases and a review of the English literature. Medicine (Baltimore) 1979; 58: 48-64.
9. Popper H, Thomas LB, Telles NC, Falk H, Selikoff IJ. Development of hepatic angiosarcoma in man induced by vinyl chloride, thorotrast, and arsenic. Comparison with cases of unknown etiology. Am J Pathol 1978; 92: 349-376.
10. Maluf D, Cotterell A, Clark B, Stravitz T, Kauffman HM, Fisher RA. Hepatic angiosarcoma and liver transplantation: case report and literature review. Transplant Proc 2005; 37: 2195-2199.
Clonchet, C.H., Hwang, C.C., Chen, Y.H., Wu, J.T., Cheung, C.S., Lin, C.L., Yen, C.L., Wang, W.Y., Chiang, K.C. Liver angiosarcoma, a rare liver malignancy, presented with intrahepatic biliary disease due to rupture—a case report. Journal of Surgical Oncology 2012; 10: 23.

Falk, S., Krishnan, J., Meis, J.M. Primary angiosarcoma of the spleen. A clinicopathologic study of 40 cases. American Journal of Surgical Pathology 1993; 17: 959-970.

Neuhausser, T.S., Derringer, G.A., Thompson, L.D., Fanburg-Smith, J.C., Miettinen, M., Saaristo, A., Abbbondanzo, S.L. Splenic angiosarcoma: a clinicopathologic and immunophenotypic study of 28 cases. Mod Pathol 2000; 13: 978-987.

Wenig, B.M., Abbondanzo, S.L., Heffess, C.S. Epithelioid angiosarcoma of the adrenal glands. A clinicopathologic study of nine cases with a discussion of the implications of finding "epithelial-specific" markers. American Journal of Surgical Pathology 1994; 18: 62-73.

Kareti, L.R., Katlein, S., Siew, S., Blauvelt, A. Angiosarcoma of the adrenal gland. Pathology Lab Med 1988; 112: 1163-1165.

Krüger, S., Kujath, P., Johannisson, R., Feller, A.C. Primary epithelioid angiosarcoma of the adrenal gland case report and review of the literature. Tumori 2001; 87: 262-265.

Nielsen, G.P., Young, R.H., Prat, J., Scully, R.E. Primary angiosarcoma of the ovary: a report of seven cases and review of the literature. International Journal of Gynecology 1997; 16: 378-382.

Nucci, M.R., Krausz, T., Liifschitz-Mercer, B., Chan, J.K., Fletcher, C.D. Angiosarcoma of the ovary: clinicopathologic and immunohistochemical analysis of four cases with a broad morphologic spectrum. American Journal of Surgical Pathology 1996; 20: 620-630.

Bradford, L., Swartz, K., Rose, S. Primary angiosarcoma of the ovary complicated by hemoperitoneum: a case report and review of the literature. Arch Gynecol Obstet 2010; 281: 145-150.

Glancy, D.L., Morales, J.B., Roberts, W.C. Angiosarcoma of the heart. American Heart Journal 1968; 21: 413-419.

Burke, A.P., Cowan, D., Virmann, R. Primary sarcomas of the heart. Cancer 1992; 69: 387-395.

Luk, A., Nwachukwu, H., Lim, K.D., Cusimano, R.J., Butany, J. Cardiac angiosarcoma: a case report and review of the literature. Cardiovascular Pathology 2010; 19: e69-e74.

Pate, A.M., Ryu, J.H. Angiosarcoma in the lung. Chest 1993; 103: 1531-1535.

Pandit, S.A., Fiedler, P.N., Westcott, J.L. Primary angiosarcoma of the lung. Ann Diag Pathol 2005; 9: 302-304.

Marchal, C., Weber, B., de Lafontan, B., Resbeut, M., Mignotte, H., du Chatellier, P., Cutuli, B., Rema-Saumo, M., Brousset-Leroux, A., Chaplain, G., Lescam, F., Dilhuydy, J.M., Lagrange, J.L. Nine breast angiosarcomas after conservative treatment of breast carcinoma: a survey from French comprehensive cancer centers. International Journal of Oncal Biol Phys 1999; 44: 113-119.

Sher, T., Hennessey, B.T., Valero, V., Braglio, K., Woodward, W.A., Trent, J., Hunt, K.K., Hortobagyi, G.N., Gonzalez-Angulo, A.M. Primary angiosarcomas of the breast. Cancer 2007; 110: 173-178.

Wang, Y.K., Jakowski, J., Tawfik, O.W., Thomas, P.A., Fan, F. Angiosarcoma of the breast: a clinicopathologic analysis of cases from the last 10 years. Ann Diag Pathol 2005; 9: 147-150.

Barclay, T.H., Schapira, D.V. Malignant tumors of the small intestine. Cancer 1983; 51: 878-881.

Ondoñez, N.G., del Junco, W.O., Ayala, A.G., Ahmed, N. Angiosarcoma of the small intestine: an immunoperoxidase study. American Journal of Gastroenterology 1983; 78: 218-221.

Tasy, J.B., Battifora, H. Angiosarcoma of the gastrointestinal tract. A report of three cases. Cancer 1988; 62: 210-216.

Khalil, M.F., Thomas, A., Aassad, A., Rubin, M., Taub, R.N. Epithelioid Angiosarcoma of the Small Intestine After Occupational Exposure to Radiation and Polynvinyl Chloride: A case Report and Review of Literature. Sarcoma 2005; 9: 161-164.

Grewal, J.S., Daniel, A.R., Carson, E.J., Catanizzo, A.T., Sheehab, T.M., Tworek, J.A. Rapidly progressive metastatic multicentric epithelioid angiosarcoma of the small bowel: a case report and a review of literature. International Journal of Colorectal Disease 2008; 23: 745-756.

Lin, C.F., DeFrías, D., Lin, X. Epithelioid angiosarcoma: a neoplasm with potential diagnostic challenges. Cytopathology 2010; 38: 154-158.

Fletcher, C.D., Beham, A., Bekir, S., Clarke, A.M., Marley, N.J. Epithelioid angiosarcoma of deep soft tissue: a distinctive tumor readily mistaken for an epithelial neoplasm. American Journal of Surgical Pathology 1999; 15: 915-924.

Carey, E.J., Leighton, J.A., Heigh, R.J., Shiff, A.D., Sharma, V.K., Post, J.K., Fleischer, D.E. A single-center experience of 260 consecutive patients undergoing capsule endoscopy for obscure gastrointestinal bleeding. American Journal of Gastroenterology 2007; 102: 89-95.

Bashir, R.M., al-Kawas, F.H. Rare causes of occult small intestinal bleeding, including aortoenteric fistulas, small bowel tumors, and small bowel ulcers. Gastrointest Endosc Clin N Am 1996; 6: 709-738.

Chami, T.N., Rainer, L.E., Henneberry, J., Smith, D.P., Hill, G., Katz, P.O. Angiosarcoma of the small intestine: a case report and literature review. American Journal of Gastroenterology 1994; 89: 797-800.

Bardwil, J.M., Meoege, E.E., Butler, J.J., Russin, D.J. Angiosarcoma of the head and neck region. American Journal of Surgery 1986; 116: 548-553.

Chen, K.T., Hoffman, K.D., Hendricks, E.J. Angiosarcoma following therapeutic irradiation. Cancer 1979; 44: 2044-2048.

NaNUS, D.M., Kelsen, D., Clark, D.G. Radiation-induced angiosarcoma. Cancer 1987; 60: 777-779.

Aitolta, P., Poutaainen, A., Nordback, I. Small-bowel angiosarcoma after pelvic irradiation: a report of two cases. International Journal of Colorectal Disease 1999; 14: 309-310.

Wolof, R.B., Sato, N., Azumi, N., Lack, E.E. Intra-abdominal "angiosarcomatosis" report of two cases after pelvic irradiation. Cancer 1991; 67: 2275-2279.

Su, C.C., Jen, Y.T., Chien, C.H., Yu, C.Y., Lin, P.W. Postirradiation angiosarcoma of the terminal ileum. Zhonghua Yi Xue Zazhi (Taipei) 1991; 48: 147-152.

Hwang, T.L., Sun, C.F., Chen, M.F. Angiosarcoma of the small intestine after radiation therapy: a report of a case. Journal of Formosan Medical Association 1993; 92: 658-661.

Hansen, S.H., Holck, S., Flyger, H., Tange, U.B. Radiation-associated angiosarcoma of the small bowel. A case of multiphoidy and a fulminating clinical course. American Journal of Pathology 1996; 104: 891-894.

Suzuki, F., Saito, A., Ishi, K., Koyatsu, J., Maruyama, T., Suda, K. Intra-abdominal angiosarcomatosis after radiotherapy. Journal of Gastroenterological Hepatology 1999; 14: 289-292.

Policarpio-Nicolás, M.L., Nicolas, M.M., Keh, P., Laskin, W.B. Postirradiation angiosarcoma of the small intestine: a case report and review of literature. Annals of Diag Pathology 2006; 10: 301-305.

Berry, G.J., Anderson, C.J., Pitts, W.C., Neitzel, G.F., Weiss, L.M. Cytology of angiosarcoma in effusions. Acta Cytologica 1991; 35: 538-542.

Allison, K.H., Yoder, B.J., Bronner, M.P., Goldblum, J.R., Rubin, B.P. Angiosarcoma involving the gastrointestinal tract: a series of primary and metastatic cases. American Journal of Surgery 2004; 28: 298-307.

Vriend, H.M., Becker, A.E. Multiple malignant (haem) angioendothelomas of the stomach and small intestine. Archives of Surgery Neer 1970; 20: 15-23.

Delvaux, V., Sciot, R., Neuvile, B., Moerman, P., Peeters, M., Filez, L., Van Beckevoort, D., Ectors, N., Geboes, K. Multifocal epithelioid angiosarcoma of the small intestine. Virchows Arch 2000; 437: 90-94.

Frazier, G., Ganti, A.K., Potti, A., Mehdi, S. Angiosarcoma of the small intestine: a possible role for thalidomide? Medical Oncology 2003; 20: 397-402.
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53 Butrón Vila T, Garcia Villar O, Alonso Garcia S, Bonachia Naranjo O, Pérez Espejo G, Lomas Espadas M, Hidalgo Pascual M. Angiosarcoma in the small intestine. Apropos of a particular case. Hepatogastroenterology 2005; 52: 1139-1142

54 Raina V, Sengar M, Shukla NK, Deo SS, Mohanty BK, Sharma D, Ray R, Das P, Rath GK. Complete response from thalidomide in angiosarcoma after treatment of breast cancer. J Clin Oncol 2007; 25: 900-901

55 Vakkalanka B, Milhem M. Paclitaxel as neoadjuvant therapy for high grade angiosarcoma of the spleen: a brief report and literature review. Clin Med Insights Oncol 2010; 4: 107-110

56 Penel N, Marréaud S, Robin YM, Hohenberger P. Angiosarcoma: state of the art and perspectives. Crit Rev Oncol Hematol 2011; 80: 257-263

57 Penel N, Italiano A, Ray-Coquard I, Chaigneau L, Delcambre C, Robin YM, Bui B, Bertucci F, Isambert N, Cupissol D, Bompas E, Bay JO, Duffaud F, Guillemet C, Blay JY. Metastatic angiosarcomas: doxorubicin-based regimens, weekly paclitaxel and metastasectomy significantly improve the outcome. Ann Oncol 2012; 23: 517-523

58 Italiano A, Cioffi A, Penel N, Levra MG, Delcambre C, Kalbacher E, Chevreau C, Bertucci F, Isambert N, Blay JY, Bui B, Antonescu C, D’Adamo DR, Maki RG, Keohan ML. Comparison of doxorubicin and weekly paclitaxel efficacy in metastatic angiosarcomas. Cancer 2012; 118: 3330-3336

59 Kelemen K, Yu QQ, Howard L. Small intestinal angiosarcoma leading to perforation and acute abdomen: a case report and review of the literature. Arch Pathol Lab Med 2004; 128: 95-98

60 Cilursu AM. Massive hemorrhage due to angiosarcomatosis diagnosed by intraoperative small bowel endoscopy. Endoscopy 1991; 23: 245

61 Usuda H, Naito M. Multicentric angiosarcoma of the gastrointestinal tract. Pathol Int 1997; 47: 553-556

62 Al Ali J, Ko HH, Owen D, Steinbrecher UP. Epithelioid angiosarcoma of the small bowel. Gastrointest Endosc 2006; 64: 1018-1021

63 Mohammed A, Aliyu HO, Liman AA, Abdullahi K, Abubakar N. Angiosarcoma of the small intestine. Ann Afr Med 2011; 10: 246-248

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