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Obscure gastrointestinal bleeding due to multifocal intestinal angiosarcoma

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ABSTRACT

INTRODUCTION: Intestinal angiosarcomas are an extremely rare and aggressive vascular tumors, with a few cases reported in the literature.
PRESENTATION OF CASE: A 45 years-old male arrived to our hospital with intermittent gastrointestinal bleeding presenting melena and weight loss, he has antecedent of pelvic radiotherapy ten years before admission for an unknown pelvic tumor. Emergency surgery was required because of uncontrolled bleeding and hemodynamic instability. Histopathological findings revealed a multifocal high-grade epithelioid angiosarcoma, with cells reactive for CD31, keratins CKAE 1/AE3 and factor VIII.
DISCUSSION: Angiosarcomas are aggressive tumors with a high rate of lymph node metastasis and peripheral organs. The diagnosis is difficult because it present nonspecific clinical presentation, radiological and histopathological findings. There are few reports of angiosarcoma involving the small intestine and the most common presentation are abdominal pain and gastrointestinal bleeding. There is not enough information for intestinal angiosarcoma secondary to radiation therapy, but there have been proposed criteria for diagnosis: no microscopic or clinical evidence of antecedent malignant lesion, angiosarcoma presented in the field of irradiation, long latency period between radiation and angiosarcoma and histological confirmation. We suspect our patient course with a secondary form of angiosarcoma. Therapy for bleeding angiosarcoma consists in control of bleeding and medical management to stabilize the patient. Once accomplished surgical resection is required.
CONCLUSION: We should keep in mind this tumors as a cause of obscure intestinal bleeding in patients with medical history of radiation therapy.

1. Introduction

Angiosarcomas are a very rare and aggressive tumors of vascular cell origin, they comprise 1–2% of all sarcomas. They can occur anywhere on the body but they occur mainly in the skin, soft tissue and breast and rarely the gastrointestinal tract [1,2]. They can be sporadic or secondary to some predisposing factors like radiotherapy, chronic lymphedema, familial syndromes and exposure to various chemicals. The distribution is similar between males and females and they are more common in old people [3]. These neoplasms have a very poor prognosis due to its diagnostic is usually delayed because of its diverse clinical presentation and none specific symptoms [4]. The occurrence in small intestine is extremely rare, with a few reports in the international journals [5]. We describe a case of patient who presented gastrointestinal bleeding due to multifocal intestinal angiosarcoma.

2. Clinical case

A 45 years-old male was admitted in our hospital with a 3 month history of intermittent gastrointestinal bleeding presenting melena and weight loss of 20 kg. At his arrive, he reported epigastric pain and occasional fever since a month ago. The patient referred a medical history of 20 pelvic radiotherapy sessions in a private hospital for unknown pelvic tumor 10 years before its admission. Diagnostic workup began with an upper endoscopy and colonoscopy with a negative report of visible bleeding and non-anatomical abnormalities. A computer tomographic scan of the abdomen showed irregular and circumferential thickening of jejunum, with 24 mm of thickness, without lymph nodes and other intra-abdominal lesions (Figs. 1 and 2). Serum levels of tumors markers ACE and Ca 19.9

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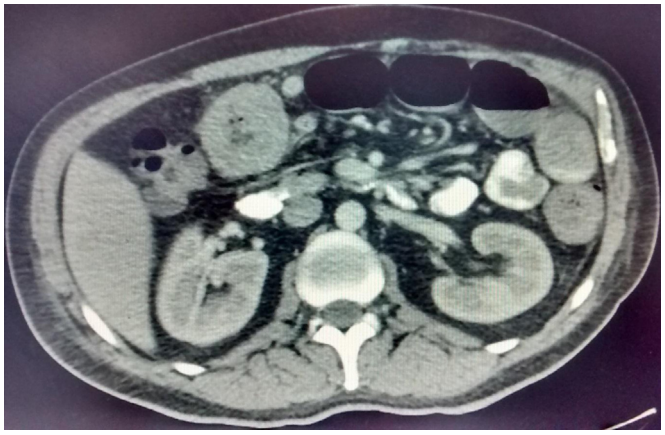

Fig. 1. CT scan, axial plane show an intestinal tumor.

were normal, except Ca 125 that was increased 4 fold normal value. Conservative management was started with hemodynamic stabilization and multiple transfusions (packed red blood cells and fresh frozen plasma).

We decided an emergency surgery in his third day of admission because high transfusional requirements and hemodinamical instability. An exploratory laparotomy was performed finding macroscopic evidence of four tumors at 15, 30, 50 and 150 cm distal to Treitz's ligament (Fig. 3); therefore, three intestinal resections with enteroenterostomy and omentectomy were performed. No transoperative complications were reported. The postoperative course was complicated by surgical site infection and the patient

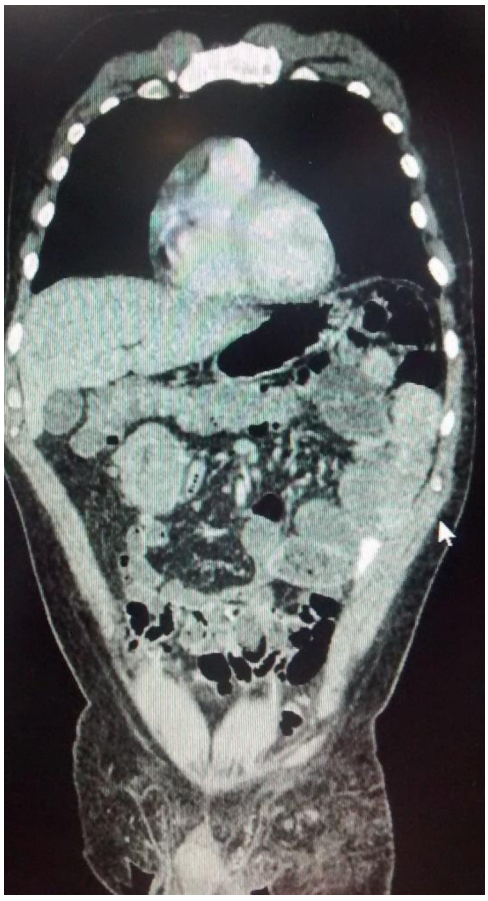

Fig. 2. CT scan, coronal plane showing thickening of intestinal wall.

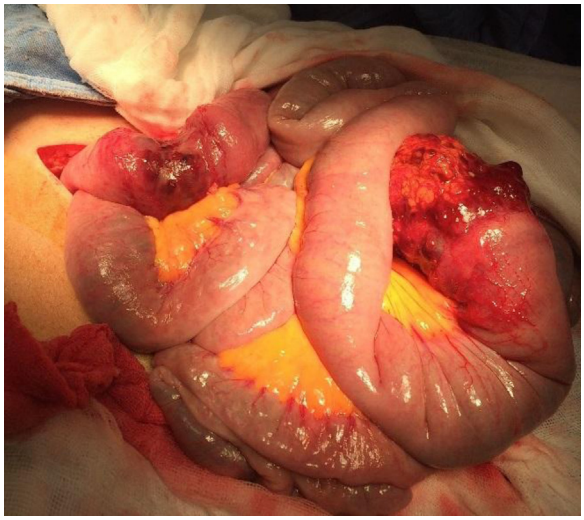

Fig. 3. Intraoperative presentation of the multifocal tumors.

was treated with IV antibiotics, he was discharged 10 days after surgery. The patient was referred to Oncology center to receive adjuvant therapy.

The pathological findings revealed a multifocal high-grade epithelioid angiosarcoma, with cells reactive for CD31, keratins CKAE 1/AE3 and factor VIII, and nonreactive for CD34 involving ileum and jejunum with diameter 4.5, 6.5 and 8.5 cm, highly vascularized, ulcerated and infiltrating tumors, with focal vascular permeation, without lymphatic and neural permeation, no necrosis. Six omentum metastatic implants were reported.

3. Discussion

Primary angiosarcoma of the small intestine is an extremely rare disease affecting mainly: liver, spleen, adrenals, ovaries, heart, lung, breast and, rarely, the middle gastrointestinal tract as in our case [2]. Angiosarcomas are aggressive tumors with a high rate of lymph node metastasis and peripheral organs. The diagnosis is difficult because of nonspecific clinical presentation, radiological and histopathological findings, so the angiosarcoma of the small intestine represents unique challenge to diagnose [6].

These tumors could have clinical presentation with bleeding of gastrointestinal tract, anemia, intestinal obstruction, abdominal pain, nausea, abdominal distention, weight loss, shortness of breath, weakness and diarrhea. In our case, present a patient with gastrointestinal bleeding like initial symptom [2,7,8]. There is a recent report presented giant abdominal angiosarcoma (diameter > 20 cm) [7].

Ni et al., reported 27 cases of angiosarcoma involving the small intestine [2]. The most common presentation was abdominal pain and gastrointestinal bleeding (37%). Twenty-three patients presented primary angiosarcoma (85.15%), 4 patients indeterminate (14.8%) and none with secondary form of angiosarcoma. Nine patients had medical history of radiation (33.3%) all of these with the primary form. One patient had multifocal intestinal of angiosarcoma and no history of radiation, being a primary form of angiosarcoma. Our case, as we have described, the patient presented gastrointestinal bleeding caused by a multifocal intestinal angiosarcoma, and because the history of pelvic radiation, we supposed that, this presentation was a secondary form of intestinal sarcoma [2].

Angiosarcomas are classified as well-differentiated, poorly differentiated, and epithelioid tumors [5]. The histopathological diagnosis is difficult because it shows high architectural and

cytological variability [9]. The vasoformative structures can range from well-formed vessels, recognized as vascular spaces to slit-like poorly developed anastomosing vascular channels [9,10].

In well differentiated areas, these tumors form functioning vascular sinusoids continuous with normal vascular channels, this dissect between collagen bundles and are often associated with monocyte infiltration [3].

In aggressive disease, cells become multilayered and form papillary-like projections into the vascular lumen, mitotic bodies are common, as are small clusters of erythrocytes within the cytoplasm of the abnormal endothelial cells. In poorly differentiated areas, the malignant endothelial cells form continuous sheets, usually with an epithelioid morphology, and with areas of hemorrhage and necrosis can be confused with other entities such as a poorly differentiated carcinoma, melanoma, or epithelioid leiomyosarcoma [3,9].

Expression of endothelial markers including von Willebrand factor, CD34, CD31, Ulex europaeus agglutinin 1, and vascular endothelial growth factor (VEGF) are present, and are very important to confirm the diagnosis [3,5]. They are the most useful markers in poorly differentiated cases. However, progressive tumors dedifferentiation can lead to a loss of these markers. The absence of melanocytic markers (S100), human melanoma black-45, and melanoma antigen can help distinguish angiosarcoma from melanoma [3,11]. Additionally, epithelioid angiosarcomas can express cytokeratins, leading to confusion with poorly differentiated carcinomas. Benefits diagnosis by immunohistochemical expression of CD31 and CD34 markers as well as the factor VIII antigen-active ated [5,11]. The role of angiogenesis and the angiogenic factors, VEGF-A are an important area of opportunity for the diagnosis because is consistently expressed at higher concentrations in angiosarcomas. The VEGFR-2 is the main receptor and its loss, was correlated with worse prognosis [3,12]. Other abnormalities have been found in metastasic angiosarcoma, TP53, KRAS mutations, overexpression of Wilms' tumor-1 and galectin-3. The overexpression of the transcription factor ETS1 result in increased production of metalloproteinases [3].

Results pooled from three separate series showed KIT positivity in 38 (50%) of 76 samples, and diffuse KIT expression in 18 (47%) of 38 samples. KIT-mutation analysis has been done for a handful of angiosarcomas [13]. Multiple chromosomal abnormalities have been described but none is specific for angiosarcom (trisomy 5, deletions on the short arm of chromosome 7, abnormalities on chromosomes 8, 20, and 22, and loss of chromosome Y [3].

There is not enough information for angiosarcoma secondary to radiation therapy, but there have been proposed criteria for diagnosis: no microscopic or clinical evidence of antecedent malignant lesion, angiosarcoma presented in the field of irradiation, long latency period between radiation and angiosarcoma and histological confirmation. As we mentioned before, we suspect our patient course with a secondary form of angiosarcoma because accomplish with this criteria [14].

CT and MRI scan has limited diagnostic utility due to lack of specificity. Endoscopy can directly detect neoplasia, and it is useful in gastric location, duodenum or colon. For tumors of the jejunum and ileum, capsule endoscopy and barium studies may be used but have limited diagnostic use. Exploratory laparotomy is often required to reach a diagnosis. In our case, we required surgical exploration due to hemodynamic instability and failure with conservative management [6].

Therapy for bleeding angiosarcoma consists in control of bleeding and medical management to stabilize the patient. Once accomplished, is followed by surgical resection [5]. Surgery is the treatment of choice, although usually is not possible due to advanced stage when the diagnosis is made. Currently, surgical excision associated with adjuvant radiotherapy and /or chemotherapy may be useful; however, the efficacy of these treatments for angiosarcoma remains unclear [5].

Guidelines for neoadjuvant and adjuvant therapy are not well described. Literature reports showed poor experience in management with adjuvant chemotherapy and a combination chemotherapy and radiation. There are experiences with adjuvant paclitaxel and combination of doxorubicin, vincristine, dacarbazine and cyclophosphamide; another combination is with doxorubicin and dacarbazine, and monotherapy with doxorrubicin but these protocols are generally empiric and based on studies of cutaneous angiosarcoma. Clinical studies on intestinal angiosarcomas are lacking due to their rarity, and results are diverse, but generally with poor prognosis [5]. No current recommendations can be made, but a combination of paclitaxel and thalidomide are commonly considered as adjuvant therapy [15].

Prognosis in these type of tumors is very poor despite the use of chemotherapy, surgery and even radiotherapy. There is no evidence which can demonstrate a better survival among trials and they are usually empiric due to the lack of experience. Patients usually die within 1 year from diagnosis or even on the late posoperatory period due to severe sepsis [5].

Although some trials report certain association of the site of presentation with prognosis, other do not do it, specifically speaking of intestinal angiosarcomas; there are no guidelines referring to the follow up, which needs overall focused to detect metastasis and recurrence. Main prognostic factors such as older age, status performance, high tumor grade and metastases are associated with a poorer prognosis, but it is unclear which is the main factor [3].

Recurrence cannot be discussed until metastases has been discarded and follow up in patients free of disease is documented. In Ni et al. report, of the 27 patients, 26% (7 patients) died during the first six months, 15% (4 cases) died of several complications after 1 year of surgery, 18.5% (5 cases) died during posoperatory period and a the rest of them (33%) did not have any follow up [2].

4. Conclusions

Our patient presented a very rare condition, that start with non specific symptoms, so we started the work-up finding an intestinal tumor and because the patient presented an hemodynamic deterioration, we decide to submit to surgery. Our patient had a history of unknown pelvic tumor and radiotherapy. So, we suggest to consider the diagnosis of intestinal angiosarcoma in other patients with these features. After the pathology results, the patient was sent to oncologic management.

Conflict of interest

None of the authors have conflict of interest.

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Ethical approval

Written informed consent was obtained from the patient for publication of this case. An Institutional Review Board approval was obtained before the publishing of this article.

Author contribution

Dr. Dolores Navarro-Chagoya, Concept. Design, Writing Paper.Dr. Marco Figueroa-Ruiz, Concept. Design, Writing

Paper.Dr. Javier López-Gómez, Concept. Design, Writing Paper. Dr. Hector Nava-Leyva, Concept. Design. Writing Paper.Dr. Carlos E. Alvarez-Ponce, Concept. Design, Writing Paper.Dr. Gustavo Guzman-Sombrerero, Concept. Design, Writing Paper.Dr. Jose Velazquez-Garcia, Concept Design, Writing Paper.

Consent

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

Guarantor

Dr. Dolores Navarro-Chagoya.

References

[1] S. Singla, P. Papavasiliou, B. Powers, J. Gaughan, M. Von Mehren, J.C. Watson, J.M. Farma, Challenges in the treatment of angiosarcoma: a single institution experience, Am. J. Surg. 208 (2) (2014) 254–259, http://dx.doi.org/10.1016/j.amjsurg.2014.01.007.

[2] Q. Ni, D. Shang, H. Peng, M. Roy, G. Liang, W. Bi, X. Gao, Primary angiosarcoma of the small intestine with metastasis to the liver: a case report and review of the literature, World J. Surg. Oncol. 25 (11) (2013) 242, http://dx.doi.org/10.1186/1477-7819-11-242.

[3] R.J. Young, N.J. Brown, M.W. Reed, D. Hughes, P.J. Woll, Angiosarcoma, Lancet Oncol. 10 (2010) 983–991, http://dx.doi.org/10.1016/S1470-2045(10) 70023-1.

[4] J. Fayette, E. Martin, S. Piperno-Neumann, A. Le Cesne, C. Robert, S. Bonvalot, D. Ranchère, P. Pouillart, J.M. Coindre, J.Y. Blay, Angiosarcomas, a heterogeneous group of sarcomas with specific behavior depending on primary site: a retrospective study of 161 cases, Ann. Oncol. 18 (12) (2007) 2030–2036.

[5] L. Zacarias Föhrding, A. Macher, S. Braunstein, W.T. Knoefel, S.A. Topp, Small intestine bleeding due to multifocal angiosarcoma, World J. Gastroenterol. 28 (November (44)) (2012) 6494–6500, http://dx.doi.org/10.3748/wjg.v18. i44.6494.

[6] D.S. Liu, H. Smith, M.M. Lee, M. Djeric, Small intestinal angiosarcoma masquerading as an appendiceal abscess, Ann. R. Coll. Surg. Engl. (2013), http://dx.doi.org/10.1308/003588413x 13511609955373.

[7] M. Takahashi, M. Ohara, N. Kimura, H. Domen, T. Yamabuki, K. Komuro, T. Tsuchikawa, S. Hirano, N. Iwashiro, Giant primary angiosarcoma of the small intestine showing severe sepsis, World J. Gastroenterol. 20 (November (43)) (2014) 16359–16363, http://dx.doi.org/10.3748/wjg.v20. i43.16359.

[8] R. Siderits, F. Poblete, B. Saraiya, C. Rimmer, A. Hazra, L. Aye, Angiosarcoma of small bowel presenting with obstruction: novel observations on a rare diagnostic entity with unique clinical presentation, Case Rep. Gastrointest. Med. 2012 (2012) 480135, http://dx.doi.org/10.1155/2012/480135.

[9] J. Al Ali, H.H. Ko, D. Owen, U.P. Steinbrecher, Epithelioid angiosarcoma of the small bowel, Gastrointest. Endosc. 64 (6) (2006) 1018–1021.

[10] V. Delvaux, R. Sciot, B. Neuville, P. Moerman, M. Peeters, L. Filez, D. Van Beckevoort, N. Ectors, K. Geboes, Multifocal epithelioid angiosarcoma of the small intestine, Virchows Arch. 437 (1) (2000) 90–94.

[11] M. Ohsawa, N. Naka, Y. Tomita, D. Kawamori, H. Kanno, K. Aozasa, Use of immunohistochemical procedures in diagnosing angiosarcoma, evaluation of 98 cases, Cancer 75 (June (12)) (1995) 2867–2874.

[12] E. Itakura, H. Yamamoto, Y. Oda, M. Tsuneyoshi, Detection and characterization of vascular endothelial growth factors and their receptors in a series of angiosarcomas, J. Surg. Oncol. 97 (1) (2008) 74–81.

[13] R. Komdeur, H.J. Hoekstra, W.M. Molenaar, E. Van Den Berg, N. Zwart, E. Pras, I. Plaza-Menacho, R.M. Hofstra, W.T. Van Der Graaf, Clinicopathologic assessment of postradiation sarcomas: KIT as a potential treatment target, Clin. Cancer Res. 9 (8) (2003) 2926–2932.

[14] P. Aitola, A. Poutiainen, I. Nordback, Small-bowel angiosarcoma after pelvic irradiation: a report of two cases, Int. J. Colorectal. Dis. 14 (6) (1999) 308–310.

[15] B. Vakkalanka, M. Milhem, Paclitaxel as neoadjuvant therapy for high grade angiosarcoma of the spleen: a brief report and literature review, Clin. Med. Insights Oncol. 4 (2010) 107–110.