

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Splenic Angiosarcoma Diagnosed on Bone Marrow Biopsy: Case Report and Literature Review

Asaph C.J. Levy, MD^{a,*}, Miriam DeFilipp, MD^a, Morgan Blakely, MD^b, Saeed Asiry, MD^c, Susan Jormark, MD^c, Allen Goodman, MD^a

^a Department of Radiology, Northwell Health System, Lenox Hill Hospital, 100 East 77th St, New York, NY 10075 USA

^b Department of Pathology, Mount Sinai Hospital Health System, Mount Sinai Hospital, New York, NY 10075 USA

^c Department of Pathology, Northwell Health System, Lenox Hill Hospital, 100 East 77th St, New York, NY 10075 USA

ARTICLE INFO

Article history:

Received 22 November 2018

Revised 21 December 2018

Accepted 22 December 2018

Available online 4 January 2019

Keywords:

Primary

Splenic

Angiosarcoma

Spleen

Bone

Metastasis

ABSTRACT

Primary splenic angiosarcoma carries a poor prognosis and is among the rarest forms of malignancy. An overwhelming majority of patients with splenic angiosarcoma will develop metastases. However, osseous metastatic disease is rare. We present an 83 year old hispanic female who was diagnosed with primary splenic angiosarcoma on bone marrow biopsy performed for a hematologic workup. We highlight key historical, laboratory, imaging, and pathological features of splenic angiosarcoma. The synthesis of both imaging features and clinical history is essential for establishing early diagnosis in these patients.

© 2019 Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license.

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Primary splenic neoplasms can be broadly categorized into lymphoid and vascular neoplasms. Lymphoid neoplasms originate from the white pulp, and vascular neoplasms arise from the red pulp [1]. Malignant primary splenic tumors include

primary lymphoma, hemangiosarcoma, and Primary Splenic Angiosarcoma (PSA). Other benign primary splenic neoplasms include hemangioma, lymphangioma, hamartoma, hemangioendothelioma, and hemangiopericytoma [2].

PSA is a rare tumor arising from splenic vascular endothelium. It is among the rarest forms of malignancy with an incidence of 0.14–0.25 cases per million individuals [3]. It tends

Acknowledgements: We would like to acknowledge the department of Radiology and Pathology at Northwell Health System's Lenox Hill Hospital, as well as the Pathology department at Mount Sinai Hospital and their collaboration on the preparation of this report.

Conflicts of Interest: We have no conflicts of interest to disclose.

* Corresponding author.

E-mail address: asaphlevy@gmail.com (A.C.J. Levy).

<https://doi.org/10.1016/j.radcr.2018.12.008>

1930-0433/© 2019 Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

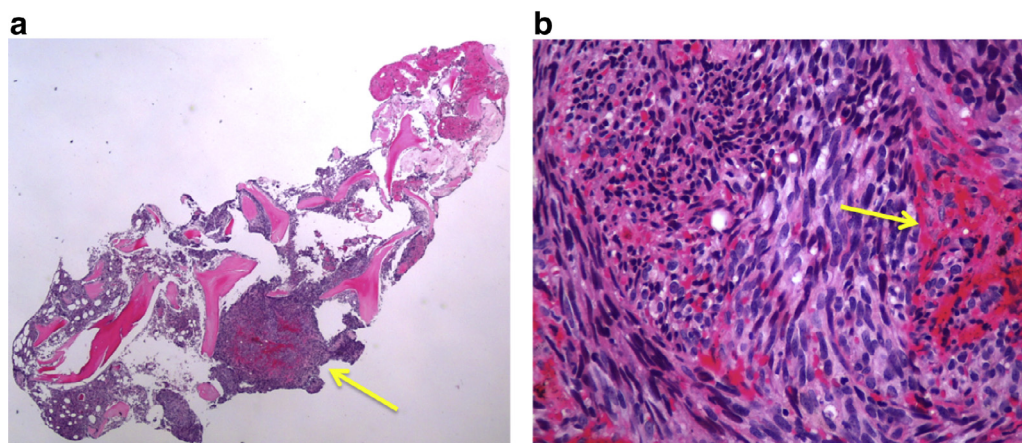


Fig. 1 – (a) Low power view (40x): Hematoxylin and Eosin (H&E) stained section of hypercellular bone marrow with focal nest of metastatic tumor (yellow arrow). (b) High power view (400x): H&E stained section show fascicles of high grade malignant spindle cells with extensive erythrocyte extravasation (yellow arrow).

to occur in patients over the age of 40, with a peak incidence during the 6th decade of life, with no clear gender predilection [4]. Risk factors for PSA are not well known.

PSA is a particularly aggressive malignancy with a propensity to metastasize, likely due to its vascular origin, and diagnosis is often delayed due to vague presenting symptoms such as abdominal pain and distension. These patients are often asymptomatic in the absence of advanced disease. Historical and physical findings suspicious for advanced disease include weight loss, ascites, and a palpable abdominal mass/splenomegaly. The most common sites of metastases have been reported to include the liver, lungs, lymph nodes, and gastrointestinal tract. However, bone metastases have also been described in a small number of cases [5–9].

Case report

The patient is an 83-year-old Hispanic female who initially presented to an outside institution with known splenomegaly and acute abdominal pain. During an outpatient hematology/oncology workup for nonHodgkin's Lymphoma and marginal zone lymphoma, she became acutely ill, presenting with spontaneous splenic rupture and underwent an urgent splenectomy. Pathology for the splenectomy specimen was interpreted as normal splenic tissue without evidence of extramedullary hematopoiesis at the time of surgery. The patient was admitted for postoperative management and discharged in stable condition.

However, 2 weeks later she presented to our Emergency Department (ED) with increasing abdominal pain, shortness of breath, and lower extremity edema. Her past medical history consisted of hypertension, hyperlipidemia, and thrombocytopenia, as well as the recent history of splenectomy. Physical exam in the ED demonstrated trace crackles, as well as moderate abdominal distension and tenderness to palpation. Her labs on admission demonstrated a WBC of 11.9 K/ μ L (Normal: 3.8–10.5 K/ μ L), hemoglobin of 9.1 g/dL

(Normal: 12.0–15.5 g/dL), platelets of 63 K/ μ L (Normal: 150–450 K/ μ L), Partial Thromboplastin Time (PTT) of >200 seconds (Normal: 25–35 seconds), Prothrombin Time (PT) of 320 seconds (Normal: 11–13.5 seconds), International Normalized Ratio (INR) of >24 (Normal: <1.1), Fibrinogen < 80 mg/dL (Normal: 150–400 mg/dL), D-dimer of 16,533 ng/mL (Normal: \leq 500 ng/mL), CA-125 of 117 U/mL (Normal: \leq 35 U/mL), and CA 19-9 of 172.3 U/mL (Normal: \leq 41.3 U/mL). The initial Computed Tomography (CT) scan performed on this presentation was a pulmonary arteriogram to exclude Pulmonary Embolism (PE), which was negative for PE but positive for mild abdominal ascites, hepatomegaly, and cholelithiasis without evidence of acute cholecystitis.

During her admission at our institution, hematology/oncology was consulted for the patient's coagulopathy, who expressed suspicion for myelofibrosis, myeloproliferative neoplasm, or infection as the underlying etiology. As a result, a bone marrow biopsy was recommended and performed. The pathology demonstrated malignant spindle cells with extensive erythrocyte extravasation (Fig. 1). By immunohistochemistry, the specimen was positive for vascular antigen/tumor markers CD34 and CD31 (Fig. 2). Human Herpesvirus-8 (HHV-8) and podoplanin (D2-40) testing was negative, ruling out Kaposi's Sarcoma (KS). These pathologic features were consistent with metastatic angiosarcoma. The patient was then started on chemotherapy regimen with doxorubicin.

In lieu of the pathology results, a diagnosis of splenic angiosarcoma was suspected, given a history of splenomegaly and spontaneous splenic rupture. A presplenectomy contrast-enhanced CT of the abdomen and pelvis, performed at the outside institution, demonstrated innumerable subcentimeter splenic hypodensities with a dominant 7.0cm splenic mass (Figs. 3 and 4).

In order to affirm a definitive diagnosis, the splenectomy pathology was re-evaluated at the outside institution. The revised pathology established a diagnosis of splenic angiosarcoma, as specimen sections stained positive for CD31 (Figs. 5 and 6).

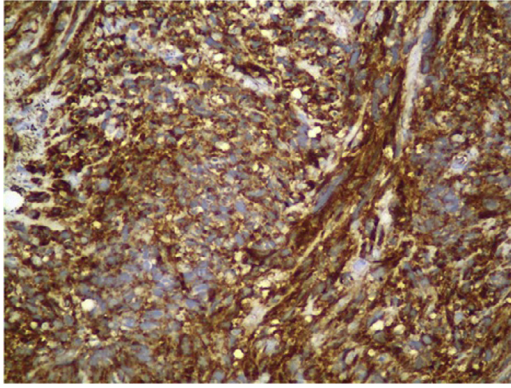


Fig. 2 – Immunohistochemistry: The tumor cells are diffusely positive for CD31 immunostain (vascular endothelial cell marker).

The patient's hospital course was complicated by severe Disseminated Intravascular Coagulation (DIC), which required multiple transfusions of cryoprecipitate, Fresh Frozen Plasma (FFP), and Vitamin K. In addition, she experienced a decline in mental status, thought to be secondary to metabolic encephalopathy versus hepatic encephalopathy; as she had a blood ammonia level up to 95 $\mu\text{mol/L}$ (Normal: 11–55 $\mu\text{mol/L}$). She eventually became unresponsive, hypotensive, and tachycardic and was transferred to the Intensive Care Unit (ICU) where she subsequently decompensated and expired despite our resuscitative efforts.

Discussion

PSA is a rare soft-tissue sarcoma with a poor prognosis. It represents less than 2% of all soft tissue sarcomas [10]. Most forms of this cancer are considered sporadic and there are no known genetic or environmental predisposing factors. Its poor

prognosis is likely due to later stage of diagnosis, given its indolent presentation. Common presenting symptoms include upper abdominal pain and fullness, fatigue, splenomegaly, anemia, thrombocytopenia, and weight loss. Patients may present with spontaneous splenic rupture, resulting in acute hemoperitoneum in up to 30% of patients [11]. Some reports suggest splenic rupture and urgent/elective splenectomy have no effect on outcomes. Conversely, others have proposed splenic rupture carries a worse prognosis due to the increased risk of dissemination of tumor cells by direct implantation within the peritoneal cavity, as well as through hematogenous spread [11]. PSA has a propensity to metastasize likely due to its vascular endothelial origin. The main reported metastatic sites are liver (89%), lungs (78%), lymph nodes (56%), and bone (22%) [11]. Although there are no standardized treatment regimens for PSA, many patients undergo a combination of treatment with surgery and chemoradiation therapy [4].

The pathogenesis of PSA is not well understood. Some studies suggest they occur as a result of malignant transformation of hemangiomas or hemangioendotheliomas [11]. There are reported risk factors for angiosarcoma in general, which include radiation and exposure to chemicals such as thorium, arsenic, and vinyl chloride [12]. However, these are not specific for PSA.

Radiographic features of PSA typically includes an aggressive-appearing splenic mass or masses with associated splenomegaly. Contrast-enhanced CT generally demonstrates multiple complex heterogeneous and hypervascular splenic masses, which is present in our case. However, they may also present as a solitary splenic mass. The heterogeneous appearance of these tumors is thought to be secondary to internal areas of hemorrhage and necrosis [2]. Calcifications are seldom reported in these lesions. If there are intrinsic calcifications, calcified hemangiomas and treated splenic lymphoma should also be considered. Reported ultrasound characteristics include multiple complex heterogeneous splenic masses with predominantly increased echogenicity with areas of decreased echogenicity. The presence of hypervascularity on color Doppler images is equivocal [13].

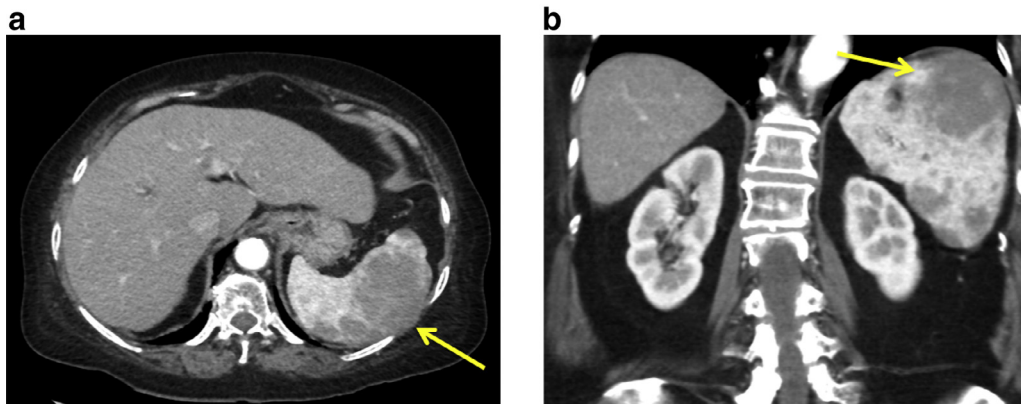


Fig. 3 – (a) Axial contrast-enhanced CT image demonstrates multiple splenic hypodensities with a dominant 7.0 cm splenic mass with findings suspicious for local invasion of the chest wall (yellow arrow). (b) Coronal contrast-enhanced CT image demonstrates an enlarged spleen with an irregular contour. The dominant mass is also depicted (yellow arrow) with intrinsic heterogeneous enhancement.

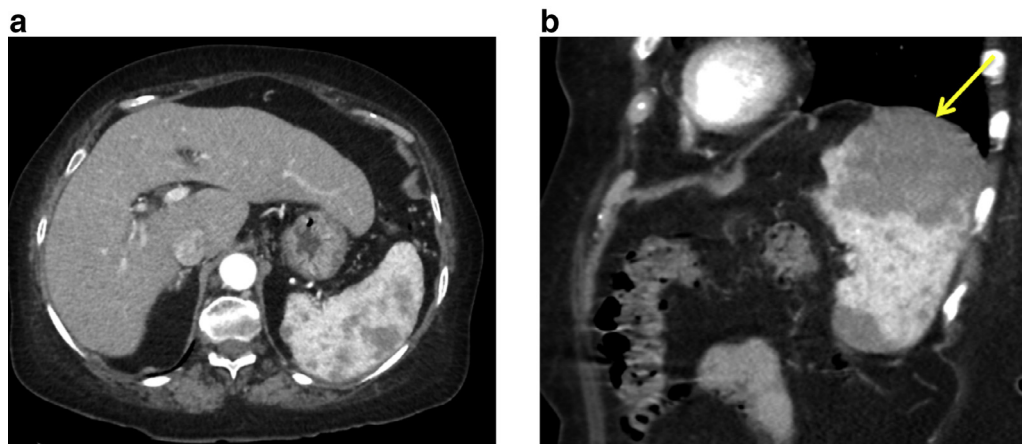


Fig. 4 – (a) Axial contrast-enhanced CT image demonstrates multiple scattered subcentimeter splenic hypodense lesions. (b) Sagittal contrast-enhanced CT image demonstrates multiple splenic hypodensities within an enlarged and irregular spleen. The dominant mass is depicted (yellow arrow) as well as a smaller hypodense mass in the inferior aspect of the spleen.

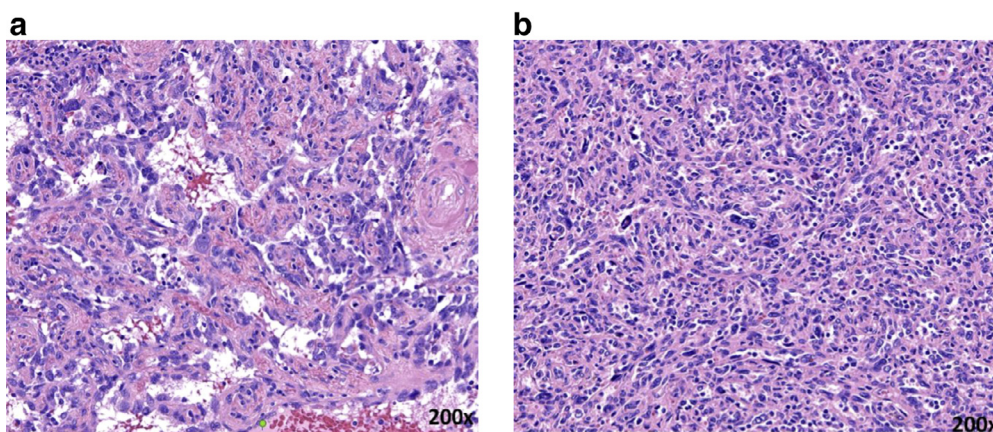


Fig. 5 – High power view (200x): H&E stained sections of the splenectomy specimen show splenic angiosarcoma displaying characteristic atypical anastomosing neoplastic vascular channels and pleomorphic nuclei.

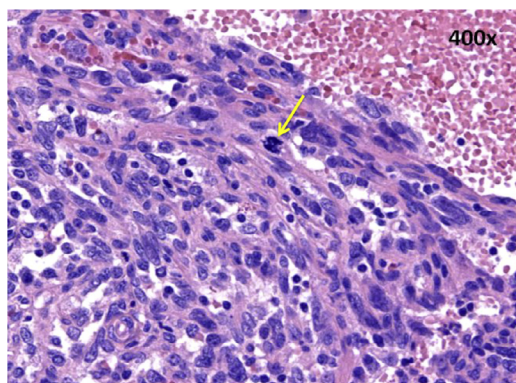


Fig. 6 – High power view (400x): H&E stained section of the splenectomy specimen shows splenic angiosarcoma displaying an atypical mitotic figure (yellow arrow) amongst pleomorphic spindle cells.

Reported Magnetic Resonance Imaging (MRI) features include nodular hypointense masses, relative to the adjacent splenic parenchyma, on both T1- and T2-weighted images. However, intrinsic increased T1 and T2 signal may be appreciated in the setting of intratumoral hemorrhage and necrosis. In all 3 modalities, attention should be made to detect concurrent liver lesions, as liver metastasis is present in approximately 89% of cases [11]. However, our patient did not have radiographically evident liver metastases at the time of diagnosis.

Given that this is a rare entity, it is even rarer to establish this diagnosis on bone marrow biopsy. To our knowledge, there have only been a small number of reported cases of metastatic disease to the bones [5–8]. Falk et al is a study of 40 cases of PSA in which 7 patients (17%) of these patients had bone or bone marrow metastasis [9]. A summary of recently reported cases with bone metastases is presented (Table 1).

PSA is a rare yet aggressive malignancy. Therefore, it is important as radiologists to raise the suspicion in the setting of splenic masses with characteristic imaging features and a compatible history; including but not limited to splenomegaly,

Table 1 – Summary of reported cases of PSA with bone metastases

Reference	# of patients	Age	Gender	Presentation	Imaging findings/ diagnostic modality (D _x)	Pathology	Involvement	Survival
Anoun et al. (2014) [5]	1	25	F	Anemia and splenomegaly	CT: Large (21cm) heterogeneous spleen with multiple lesions measuring up to 1cm Dx: bone marrow biopsy (splenectomy was subsequently performed)	Spindle cell proliferation and slit-like vascular channels. CD34 (+); CD31 (-); HHV-8 (-)	Bone and local lymph node metastasis (14 N+ of 15)	12 months (following splenectomy)
Pathan et al. (2008) [6]	1	43	F	Anemia, thrombocytopenia, and LUQ abdominal mass	CT: not performed US: splenomegaly and echogenic liver mass Dx: splenectomy (bone marrow biopsy was subsequently performed 2 weeks post splenectomy)	Spindle tumor cells and anastomosing vascular channels. CD34 (+); CD31 (+); Factor VIII (+)	Bone marrow and liver metastases	Not Reported
Wang et al. (2004) [7]	1	36	M	Splenic mass	Dx: splenectomy (bone marrow biopsy was performed 3 years following splenectomy for anemia)	High-grade Angiosarcoma. CD31 (+); CD34 (+); vWF (+)	Bone marrow	Not reported
Gao et al. (2017) [8]	1	68	F	Skull masses, anemia, and thrombocytopenia	CT: diffuse skull destruction/soft tissue scalp mass MRI: splenomegaly and multiple splenic/hepatic lesions Dx: resection of skull tumor	Spindle Cells, atypia, nuclear fission, & necrosis. CD34 (+); CD31 (+)	Parietal and occipital calvarium	Not reported
Levy et al. (current report)	1	83	F	Spontaneous splenic rupture, abdominal pain/distension, SOB, lower extremity edema, and anemia	CT: splenomegaly and innumerable splenic hypodensities with a dominant 7cm mass Dx: bone marrow biopsy	Spindle cell proliferation and slit-like vascular channels. CD34 (+); CD31 (-); HHV-8 (-)	Bone marrow	3 months (following splenectomy)

LUQ, Left Upper Quadrant; SOB, Shortness Of Breath; HHV-8, Human Herpes Virus-8; vWF, von Willebrand Factor

spontaneous splenic rupture, splenectomy, or coagulopathy of unclear etiology. The synthesis of both imaging features and clinical history may lead us to suggest PSA in these patients.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2018.12.008](https://doi.org/10.1016/j.radcr.2018.12.008).

REFERENCES

- [1] Frontario SC, Goldenberg-Sandau A, Roy D, Sandau R. Primary splenic angiosarcoma presenting as idiopathic thrombocytopenic purpura: a case report and review of the literature. *Case Rep Surg* 2016;2016:4173060. doi:[10.1155/2016/4173060](https://doi.org/10.1155/2016/4173060).
- [2] Kaza RK, Azar S, Al-Hawary MM, Francis IR. Primary and secondary neoplasms of the spleen. *Cancer Imaging* 2010;10(1):173–82. doi:[10.1102/1470-7330.2010.0026](https://doi.org/10.1102/1470-7330.2010.0026).
- [3] Xu B, Xie X, Zhou X, Zhai M, Yang W. Spontaneous rupture of primary splenic angiosarcoma: a case report. *Oncol Letters* 2015:3271–3. doi:[10.3892/ol.2015.3714](https://doi.org/10.3892/ol.2015.3714).
- [4] Hamid K, Rodriguez J, Lairmoire T. Primary splenic angiosarcoma. *J Society Laparoendosc Surg* 2010;14(3):431–5. doi:[10.4293/108680810X12924466006521](https://doi.org/10.4293/108680810X12924466006521).
- [5] Anoun S, Marouane S, Quessar A, Benchekroun S. Primary splenic angiosarcoma revealed by bone marrow metastasis. *Turk J Haematol* 2014;31(4):408–10. doi:[10.4274/tjh.2013.0049](https://doi.org/10.4274/tjh.2013.0049).
- [6] Pathan M, Ben-Ezra J, Riley R. A rare case of bone marrow metastasis of a splenic angiosarcoma. *Int J Endovasc Med* 2008;1(2):1–4.
- [7] Wang C, Rabah R, Blackstein M, Riddell RH. Bone marrow metastasis of angiosarcoma. *Pathol Res Pract* 2004;200(7-8):551–5. doi:[10.1016/j.prp.2004.05.003](https://doi.org/10.1016/j.prp.2004.05.003).
- [8] Gao L, Xu W, Li T, Luo H, Gai S, Xing R, et al. A rare case of angiosarcoma with skull masses and erythropenia and thrombocytopenia: a case report and review of literature. *Medicine* 2017;96(49):e8787. doi:[10.1097/MD.00000000000008787](https://doi.org/10.1097/MD.00000000000008787).
- [9] Falk K, Krishnan J, Meis JM. Primary angiosarcoma of the spleen: a clinicopathologic study of 40 cases. *Am J Surg Pathol* 1993;17:959–70.
- [10] Shukla M, Basu S, Shukla VK, Kumar M. Fever, anemia, and splenomegaly: a rare presentation of splenic angiosarcoma. *Indian J Med Paediatr Oncol* 2011;32(4):230–2. doi:[10.4103/0971-5851.95148](https://doi.org/10.4103/0971-5851.95148).
- [11] Ferreira BP, Rodler ET, Loggers ET, Pollack SM, Jones RL. Systemic therapy in primary angiosarcoma of the spleen. *Rare Tumors* 2012;4(4):e55. doi:[10.4081/rt.2012.e55](https://doi.org/10.4081/rt.2012.e55).
- [12] Kohutek F, Badik L, Bystricky B. Primary angiosarcoma of the spleen: rare diagnosis with atypical clinical course. *Case Rep in Oncol Med* 2016;6 pages. doi:[10.1155/2016/4905726](https://doi.org/10.1155/2016/4905726).
- [13] Thompson WM, Levy AD, Aguilera NS, Gorospe L, Abbott RM. Angiosarcoma of the spleen: imaging characteristics in 12 patients. *Radiology* 2005;235:106–15. doi:[10.1148/radiol.2351040308](https://doi.org/10.1148/radiol.2351040308).