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Krol, John J.; Krol, Vera V.; Dawkins, Adrian; and Ganesh, Halemane S., "Case 213: Primary Spenic Angiosarcoma" (2015). *Radiology Faculty Publications*. 4.

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Notes/Citation Information

Published in *Radiology*, v. 274, no. 1, p. 298-303.

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Digital Object Identifier (DOI)

<http://dx.doi.org/10.1148/radiol.14110919>

Case 213: Primary Splenic Angiosarcoma¹

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History

A 75-year-old woman with a medical history of gastroesophageal reflux disease and type II diabetes presented to the hospital with a 3-month history of gradually worsening headaches, vague upper abdominal pain, and lower back pain. The patient denied fevers, night sweats, contact with sick individuals, occupational exposure to infection, bleeding, immunodeficiency, intravenous drug use, alcohol or tobacco abuse, history of malignancy, family history of genetic disorders, and international travel. Physical examination revealed a skin-colored mass protruding from the right side of her forehead, but there were no other notable abnormalities. Her diabetes was managed with diet, and the only prescription medication she was taking was esomeprazole. She was not taking anti-coagulants. Initial laboratory work-up revealed anemia and profound thrombocytopenia (hemoglobin level, 9.4 g/dL; platelet count, $16 \times 10^9/L$); these were refractory to aggressive treatment, including plasmapheresis, immunosuppression with prednisolone, and numerous transfusions. Contrast material-enhanced magnetic resonance (MR) imaging of the head was performed at admission to further evaluate the patient's headache and the mass on the patient's forehead. Ultrasonography (US) of the abdomen was performed to evaluate the cause of abdominal pain. The discovery of liver lesions at US led us to perform contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis. Contrast-enhanced MR imaging of the abdomen was performed to narrow the diagnostic considerations for the lesions identified at CT. Bone marrow biopsy revealed no evidence of infectious or neoplastic processes. Endoscopy and colonoscopy were performed; however, they revealed no abnormalities. Further laboratory work-up included extensive testing for parasites, fungi, bacteria, and viruses, including the human immunodeficiency virus (HIV). All of the results were negative. On the 17th day of admission, the patient became acutely unresponsive, her condition deteriorated rapidly, and she died. Unenhanced head CT was performed at the time of the patient's acute decompensation.

Part one of this case appeared 4 months previously and may contain larger images.

Published online

10.1148/radiol.14110919 Content code: **GI**

Radiology 2015; 274:298–303

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Conflicts of interest are listed at the end of this article.

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Imaging Findings

Figure 1 is an axial contrast-enhanced T1-weighted MR image of the head that was obtained to assess the patient's initial report of headache and the lesion on the patient's forehead.

There is an extra-axial peripherally enhancing soft-tissue lesion extending through the diploic space and showing mass effect in the right frontal lobe. Figure 2 is a transverse gray-scale US image of the upper abdomen obtained to evaluate the patient's vague upper

Figure 1

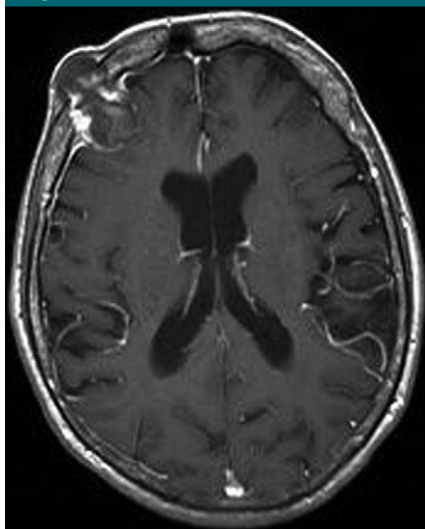


Figure 1: Axial T1-weighted (repetition time msec/echo time msec, 400/17; 5-mm section thickness) contrast-enhanced MR image of the brain (10 mL of gadopentetate dimeglumine administered intravenously over 15 seconds, Magnevist; Bayer Healthcare Pharmaceuticals, Leverkusen, Germany) shows a peripherally enhancing soft-tissue lesion extending through the diploic space into the parenchyma of the right frontal lobe.

abdominal pain. This image shows ill-defined heterogeneous hypoechoic lesions, some of which contain internal echoes. There is a heterogeneous rim surrounding some of the lesions. The visualized hepatic parenchyma demonstrates diffuse heterogeneity. These lesions were not suspected clinically and shifted the focus to differential diagnostic considerations of infectious and neoplastic processes; however, laboratory tests did not enable us to confirm a specific diagnosis. Torso CT was performed with intravenous administration of contrast material to establish the distribution of lesions and to identify the source. Figure 3 is a representative image of the chest obtained through the breasts that shows no breast or lung mass. Figure 4a is an axial dynamic contrast-enhanced CT image obtained in the arterial phase that depicts multiple complex low-attenuation lesions throughout the liver. A similar large complex low-attenuation lesion is seen in the spleen. There

Figure 2

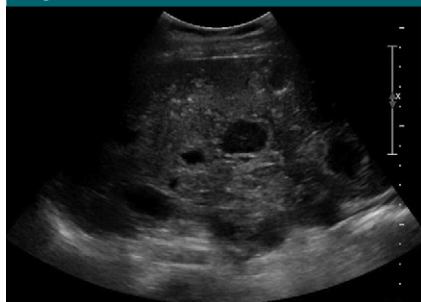


Figure 2: Transverse gray-scale US image of the upper abdomen shows ill-defined heterogeneous hypoechoic lesions. Some of the lesions contain internal echoes, and some have relatively hyperechoic rims. The visualized hepatic parenchyma demonstrates diffuse heterogeneity.

Figure 3



Figure 3: Axial contrast-enhanced CT image of the chest acquired during the arterial phase (80 mL of iohexol 300 administered at a rate of 4 mL/sec, Omnipaque 300; GE Healthcare, Milwaukee, Wis). There is no lung or breast mass.

is slight heterogeneous enhancement of the splenic lesion but no enhancement of the liver lesions. Figure 4b shows the pancreas is fatty and atrophied, without focal mass. There is no renal mass. We identified soft-tissue masses in the L1 and L2 vertebral bodies on this image. In combination with chest CT images, the dynamic contrast-enhanced CT images helped us exclude the most common malignancies, including those in the breast, lung, pancreas, uterus, cervix, ovary, and kidney. Endoscopy and colonoscopy were also performed and revealed no mass, which enabled us to virtually exclude gastric and colon primary malignancies. Infectious and neoplastic processes were still the major differen-

Figure 4



a.



b.

Figure 4: Axial contrast-enhanced CT images of the liver during the arterial phase (80 mL of iohexol 300 administered at a rate of 4 mL/sec) show (a) a large complex low-attenuation lesion in the spleen and multiple complex low-attenuation lesions throughout the liver and (b) fatty atrophy of the pancreas, without focal mass, and no renal mass.

tial considerations; thus, fluorodeoxyglucose (FDG) combined positron emission tomography (PET) and CT were ordered in an attempt to distinguish between the two major differential diagnoses. Figure 5 is the FDG PET/CT image, which did not show abnormal FDG uptake in the lesions and added little information to the clinical picture. MR images of the abdomen were then obtained to better characterize the hepatic and splenic lesions. Figure 6 is an ultrafast spin-echo sequence that reveals a large heterogeneous T2 hyperintense lesion in the spleen and multiple heterogeneous T2 hyperintense lesions throughout the liver. Figure 7 was obtained with a dynamic postcontrast axial T1-weighted

Figure 5

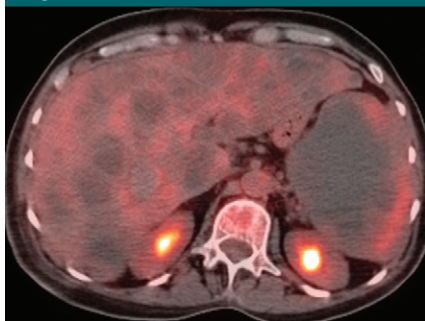


Figure 5: Representative axial FDG (13.9 mCi, infused at a blood glucose level of 113 mg/dL and incubated for 62 minutes) PET/CT image through the upper abdomen shows low-grade uptake of the radiotracer in the periphery of the cystic necrotic lesions within the spleen and liver.

Figure 6

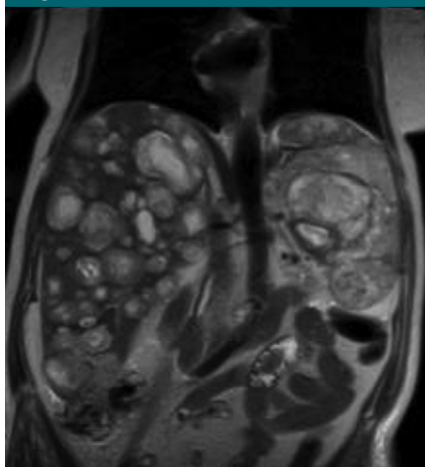
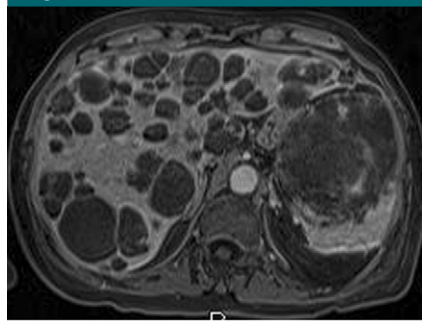


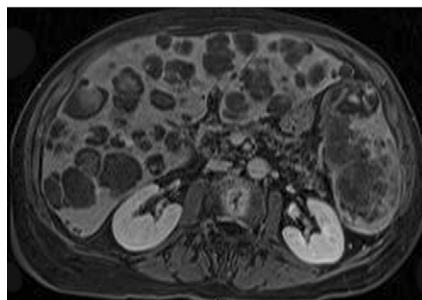
Figure 6: Coronal T2-weighted (900/78, 6-mm section thickness) ultrafast spin-echo MR image of the abdomen (Symphony; Siemens Medical Systems, Erlangen, Germany) shows a large complex T2 heterogeneous hyperintense lesion in the spleen and multiple heterogeneous T2 hyperintense lesions throughout the liver.

fat-suppressed gradient-echo sequence, and it depicts areas of heterogeneous enhancement of the large splenic lesion and peripheral enhancement of several of the hepatic lesions on the early arterial phase image (Fig 7a). Figure 7b was obtained in the late arterial phase and shows an additional peripherally enhancing lesion in the L1 vertebral body. The imaging and laboratory results failed to yield a specific

Figure 7



a.



b.

Figure 7: Axial T1-weighted (4.3/2, 2-mm section thickness) dynamic contrast-enhanced ultrafast gradient-echo MR images of the abdomen (10 mL of gadopentetate dimeglumine) obtained during the (a) early and (b) late arterial phases. Images show areas of heterogeneous enhancement of the large splenic lesion and several of the hepatic lesions (a) and an additional peripherally enhancing mass in the L1 vertebral body (b).

diagnosis, so biopsy was requested. Angiosarcoma was not suspected by those who performed the procedure. Routine CT-guided biopsy of one of the liver lesions was attempted, but the results were nondiagnostic, as the lesions yielded only inflammatory cells and necrotic tissue. Substantial intraperitoneal bleeding was recognized several hours after biopsy and required multiple transfusions. The patient remained hemodynamically stable; however, at autopsy several days later, there was an estimated 3–4 L of blood in the abdomen. Figure 8 is an axial CT image of the head without intravenous contrast material obtained at the time of the patient's spontaneous acute clinical decompensation several days after biopsy. It shows the extra-axial mass associated with acute extra-axial

Figure 8



Figure 8: Unenhanced axial CT image of the head at the time of acute mental status changes and clinical deterioration shows acute subdural and epidural hemorrhage causing mass effect in the brain and subfalcine herniation.

Figure 9

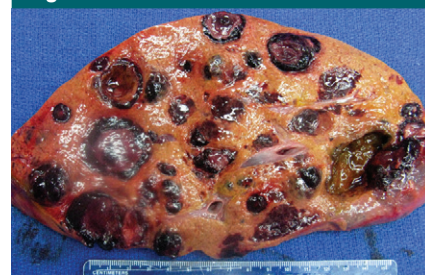


Figure 9: Gross pathologic image of the liver shows parenchymal involvement by ill-defined hemorrhagic and necrotic foci of angiosarcoma.

hemorrhage and associated mass effect, including subfalcine herniation. Figure 9 is the liver specimen at autopsy. It shows parenchymal involvement by ill-defined, hemorrhagic, and necrotic foci of angiosarcoma. Figure 10 is the spleen specimen at autopsy. It shows gross organ distortion and involvement by one dominant lesion and numerous cystic, necrotic, and hemorrhagic lesions that surround the larger lesion. Figure 11 is the histologic slice of the spleen. It shows an area of haphazard anastomosis of poorly formed vascular channels adjacent to an area of hemorrhage and necrosis. The vas-

Figure 10



Figure 10: Gross pathologic image of the spleen shows a markedly distorted organ with one dominant lesion and numerous surrounding cystic, necrotic, and hemorrhagic lesions.

cular channels are lined by highly pleomorphic epithelioid cells of high nuclear grade. The autopsy findings of a large dominant splenic angiosarcoma and multiple smaller foci of angiosarcoma involving the liver and bones enabled us to confirm the diagnosis of splenic angiosarcoma.

Discussion

The distribution, behavior, and imaging characteristics of the lesions suggest a neoplastic or infectious origin. There is easily identifiable multifocal disease, with one of the lesions extending through the skull and compressing the right frontal lobe parenchyma. Thus, the most likely categories of disease processes that would explain these findings are infection and neoplasm.

The major infectious differential considerations for this patient would be echinococcal infection, bacillary angiomatosis, schistosomiasis, and multiple abscesses, including those caused by amoebic species. Abscesses and bacillary angiomatosis virtually always cause high fevers and leukocytosis and are therefore unlikely, given this patient's history and laboratory results. Echinococcal infection was excluded clinically with echinococcal antigen testing. Schistosomiasis represents a reasonable differential diagnosis for the liver lesions, but it would not explain the soft-tissue mass in the skull. Other overwhelmingly rare or atypical infections

Figure 11

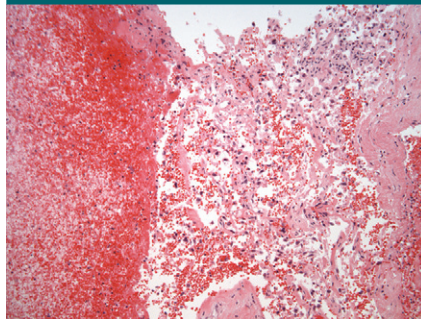


Figure 11: Hematoxylin-eosin stained slice of the spleen (original magnification, $\times 20$) shows an area of haphazard anastomosis of poorly formed vascular channels adjacent to an area of hemorrhage and necrosis. The vascular channels are lined by highly pleomorphic epithelioid cells of high nuclear grade.

were excluded because of the negative HIV test results, a lack of immunodeficiency, and a negative history of travel. In summary, the lack of signs and symptoms of infection and the negative results of extensive infectious disease testing make an infectious origin unlikely.

An extensive neoplastic process would better explain the behavior and distribution of the lesions in this patient. The most likely cause of multiple hepatic, splenic, and bone lesions would be metastatic disease from a common primary malignancy, such as the lung, breast, pancreas, kidney, or colon. Additionally, diffuse malignant processes, such as lymphoma, leukemia, or melanoma, would be a reasonable consideration. Primary breast, renal, lung, pancreatic, and gastrointestinal malignancies were excluded on the basis of the normal appearance of these organs at CT, other imaging studies, and endoscopy. Melanoma is less likely, as it tends to appear as T1 shortening on MR images from the cellular melanin content and as arterial phase enhancement on dynamic images (1). The centrally necrotic lesions could reasonably represent a common appearance of melanoma in a patient undergoing chemotherapy; however, this patient never underwent treatment for malignancy (2). Leukemia and lymphoma will be discussed later in this report.

Since metastases from the most common malignancies in this case are

considered unlikely, the differential diagnosis for multiple hepatic lesions should be expanded to include other, more rare processes. Lymphatic malformations and multiple hemangiomas could have an appearance similar to that of the hepatic and splenic lesions seen in this patient, but this would not explain the spontaneously hemorrhaging lesion in the skull. Kaposi sarcoma is known to involve the liver in patients with HIV; however, this patient did not have HIV, and primary hepatic or splenic Kaposi sarcomas are very rare. Epithelioid hemangioendothelioma is an important differential diagnosis in this case. Epithelioid hemangioendothelioma is often multifocal within the liver and can produce similar-appearing lesions at imaging; however, splenic and bone metastases are extremely rare (3). Primary liver hemangiopericytoma is very rare and may mimic angiosarcoma (4). However, it is less common than angiosarcoma and preferentially metastasizes to lung and bone (5).

There are several primary splenic neoplasms that could have imaging characteristics similar to those in this case. Lymphoma and leukemia could explain the distribution of the lesions, as well as the anemia and thrombocytopenia in this patient. However, these are virtually excluded in the setting of a negative bone marrow biopsy. Littoral cell angioma produces hypoattenuating splenic lesions and can have malignant characteristics; however, bone metastases are rare in this diagnosis (6). Primary splenic hemangiopericytoma is a very rare neoplasm that mimics splenic angiosarcoma in many ways, but it is less common than angiosarcoma and tends to metastasize to lung and bone (5).

Metastatic splenic angiosarcoma is the best diagnosis in this case. The spleen is the most likely primary organ in this patient for two reasons: First, the dominant lesion in the spleen is much larger than the metastases elsewhere in the body. Second, the pattern of metastasis demonstrated by imaging is most consistent with the pattern observed in patients with splenic angiosarcoma (7).

Primary splenic angiosarcoma is a rare aggressive neoplasm with the propensity to spontaneously hemorrhage, as demonstrated by this patient's skull metastasis. These lesions are known to hemorrhage significantly after biopsy, which was also seen in this patient, who had an estimated 3–4 L of blood in her abdomen at autopsy. Radiologists should be familiar with the appearance of angiosarcoma, as well as the potential for abnormal platelets with this diagnosis, so that they can make informed decisions regarding potential biopsy of similar-appearing lesions. The mean age for women to develop splenic angiosarcoma is 68 years (8). The most common presenting symptom is vague abdominal pain, as in this patient. This pain can be acute if there is spontaneous splenic rupture. Chest pain, weight loss, and fatigue are other signs and symptoms at presentation in a minority of patients. The most common laboratory abnormality is cytopenia, which was seen in up to 91% of patients in one large study (9). In that study, anemia was found in 62% of patients, and thrombocytopenia was found in up to 33% of patients with a diagnosis of angiosarcoma. This patient had both of these laboratory abnormalities. In spite of hepatic metastases being common in the setting of primary splenic angiosarcoma, hepatic enzyme test results are typically within normal limits (8). The most common sites of metastases for splenic angiosarcoma are liver and bone, specifically the vertebrae, as in this patient; however, lung metastases are not uncommon. Abdominal and mesenteric lymphadenopathy is reported less frequently (7). Treatment often includes splenectomy and chemotherapy, but prognosis is poor and most patients die within 1 year of initial diagnosis despite treatment (9).

The imaging findings of primary splenic angiosarcoma are somewhat variable, but certain trends appear to exist. The spleen is commonly enlarged, measuring more than 12 cm in maximum dimension. This patient's spleen measured 15.7 cm in maximum dimension. The majority of patients have diffuse involvement of the spleen either as a single large lesion or as a large mass

with multiple smaller nodules. The lesions frequently show central necrosis with a rim of soft tissue. At Doppler US, the necrotic centers of the lesions tend to appear cystic, with internal echoes secondary to debris or hemorrhage, while the soft-tissue rim generally appears heterogeneous in echo texture. Typically, on both CT and MR images, the primary splenic lesion is poorly defined (60% of cases) and irregularly shaped, and it shows irregular heterogeneous enhancement on postcontrast images (7). On T1-weighted MR images, the splenic and hepatic lesions tend to appear hypointense in the center and periphery, with focal areas of high signal intensity in the necrotic center in some of the lesions. On T2-weighted MR images, the splenic and hepatic lesions appear as ill-defined heterogeneously hyperintense lesions (7). There has been only one published case report in the English literature to date of splenic primary angiosarcoma imaged with FDG PET/CT, and that case showed avid uptake of FDG in the neoplasm (10). In the current case, FDG PET/CT showed no significant avidity for FDG, which is best explained by the cystic and necrotic qualities of the lesions in this patient (11). This case demonstrates the most common imaging findings of splenic angiosarcoma for US, CT, and MR imaging.

Splenic angiosarcoma is a rare aggressive neoplasm that presents many challenges to the clinician and radiologist. The clinical presentation is often nonspecific, and the imaging characteristics that differentiate angiosarcoma from more common diagnoses can be subtle. The importance of knowing the imaging and clinical features of splenic angiosarcoma is most crucial when one is considering lesion biopsy. As was seen in this patient, this neoplasm is known to spontaneously hemorrhage. Biopsy will produce hemorrhage, as was also seen in this patient, and most importantly, there is potential to produce hemorrhage that is difficult to control. Additionally, patients may have thrombocytopenia, which can further alter the ability to achieve hemostasis after the procedure. This knowledge

will help the physician to choose the best technique and location for biopsy and to manage potentially catastrophic complications.

Acknowledgment: We acknowledge Estill Robinson, BFA, for his contributions to the manuscript.

Disclosures of Conflicts of Interest: J.J.K. disclosed no relevant relationships. V.V.K. disclosed no relevant relationships. A.D. disclosed no relevant relationships. H.S.G. disclosed no relevant relationships.

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Congratulations to the 63 individuals and four resident groups that submitted the most likely diagnosis (metastatic angiosarcoma) for Diagnosis Please, Case 213. The names and locations of the individuals and resident groups, as submitted, are as follows:

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