Spontaneous Splenic Hemorrhage Leading to Diagnosis of Metastatic Adenocarcinoma of Unknown Origin

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ABSTRACT

Introduction: Spontaneous splenic hemorrhage is a rare initial presentation of malignancy. The objective of this case report is to elucidate the complexities of early diagnosis of splenic metastases and the complications associated with advanced malignancies of the spleen. It is also a reminder to consider splenic metastases and hemorrhage in the differential diagnosis for nonspecific presentations, such as acute abdomen, in adults.

Case Presentation: A 58-year-old female with 1 month of vague, worsening systemic symptoms and computed tomography findings suspicious for a subcapsular splenic hematoma was found to have splenic rupture. After undergoing emergency laparotomy with splenectomy, pathological samples revealed metastatic poorly differentiated adenocarcinoma of unknown origin. During a subsequent admission, she was found to be hemodynamically unstable, deemed a poor candidate for inpatient chemotherapy, and elected to proceed with comfort measures after which she died from multiorgan failure 3 weeks after initial presentation.

Discussion: Spontaneous (nontraumatic) splenic hemorrhage secondary to metastasis should remain a differential diagnosis for patients with acute abdomen and associated risk factors for primary malignancies.

INTRODUCTION

Malignancy of the spleen can be categorized broadly as having primary involvement or secondary involvement, with the latter being much more common. Despite the spleen being the most vascular organ in the body, it remains a rare site of tumor metastases.[1-3] Previous autopsy record review of secondary nonlymphoid splenic tumors in patients over a 25-year period demonstrated only 5.3% of splenic metastases as solitary lesions and 95% of secondary splenic tumors as carcinomas.[3] The lung was identified as the most common primary tumor site in 21% of cases.[3] Other tumors that commonly metastasize to the spleen include melanoma and tumors of the stomach, pancreas, colon, breast, and ovary.[1]

Metastasis to the spleen often is detected at a more advanced stage frequently stemming from the organ's asymptomatic nature and nonspecific symptoms at presentation, among a few other factors. The most common primary malignant neoplasm of the spleen is lymphoma, accounting for less than 1% of all lymphomas, which is far more rare than secondary splenic neoplasms.[1-2] The most common primary non-hematopoietic malignant splenic tumor is angiosarcoma, which carries a poor prognosis.[1] Benign neoplasms of the spleen include hemangioma (most common), splenic hamartoma, littoral cell angioma, splenic cyst, and other primary mesenchymal tumors, such as angiomyolipoma or fibroma.[1]

Given the frequency of incidental splenic lesion discovery on imaging, little guidance has been published previously on classifying splenic lesions and best approaches for formulation of a differential diagnosis. Kim et al recognized the existing gap in literature and importance of being able to differentiate various splenic pathologic conditions to inform early treatment decisions and thus developed an image-based algorithm for splenic lesion characterization.[4] This algorithm classifies splenic lesions into 2 primary categories—cystic and solid—before further delving into pathological features, such as whether they are solitary versus multiple, vascular versus nonvascular, or whether they contain unique features such as fluorodeoxyglucose avidity in lymphoma.[4] Accurate diagnosis must be achieved in a timely fashion due to the

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risk for hypersplenism or even splenic hemorrhage and rupture in more critical cases involving primary and secondary malignant splenic neoplasms.

CASE PRESENTATION

A 58-year-old female came to the emergency department (ED) with 1 month of generalized worsening weakness, malaise, and diaphoresis. Her medical history included severe Crohn's disease, osteoporosis, former tobacco use (10 pack years), and right kidney atrophy. Her surgical history was negative for any bowel resection surgeries. Her outpatient medications included propranolol, trazodone, zoledronic acid, gabapentin, and infliximab every 8 weeks for Crohn's management. She had presented to her primary care clinician with a cough 1 week prior and was found to have a COVID infection but did not have other visits or labs for her presenting symptoms prior to arriving to the ED. An outpatient computed tomography (CT) scan also had been completed 3 weeks prior to further evaluate results of a colonoscopy done 2 months prior.

Initial exam findings in the ED included decreased breath sounds at the lung bases, abdominal distension, left upper quadrant tenderness, and anasarca. Given the patient's nonspecific presentation and exam findings, a Crohn's flare was a primary concern; however, the differential diagnosis was kept broad. Labs upon arrival to the ED revealed new anemia (hemoglobin 8.6), normal white blood cell count, new thrombocytopenia (platelet count 35000) (Table), and a normal reticulocyte count, with elevated erythrocyte sedimentation rate, C-reactive protein, and lactate dehydrogenase. Imaging revealed bilateral pleural effusions and a pericardial effusion. Computed tomography (CT) scan of the abdomen and pelvis revealed new interval splenic enlargement compared to 3 weeks prior. The patient was admitted for a probable Crohn's flare and started on prednisone but overnight was found unresponsive in respiratory arrest, despite lack of respiratory symptoms on admission. She underwent resuscitation measures including intubation and was transferred to the medical intensive care unit (ICU).

Upon ICU transfer, the patient was hypotensive and hypothermic. Labs revealed worsening anemia and thrombocytopenia (Table) and a low haptoglobin with a negative Coombs test. An urgent repeat CT was ordered 12 hours after the initial scan, which revealed findings suspicious for a subcapsular splenic hematoma with hemorrhage and worsening significant lymphadenopathy throughout, increasing the team's concern for lymphoma (Figures 1 and 2). Given that she had an increasing vasopressor requirement with worsening renal function and acidosis, Surgery elected to complete an emergency laparotomy with splenectomy on day 2 of admission. In the operating room, the patient was found to have splenic rupture with 3 liters of blood evacuated. Diffuse small mesenteric peritoneal studding also was noted throughout the abdomen. Postoperatively, she was extubated on day 3 and no longer required vasopressor support. Repeat postoperative labs revealed improving anemia and thrombocytopenia (Table).

Table. Lab Values for Hospital Course

	Day 1	Day 2 (Pre-Laparotomy)	Day 2 (Post-Laparotomy)	Day 19
Hemoglobin (g/dL)	8.6	5.3	11.9	10
Hematocrit (%)	25.0	15.6	35	30.4
WBC (10e3/uL)	10.7	13.9	15.3	18.5
Platelet (10e3/uL)	35	20	39	372
Neutrophil (%)	86.8%	75%	N/A	83%
Lymphocyte (%)	6.2%	6%	N/A	2%
CA-125				524
CA 19-9				18.2
CEA				707
Chromogranin				218

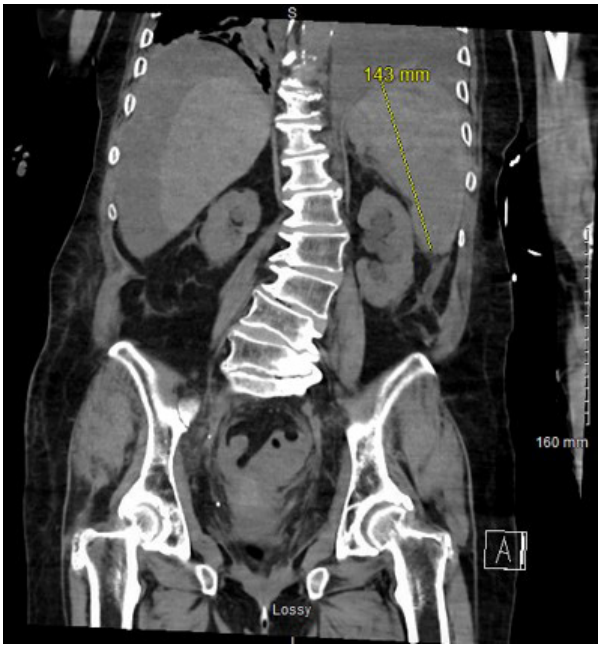
Abbreviations: WBC, white blood cells; CA, cancer antigen; CEA, carcinoembryonic antigen.

Pathology samples of the spleen and omentum were sent and returned on day 9, revealing metastatic poorly differentiated adenocarcinoma of unclear origin with signet ring cell morphology and a nonspecific immunohistochemical profile. The patient's hospital course was further complicated by acute tubular necrosis and worsening bilateral pleural effusions requiring thoracentesis, with lab results confirming malignant pleural effusions. Hematology, oncology, gastroenterology, and gynecologic oncology were consulted during her admission to continue workup of adenocarcinoma of unknown origin (Table). She was discharged after a 16-day hospitalization, with scheduled follow-up with medical oncology for suspected adenocarcinoma of small bowel versus colon.

Of note, the patient was diagnosed with Crohn's disease approximately 22 years prior and had regular screening colonoscopies every 1 to 3 years. Her disease was poorly controlled with initial management (mesalamines, 6-mercaptopurine, methotrexate), and she was receiving infliximab every 8 weeks at time of admission. Her most recent screening colonoscopy was done approximately 2 months prior to admission, with new findings of cecal pseudopolyps and abnormal-appearing mucosa near the ileocecal valve and appendiceal orifice. Biopsies of the mucosa returned negative for malignancy. A CT scan was obtained to further evaluate the colonoscopy findings, which revealed active disease with a new fistulous connection with the appendix and prominent mesenteric lymph nodes, with no splenic enlargement at the time. Given the recent colonoscopy, there was no indication for a repeat colonoscopy during her admission; however, an esophagogastroduodenoscopy was performed and was negative for a primary source.

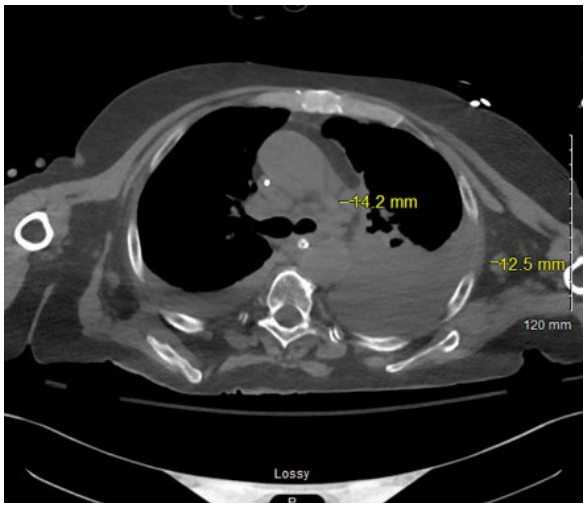
The patient returned to the ED 3 days after discharge with worsening shortness of breath and jaundice. CT imaging revealed a new soft tissue mass at the head of the pancreas with biliary obstruction (Figure 3), which was later noted to be peripancreatic

Figure 1. Computed Tomography Chest/Abdomen/Pelvis



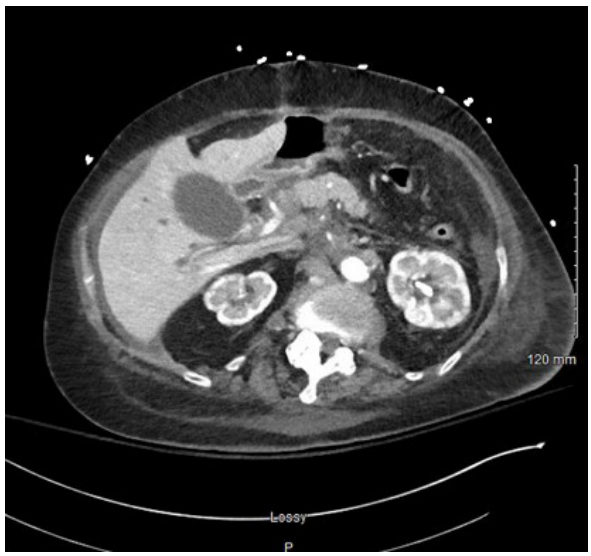
CT demonstrates splenomegaly measuring up to 14.7 cm with new heterogenous attenuation and increased hyperdense perisplenic fluid.

Figure 2. Computed Tomography Chest/Abdomen/Pelvis



CT shows multiple enlarged supraclavicular, axillary, and mediastinal lymph nodes. Representative lesions include 1.3 cm left axillary lymph node and 1.4 cm aortopulmonary window lymph node.

Figure 3. Computed Tomography Abdomen/Pelvis



CT demonstrates an aggressive mass involving the head of the pancreas that extends within the retroperitoneal space and encases the common hepatic artery and superior mesenteric artery.

soft tissue rather than a mass. Due to her hemodynamic instability, significant deconditioning and recovering kidney function, she was considered a poor candidate for inpatient chemotherapy. She ultimately elected to transition to comfort measures 3 days after readmission and died from multi-organ failure 3 weeks after her initial presentation. An autopsy was not performed.

DISCUSSION

Splenic rupture secondary to metastatic cancer is a rare complication that can occur late in the progression of a diagnosed or undiagnosed cancer. Splenic metastases are a result of advanced disease involving multiple other sites. Much of the data on splenic metastases is collected through postmortem studies, many showing the incidence to be 2.3% to 12.9%.[5] The most reported primary sites for splenic metastases include choriocarcinoma (13.3%), melanoma (10%), and gastric carcinoma (6.7%).[6] In clinical presentation, splenic metastasis is often asymptomatic but may present with discomfort in the left upper quadrant and symptoms related to pressure on other organs, such as early satiety, nausea, and dyspnea.[5,7] Symptoms of disseminated systemic disease are not uncommon either, namely cachexia and hematologic abnormalities.[5]

Several theories exist explaining the rarity of metastases to the spleen. These theories can be grouped into 3 main categories: anatomical factors, mechanical factors, and immunological factors. Anatomically, the rare occurrence of metastases to the spleen is attributed to the constant blood supply, the sharp angle of the splenic artery with the celiac axis, and the lack of afferent lymphatic vessels to the spleen.[3] Mechanical contractions of the splenic sinusoids and the presence of a splenic capsule act as a physical barrier to parenchymal metastases.[5] The microenvironment of the spleen is also particularly unfavorable for metastases. High concentrations of angiogenesis inhibition factors associated with the high density of lymphoid cells in the spleen prevent growth of metastatic cancers.[8]

In terms of the mechanism of splenic rupture secondary to malignancy, 2 theories have been proposed. Destruction of the architecture and integrity of the splenic capsule by invading neoplastic cells leading to rupture is the principal theory.[9] The other theory involves necrosis of the malignancy leading to bleeding within the tumor. Eventually, pressure builds up in the spleen leading to capsular rupture.[9]

CONCLUSIONS

Splenic metastases always should be considered part of the differential diagnosis in the context of an acute abdomen in a patient with or without cancer as a primary diagnosis. Consideration of this differential may be lifesaving—especially in the context of spontaneous splenic rupture, with first-line treatment being emergency splenectomy. In the case that a primary malignancy is identifiable and can be treated accordingly, this would not only prolong the patient's life but offer the opportunity for alternative curative therapies to be pursued, which was not consistent with this specific case.

Furthermore, it is important to emphasize the necessity for regular screening and medical management for patients with inflammatory bowel disease, as patients with these diagnoses are at increased risk of developing cancer overall. Even with stringent screening adherence and treatment optimization, it is possible that patients could present similarly to this case with a malignancy of unknown origin. In that situation, discovery of the primary malignancy may prove difficult, and with severe presentations such as this one, metastases may be an indicator of poor prognosis.

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