Multifocal Intrahepatic Artery Aneurysm with FDG-avid Thrombosis Simulating Metastasis: Report of a Rare Case

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Hepatic artery aneurysm (HAA), although rare, represents a serious diagnostic and therapeutic challenge due to high rupture rate and associated mortality. Early detection and accurate diagnosis are essential for successful management. Here, we present an extremely rare case of multi-focal intrahepatic HAA with confined intrahepatic rupture and hypermetabolic activity at PET imaging, simulating metastasis of melanoma. A retrospective review found only two other HAA at our institution between 2000 and 2015, both of which involved the extrahepatic artery. This report highlights the importance of clinical, radiological, and pathological correlation in the management of this rare condition. (J CLIN EXP HEPATOL 2016;6:321–325)

Hepatic artery aneurysm (HAA) is a rare condition, with approximately 500 cases reported since it was first described in 1809.^{1,2} It accounts for only ~0.4% of all arterial aneurysms, but more than ~20% of all visceral artery aneurysms (VAAs), making it the second most common type of VAA, following only splenic artery aneurysm.³ By definition, HAAs are true aneurysms, in which hematoma is bound by all three layers of the arterial wall. This is in contradistinction to pseudoaneurysms, which are vessel rupture with the hematoma confined only by tissue outside the arterial wall, with the tunica intima and/or media absent in the aneurysm wall. Unlike pseudoaneurysms, which are mostly secondary to trauma or surgery, HAA is associated with many different conditions. About 80% of HAAs occur extrahepatically.^{4–6} While HAA may be congenital, the vast majority are acquired. Atherosclerosis, as the most common etiologic factor for HAA, is responsible for approximately 30% of HAA cases. Iatrogenic etiologies are the second most common, among which liver transplantation accounts for about 17% of cases. Other relatively less common etiologic factors for HAA include infectious vasculitides, systemic vasculitides, including polyarteritis nodosa, Churg-Strauss vasculitis

(eosinophilic granulomatosis with polyangiitis) and those related to systemic autoimmune diseases like lupus and rheumatoid arthritis, fibromuscular dysplasia, segmental arterial mediolysis, and inherited connective tissue aberrations, such as Ehlers–Danlos and Marfan syndromes.^{7,8}

True HAAs tend to be asymptomatic until rupture, when they present as life-threatening emergencies. The estimated rate of HAA rupture is 65% with a mortality rate of 21%, which is the highest among aneurysms in the splanchnic circulation.⁹ In the last two decades, the implementation of advanced cross-sectional imaging modalities has allowed the early detection of HAAs. Moreover, since the first successful treatment of HAA by ligation in 1903, multiple other therapeutic methods have been developed, including endovascular coil embolization and endoaneurysmorrhaphy. Despite these advancements, acute rupture of HAA still has a high mortality and represents a serious diagnostic and therapeutic challenge. Here, we present a rare case of multifocal intrahepatic HAA simulating metastasis.

CASE

Clinical and Laboratory Assessment

The patient was a 76-year-old woman who presented to the Emergency Room (ER) at an outside hospital with fluctuating epigastric pain radiating to the back, nausea, and vomiting. The patient had no history of underlying chronic liver disease. Her medical history was significant for melanoma in the right upper extremity in 1973, status post-excision with wide margins; atrial fibrillation controlled by rivaroxaban; glaucoma; and a remote episode of pancreatitis. She denied any history of previous trauma, surgery, or any other procedures. On the day of transfer to

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Abbreviations: HAA: hepatic artery aneurysm; FDG: fluorodeoxyglucose; PET: positron emission tomography; VAA: visceral artery aneurysm; CT: computed tomography; MRI: magnetic resonance imaging; MRCP: magnetic resonance cholangiopancreatography; SUV: standard uptake value <http://dx.doi.org/10.1016/j.jceh.2016.08.002>

Figure 1 A 75-year-old woman with liver lesions. Contrast-enhanced CT demonstrates a 1.1 cm homogeneously and avidly enhancing lesion in segment 3 (arrow). (A) Contrast-enhanced MRI performed the following day demonstrates that only the anterior aspect of the lesion is enhancing (arrow). (B) The posterior portion of the lesion is non-enhancing. Ultrasound performed two days later confirms these findings, demonstrating internal echoes and a fine septation (arrow). (C) With color Doppler, the anterior aspect of the lesion shows vascular flow (arrow). (D) The posterior portion of the lesion containing internal echoes, lack of color flow at US and enhancement on MRI is most consistent with the partial thrombosis and contained rupture of the hepatic artery aneurysm.

our institution, her vital signs were remarkable for hypertension, with blood pressure of 183/115. Her serum transaminase activities were within normal range (alanine transaminase 33 U/L and aspartate transaminase 47 U/L) and alkaline phosphatase was slightly increased (151 U/L, normal range 30–110). All other laboratory values were within normal range.

Imaging Assessment

Abdominal computed tomography (CT) was performed during the portal venous phase following the injection of iodinated contrast. Five discrete hypervascular lesions in the liver were identified: in segment 3 measuring 11 mm, in segment 7 measuring 4 mm, and three in segment 6 measuring 6, 4, and 4 mm. The largest lesion in segment 3 demonstrated homogenous enhancement (Figure 1A). Two low-attenuation areas, each measuring 5 mm in diameter, were also incidentally noted in the uncinate process of the pancreas. None of these changes were present on a CT performed 10 years prior. Contrast-enhanced magnetic resonance imaging (MRI) was performed the following day, which demonstrated heterogeneous intermediate T1 signal within the segment 3 lesion with partial enhancement along the anterior aspect (Figure 1B). On MRCP sequence, no clear communication between the subcentimeter pancreatic lesions and pancreatic duct could be identified. Subsequent hepatic ultrasound showed a 21 mm complex hypoechoic structure with internal echoes and

septation in the left lobe of the liver, corresponding to the segment 3 lesion noted on CT and MRI (Figure 1C). Blood flow was noted along the periphery of this lesion (Figure 1D). Two adjacent anechoic structures, up to 12 mm, with surrounding vascularity were noted in the porta hepatis, which demonstrated continuity with surrounding vessels. Multiple smaller anechoic structures, measuring up to 9 mm in diameter, were also noted in the left hepatic lobe, appearing in continuity with the surrounding vessels. A separate anechoic structure containing internal vascularity and measuring 12 mm was noted in the right lobe, consistent with the lesions in segments 6 and 7 identified on CT. Two sub-centimeter splenic artery aneurysms were also noted on the CT and MRI (not shown). The abdominal aorta was normal in course and caliber. Trace abdominal ascites were present on the MRI; however, there was no frank intraperitoneal hemorrhage.

Given the patient's history of melanoma, positron emission tomography (PET) scan was performed to further characterize the liver lesions. On fused PET-CT imaging, the liver demonstrated mild focal FDG uptake corresponding to the enhancing lesions seen on CT and ultrasound (Figure 2). The maximum standard uptake value (SUV-max) of these lesions was 3.2. Although the lesions were not markedly FDG avid, the consensus was that surgical resection was preferable and to repeat PET/CT scan in two months. The patient underwent elective resection. Two additional masses were identified intraoperatively in the

Figure 2 Fused PET/CT image of the liver lesion. The lesion in segment 3, corresponding to lesions identified on the prior abdominal imaging, demonstrating mild hypermetabolic activity (arrow).

left lobe, in the falciform fissure and in the anterior portion of segment 4. The transection plane incorporated these lesions, resulting in an extended left lateral segmentectomy. The patient tolerated the procedure well without complication.

Pathologic Assessment

The liver resection specimen measured 16.0 cm × 9.5 cm × 3.0 cm and weighed 256 grams. Serial

sectioning revealed dilated and thick-walled blood vessels with occluding dark red thrombi, measuring up to 2 cm in diameter (Figure 3A). The thrombi are present throughout the large and small branches of vessels in the portal tracts. Histologically, the lesions were composed of dilated, thick-walled muscular vessels containing fresh thrombi. Focally, the thrombus was organized and recanalized. Thrombus was seen within the lumen and within the arterial wall at the site of dissection (Figure 3B). Dilated and thrombosed arteries with fragments of internal elastic layers confirm true HAAs (Figure 3C and D). No active, chronic, or granulomatous arteritis was noted; however, adjacent arteries showed atherosclerotic changes. No malignant cells were identified, and immunohistochemical stains for HMB-45 and Melan A performed on multiple levels were all negative, excluding metastatic melanoma. These histopathological findings were consistent with rupture of multifocal HAAs.

DISCUSSION

We demonstrate here a case of a 76-year-old patient with rare multifocal intrahepatic HAA. There was spontaneous thrombosis of the HAA following confined intrahepatic rupture, and thus the patient avoided serious hemorrhage. Given that the patient had no history of trauma, surgery, or chronic liver disease and the finding of intrahepatic arterial atherosclerosis, it is believed that atherosclerosis

Figure 3 Gross image showing dilated and thick-walled blood vessels with occluding dark red thrombi throughout the large and small branches of the portal tree. (A) Histopathological slides showing organizing and fresh thrombi in the lumen (left) and within the wall of this ruptured hepatic artery aneurysm (right). (B) Elastic van Gieson stain, ×100; and organized thrombus in a markedly dilated hepatic artery with small fragments of the internal elastic layer remaining (arrows), consistent with true hepatic artery aneurysm. (C) Elastic van Gieson stain, ×40. (D) highmagnification view of the thrombus identified on the prior abdominal imaging, ×100.

may be the cause of HAA in this interesting case. Furthermore, the patient had a remote history of pancreatitis, and two incidentally identified small cystic lesions in her pancreas at presentation. Pancreatitis is one of the established risk factors for HAA, and the subcentimeter lesions in pancreatic uncinate process could represent small pseudocysts in the context of subclinical pancreatitis and could potentially be one of the etiologic factors for this case.

In this case, the patient first presented with nonspecific symptoms such as nausea, vomiting, and abdominal pain. However, she also described “epigastric pain radiating to the back”, possibly related to the acute rupture of the aneurysm. Studies have shown that multifocal aneurysms have higher chances of rupture, especially HAAs associated with polyarteritis nodosa.^{4,10} In our case, the patient had multifocal HAAs; however, there was no evidence of polyarteritis nodosa in the history or histology. It has also been shown that HAAs with atherosclerotic origin are less likely to rupture.⁴ Rupture of HAA is a life-threatening emergency and has a mortality of 21%.^{2,9,11} However, in this case, the ruptured aneurysm was spontaneously thrombosed and contained by portal stroma and hepatic parenchyma, possibly preventing massive hemorrhage. Although spontaneous thrombosis has been reported after rupture of hepatic artery pseudoaneurysms,¹² to the best of our knowledge, the present case is the first case of spontaneous thrombosis in a true aneurysm of the hepatic artery in the English literature.

The HAA presented in this case has multiple unique anatomical and radiological features that merit further discussion. The vast majority of HAAs, both true aneurysms and pseudoaneurysms, are solitary extrahepatic aneurysms. Studies have shown that approximately 80% of true aneurysms in hepatic arteries are extrahepatic; and about 92% of them are solitary.⁴⁻⁶ The most common location for HAA is the common hepatic artery, where 63% of cases occur, followed by right and left hepatic artery, where 28% and 5% of HAAs occur, respectively.^{1,13} In this case, the patient's HAA occurred intrahepatically in a multifocal manner. To the best of our knowledge, this is the first case of HAAs occurring at this anatomical location in this atypical pattern. In fact, this atypical multifocal pattern in a patient with a prior history of melanoma, raised concern for metastatic disease leading to the surgical treatment.

The radiological manifestation of the present case is also intriguing. Although angiography is considered as the gold standard for diagnosis of HAA, it is seldom used as the first line technique because of its invasiveness. Other imaging modalities, such as ultrasound, CT, and MRI, are usually used as screening for HAA. In this case, the hepatic ultrasound showed hypoechoic structures with internal blood flow and continuity with adjacent blood vessels, suggesting thrombosis and recanalization of aneurysm in retrospect. However, given the patient's history of

melanoma, a FDG-PET scan was performed to evaluate for the possibility of metastases. Of note, melanoma metastasis can hemorrhage, further confounding the findings in this case.¹⁴ Interestingly, on PET scan, the lesion was multifocal and demonstrated increased accumulation of FDG, raising the concern for metastatic or primary malignancy. Although FDG-PET is highly sensitive and specific in distinguishing malignant from benign lesion based on the high glucose metabolic activity of malignant cells, anecdotal reports have shown that benign thrombosis can also be FDG avid,¹⁵⁻¹⁷ sometimes reaching SUV levels as high as 10.4.¹⁸ The increased FDG accumulation in thrombosis is thought to be due to either inflammatory cells infiltrates in the thrombus or focally localization of inflammatory cells in the aneurysm wall.^{15-17,19} Another study showed that the increase of FDG uptake by a benign thrombosis is a sign of atherosclerotic plaque destabilization and raises the concern for subsequent adverse events.²⁰ Although studies have also shown that the SUVmax of tumor thrombus and benign thrombus overlap, the SUVmax of tumor thrombus is usually significantly higher. When using a cutoff value of SUVmax = 3.35 as a criterion, the sensitivities and specificity of using SUVmax differentiating benign and malignant thrombosis can reach 71.4% and 90%, respectively.^{15,17}

CONCLUSION

In conclusion, we present a rare symptomatic case of intrahepatic HAA, which occurred in an atypical, multifocal pattern. Following rupture, the aneurysms spontaneously thrombosed with an imaging appearance that mimicked metastatic malignancy. This case highlights the importance of clinical-radiological-pathological correlation when encountering this rare but challenging entity for early identification and intervention.

CONFLICTS OF INTEREST

The authors have none to declare.

REFERENCES

1. Arneson MA, Smith RS. Ruptured hepatic artery aneurysm: case report and review of literature. *Ann Vasc Surg*. 2005;19(4):540-545.
2. Shannon R. Hepatic artery aneurysm. *Med J Aust*. 1991;154(11):773-774.
3. Lu M, Weiss C, Fishman EK, Johnson PT, Verde F. Review of visceral aneurysms and pseudoaneurysms. *J Comput Assist Tomogr*. 2015;39(1):1-6.
4. Abbas MA, Fowl RJ, Stone WM, et al. Hepatic artery aneurysm: factors that predict complications. *J Vasc Surg*. 2003;38(1):41-45.
5. Bachar GN, Belenky A, Lubovsky L, Neuman-Levine M. Sonographic diagnosis of a giant aneurysm of the common hepatic artery. *J Clin Ultrasound*. 2002;30(5):300-302.

6. Kim JH, Rha SE, Chun HJ, et al. Giant aneurysm of the common hepatic artery: US and CT imaging findings. *Abdom Imaging*. 2010;35(2):212–214.
7. Alhawsawi AM, Aljiffry M, Walsh MJ, Peltekian K, Molinari M. Hepatic artery aneurysm associated with prune belly syndrome: a case report and review of the literature. *J Surg Educ*. 2009;66(1):43–47.
8. Hulsberg P, Garza-Jordan Jde L, Jordan R, Matusz P, Tubbs RS, Loukas M. Hepatic aneurysm: a review. *Am Surg*. 2011;77(5):586–591.
9. Shanley CJ, Shah NL, Messina LM. Common splanchnic artery aneurysms: splenic, hepatic, and celiac. *Ann Vasc Surg*. 1996;10(3):315–322.
10. Pasha SF, Gloviczki P, Stanson AW, Kamath PS. Splanchnic artery aneurysms. *Mayo Clin Proc*. 2007;82(4):472–479.
11. O'Driscoll D, Olliff SP, Olliff JF. Hepatic artery aneurysm. *Br J Radiol*. 1999;72(862):1018–1025.
12. Soudack M, Epelman M, Gaitini D. Spontaneous thrombosis of hepatic posttraumatic pseudoaneurysms: sonographic and computed tomographic features. *J Ultrasound Med*. 2003;22(1):99–103.
13. Schroeyers P, Lismonde M, Vermonden J, Six C. Management of hepatic artery aneurysm. Case report and literature review. *Acta Chir Belg*. 1995;95(2):89–91.
14. Dousei T, Miyata M, Yamaguchi T, Nagaoka M, Takahashi E, Kawashima Y. Rupture of liver metastasis of malignant melanoma – a case of hepatic resection. *Jpn J Surg*. 1991;21(4):480–484.
15. Hu S, Zhang J, Cheng C, Liu Q, Sun G, Zuo C. The role of 18F-FDG PET/CT in differentiating malignant from benign portal vein thrombosis. *Abdom Imaging*. 2014;39(6):1221–1227.
16. Muzaffar R, Kudva G, Nguyen NC, Osman MM. Incidental diagnosis of thrombus within an aneurysm on 18F-FDG PET/CT: frequency in 926 patients. *J Nucl Med*. 2011;52(9):1408–1411.
17. Sharma P, Kumar R, Jeph S, et al. 18F-FDG PET-CT in the diagnosis of tumor thrombus: can it be differentiated from benign thrombus? *Nucl Med Commun*. 2011;32(9):782–788.
18. Kikuchi M, Yamamoto E, Shiomi Y, et al. Case report: internal and external jugular vein thrombosis with marked accumulation of FDG. *Br J Radiol*. 2004;77(922):888–890.
19. Xu XY, Borghi A, Nchimi A, et al. High levels of 18F-FDG uptake in aortic aneurysm wall are associated with high wall stress. *Eur J Vasc Endovasc Surg*. 2010;39(3):295–301.
20. Rominger A, Saam T, Wolpers S, et al. 18F-FDG PET/CT identifies patients at risk for future vascular events in an otherwise asymptomatic cohort with neoplastic disease. *J Nucl Med*. 2009;50(10):1611–1620.