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Magnetic resonance imaging features of intrahepatic extramedullary hematopoiesis: Three case reports

MRI features of intrahepatic extramedullary hematopoiesis

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Abstract

BACKGROUND

Extramedullary hematopoiesis rarely occurs within the liver alone, and it was found to be easily misdiagnosed. The radiological literature covering this disease includes exclusive case reports. There is a paucity of literature on the role of magnetic resonance imaging (MRI). The most common imaging modalities were CT and ultrasound. This report aims to provide more radiologic appearance of MRI and help radiologists establish diagnostic consideration.

CASE SUMMARY

Three patients (one male and two females) were incidentally found to have hepatic mass or nodule, without hepatomegaly or splenomegaly. Laboratory tests including liver function, serum hepatic tumor markers, and hepatitis serologic markers were normal. On MRI scans, all lesions showed lower signal intensity on in-phase image than those on out-phase image. One of a case showed changes in signal intensity on T2 weighted images and diffusion weighted images, which shifted from hyperintensity to hypointensity with size enlargement between two rounds of imaging examination. These lesions exhibited different enhancement patterns on dynamic contrast enhancement series.

CONCLUSION

The MRI signal change and in-/out-phase image might provide useful information and help radiologists establish diagnostic consideration.

Key Words: Liver; Extramedullary hematopoiesis; Signal intensity; Magnetic resonance imaging; Case report

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Core Tip: The MRI signal change and in-/out-phase image might provide useful information and help radiologists establish diagnostic consideration.

INTRODUCTION

Extramedullary hematopoiesis seldom occurs within the liver alone[1]. In this rare condition, the lesion can manifest as a mass with no typical radiologic findings, making it difficult to diagnose and differentiate from other hypervascular neoplasms[2]. We here present three cases of intrahepatic extramedullary hematopoiesis (IEMH) occurring solely in the liver. These lesions showed lower signal intensity on in-phase image than those on out-phase image. In addition, the first case is unique in that the lesion showed changes in magnetic resonance imaging (MRI) signal intensity with size enlargement between two rounds of imaging examination. These manifestations have never been reported before.

CASE PRESENTATION

Chief complaints

Case 1: A 50-year-old woman without any discomfort was admitted to our hospital due to an intrahepatic mass with interval growth.

Case 2: A 30-year-old female with a five-month history of Hodgkin's lymphoma (nodular sclerosis) was referred to hospital.

Case 3: A 52-year-old male was admitted to our hospital after he was found to have hepatic nodules incidentally. He had no history of alcoholism.

History of present illness

Case 1: Negative.

Case 2: She denied alcoholism and said she had no other symptoms or discomfort.

Case 3 : No symptom or discomfort was complained.

History of past illness

Case 1: Negative.

Case 2: Negative.

Case 3: Negative.

Personal and family history

Case 1: The patient's medical history included thyroid carcinoma and lung adenocarcinoma. She had undergone total thyroidectomy in November 2014 and lobectomy of the right lower lobe in October 2019, without radiotherapy or adjuvant chemotherapy in the subsequent follow-up.

Case 2: Before her initial treatment, there was no focal liver lesion detected by ultrasound or PET/CT. She had underwent 5 cycles of chemotherapy, and the regimen was BV+AVD (Brentuximab Vedotin+ Adriamycin, Vinblastine, Dacarbazine).

Case 3: The patient had a free previous medical and family history.

Physical examination

Case 1: Her physical examination was normal.

Case 2: Her physical examination was normal. The liver and spleen were impalpable.

Case 3: Physical examination was negative.

Laboratory examinations

Case 1: The laboratory tests, including blood, liver function, and serum tumor marker tests (Alpha fetal protein, carbohydrate antigen19-9, carbohydrate antigen125, carcinoembryonic antigen, and protein induced by Vitamin K absence or antagonist-II), were all within normal range. Hepatitis serologic markers such as HBs Ag and HCV Ab were negative, with no history of alcoholism.

Case 2: The platelet, white, and red blood cell counts were normal. The serum tumor markers and hepatitis serologic markers were negative.

Case 3: Laboratory tests revealed that the liver function, serum hepatic tumor markers, and hepatitis serologic markers were all normal.

Imaging examinations

Case 1: In September 2019, pre-operative ultrasound showed a hyperechoic lesion with size measuring 24 mm × 23 mm in the Segment VIII. The lesion was diagnosed as possible hemangioma.

In January 2020, during a routine examination, the lesion showed an increase in size on abdominal ultrasound. Then the abdominal CT scan (Discovery 750 HD, GE Healthcare, Milwaukee, WI, USA) was performed. The lesion appeared heterogeneously hypodense on unenhanced CT (40 HU), with 35 mm × 32 mm × 20 mm in size. The lesion became moderately hyperdense in the arterial phase (81 HU) and markedly hyperdense in the portal venous phase (106 HU), and it showed persistent enhancement in the 5-min delayed phase (110 HU) (Figure 1a–d). The next day, liver MRI was performed for further characterization and assessment of the lesion (Trio 3.0 T, Siemens, Erlangen, Germany). The lesion was hypointense relative to surrounding liver tissue on T1 weighted images (WI) with and without fat saturation (FS), and it was heterogeneously hyperintense on T2WI or T2WI-FS with clear demarcation. On dynamic contrast enhancement series, the lesion showed considerable enhancement on the arterial phase, remaining hyperintense relative to surrounding liver tissue in both portal venous and delayed phases (6 min) following the injection of 0.1 mmol/kg of Gd-DTPA (Magnevist, Bayer Healthcare, Berlin, Germany) (Figure 1e–k). The initial diagnosis included atypical angioleiomyolipoma, adenomas, and single metastasis. The patient declined to undergo surgery and remained for observation.

In June 2020, she had another abdominal MRI examination. The lesion had enlarged to 50 mm × 46 mm × 43 mm, and it was heterogeneously hypointense on T1WI-FS with scattered foci of hyperintense areas. The signal intensity was significantly lower on the in-phase image than that on the out-phase image. The lesion became isointense or mildly hypointense relative to liver on diffusion-weighted images, T2WI, and T2WI-FS.

The pattern of enhancement was overt on arterial phase and remained hyperintense on delayed phase, without vessel encasement or invasion (Figure 1 L–r).

Case 2: In April 2020, abdominal ultrasound was performed during her routine examination. Sonography found that there was a slightly hyperechoic lesion in Segment VII. Then she had MRI scan (Discovery 750W, GE Healthcare, Milwaukee, WI, USA). A 10 mm × 8 mm sized, slight hyperintensity and hypointensity lesion was showed on T2WI-FS and T1WI-FS, respectively (Figure 3a–b). The signal intensity was lower on the in-phase image than that on the out-phase image (Figure 3c–d). The signal intensity was loss on SWI (Susceptibility weighted imaging) (Figure 3e). After the administration of Gd-DTPA, the lesion showed poor enhancement on the arterial phase and enhanced gradually and persistently until six minutes (Figure 3f-h). The initial diagnosis was lymphoma infiltration.

Case 3: MRI (Trio 3.0 T, Siemens, Erlangen, Germany) scans showed a lesion located in the transitional area (34 mm × 27 mm in size) between Segment V and VIII, showing homogeneously low and high signal intensity on T1WI-FS and T2WI-FS, respectively. The signal intensity on the in-phase image was apparently lower than that on the out-phase image (Figure 4a–b). After the administration of Gd-EOB-DTPA, the lesion showed intense enhancement in the arterial phase, with no persistent enhancement in the portal venous and transitional phases and hypointense in the hepatobiliary phase (Figure 4f-h). The possible diagnosis at that time included hepatoma, adenoma, and angiomyolipoma.

FINAL DIAGNOSIS

Case 1: Macroscopically, a mass with reddish appearance without necrosis or hemorrhage was seen in the resection specimen. Microscopically, megakaryocytes, and erythroid cells were scattered within the hepatocyte cords (Figure 2). Immunohistochemical staining including the CD3, CD20, CD61, CD235, and MPO was

performed, and the cells were positive for these markers. These findings were consistent with EMH.

Case 2: Percutaneous fine-needle aspiration biopsy was performed under ultrasound guidance, and cytology showed EMH.

Case 3: The final histopathological conformation was EMH (Figure 5).

TREATMENT

Case 1: The patient underwent hepatic segmentectomy.

Case 2: After another 4 cycles of chemotherapy, liver MRI (August 2020) showed similar findings, without any increase in the size of the lesion. Because the diagnosis was uncertain and the lesion was small, we decided to obtain histopathologic confirmation.

Case 3: As the possibility of malignancy could not be excluded completely, he underwent hepatic segmentectomy, although he did not have any predisposing factors for hepatoma.

OUTCOME AND FOLLOW-UP

Case 1: The patient has no recurrent lesions or evidence of new lesions.

Case 2: The patient has no recurrent lesions or evidence of new lesions.

Case 3: The patient has no signs of recurrence.

DISCUSSION

IEMH is a rare, benign condition of the liver. The radiological literature covering this disease is exclusively case reports. All of these cases were misdiagnosed, and IEMH was not considered in the preoperative imaging diagnosis and differentiation. The most common imaging modalities were CT and ultrasound[3-7]. There is a paucity of literature on the role of MRI, which might be due to the limitations of imaging technology at that time. Moreover, the quality of the images provided in those studies was low. Thus, the radiologic features seemed to be unspecific, and it might be difficult to make correct diagnosis preoperatively.

From the pathological aspect, EMH is characterized as plenty of hematopoietic cells. Granulocytes, megakaryocytes, and erythrocytes are mixed distributed within the lesion, in which adipocyte and fibrous tissue can also be seen. Thus, EMH is positive for MPO, CD61, and CD235. Due to large number of erythrocytes scattered within EMH, the CD235 staining is strong and diffuse positive. The iron in the erythrocytes and different amounts of adipose can potentially affect the radiologic appearance.

In recent years, with the development of MRI, there have been sporadic reports regarding the published MRI findings of IEMH. Abel *et al*[8] provided the first description of T2*WI in their case, considering this technique might have potential role in MRI diagnosis. The lesion was hypointense on T2*WI, similar to the signal intensity of hepatic background on this GRE (Gradient recalled echo) sequence, indicating the lesion had as much iron deposition as the liver parenchyma in the setting of secondary hemochromatosis owing to the repeated blood transfusions. Lee *et al*[2] reported the superparamagnetic iron oxide-enhanced MRI in their case, while Zhang *et al*[9] applied the chemical shift images in their report. In our three cases, lesions on in-phase image exhibited lower signal intensity than those on out-phase image. In Case 2, the lesion was hypointense in the SWI. In Case 1, there were signal changes across two time intervals on T1WI, T2WI, and DWI (Diffusion weighted imaging), which shifted from hyperintensity to hypointensity, and without restricted diffusion in two sets of ADC (Apparent diffusion coefficient) maps. We speculate that these manifestations and signal changes could be mainly ascribed to iron deposition, depending on iron evolution in the lesion, instead of the increase of cell density or change of intralesional content such as mucin, necrosis, fibrosis, or even calcification. Iron could impact the magnetic field intensity and homogeneity; thus, the signal on DWI could be diverse due to iron content and evolution in IEMH but not really due to the diffusion restriction on ADC map. However, there is limited data about EMH on DWI. Rasche *et al*[10] observed that EMH in the spleen could impact the DWI signal. The GRE sequence was unequivocally sensitive to the presence of small amounts of iron. It should also be noted that, as the echo time was longer over time, the signal indicating iron deposition in the

lesion grew less intense[11]. Such lesions often showed lower signal intensity on SWI and in-phase images relative to the out-phase image.

Some cases report using scintigaphy to diagnose IEMH[3, 12, 13], and they presented Tc-99m uptake. Besides, positron emission tomography (PET) was applied in the diagnosis of EMH locating in the paraspinal, peritoneum and lung[1, 13, 14]. They were illustrated as high uptake value. However, there is no report about PET characteristics of IEMH. We speculate its property on ^{18}F-FDG might be from mild to intense activity, which the possible reason was the different stage of disease course. In the fresh stage, the synthesis and proliferation of hematopoietic cells were active, thus presenting as hypermetabolism, whereas in the static stage, IEMH could be low uptake.

There have been discrepancies on the radiologic characteristics of different studies (Table 1). IEMH was described as fat-containing lesion. For example, in reports published by Gupta *et al*[15], Navarro *et al*[6] and Cao *et al*[16], multiple lesions contained fat density. However, the case from Zhang *et al*[9] showed solitary lesion without any fat content, as indicated by the lack of fat signal alteration. In regard to enhancement pattern, the lesion presented as hypervascular mass with heterogeneous enhancement in the Wong *et al* report and homogeneous avid enhancement in the Zhang *et al* report, while mild enhancement was reported from Tamm *et al*[12]. Elsayes *et al*[17] considered that active lesion exhibited iso or hyperintensity on T1WI and T2WI, and enhanced after contrast material injection, while older lesions could present as hypointense on T1WI and T2WI, and might show no enhancement. Nevertheless, Kumar *et al*[18] provided a case that the lesion was isointense on T1WI and T2WI, but it showed nearly no enhancement. Belay *et al*[8] showed the lesion was low signal intensity on both T1WI and T2WI with markedly enhancement. Some authors indicated that iron deposition and fat infiltration might refer to old stage in course of disease[19], while other authors thought that iron and fat content were also detectable in the active stage[20]. MRI was found to concretely reflect different stages of hematopoiesis, depending on iron signal evolution, fat content, degree of fibrous organization, and vascular enrichment in the lesion. In this way, the difference in hematopoietic materials, fibrous tissue, and fat

content could explain the diverse radiologic description and the lack of exclusive imaging patterns.

Although most of the patients with IEMH had hematological disease, a few cases had no evidence of this underlying condition (as shown in the Case 1 and Case 3). For example, patients with small cell lung cancer and Noonan syndrome were reported in two cases[4, 15], and the cause of IEMH in another two cases remains unknown[21, 22].

Two factors differentiate these three cases from those in other reports. First, no hepatomegaly or splenomegaly was found in either. Second, a change in MRI signal was observed at two different points in time in Case 1, and it presented more radiologic characteristics over the course of the disease. Interestingly and accidentally, all our reported lesions were either in the Segment VII or VIII. Other segments of IEMH were also reported in other cases. More reports are warranted to be documented in the future.

The differential diagnosis includes benign, primary, and secondary liver malignant lesions. IEMH may mimic these lesions leading to troublesome diagnosis. In the "fat deposition" stage, the characteristic signal intensity on the in-phase image is higher than that on the out-phase image. The differential diagnosis in cirrhotic liver includes fatty metamorphosis in HCC, while that in non-cirrhotic liver includes benign lesions such as focal fatty infiltration (without mass effect), adenoma (hepatocyte nuclear factor 1a–mutated subtype) and lipoma (no enhancement). Angiomyolipoma should be also taken into consideration. In the "iron deposition" stage, the characteristic signal intensity on the in-phase image is lower than that on the out-phase image. The differential diagnosis (intratumoral bleeding) includes benign lesions such as adenoma (inflammatory subtype) and hemangioma. Malignant lesions include hemorrhagic HCC and metastasis. When IEMH demonstrates strong and persistent enhancement, FNH, adenoma and hypervascular metastasis need to be considered. An appropriate clinical setting and the application of Gd-EOB-DTPA or superparamagnetic iron oxide are helpful for diagnosis. When IEMH shows mild enhancement or avid enhancement with "washout", atypical metastasis, HCC, or even fibrolamellar carcinoma in young

patients should be considered in the differential list. Lymphoma is homogenous isointense with moderate enhancement. Fat and bleeding content is seldom seen in lymphoma.

CONCLUSION

IEMH was found to manifest with variable radiologic appearance and to be easily misdiagnosed. Given its rarity and the lack of pathognomonic imaging findings, awareness of these presentations might help radiologists establish diagnostic consideration.

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