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FULL PAPER

Changes in liver morphology in patients with extrahepatic portal venous obstruction: a retrospective magnetic resonance imaging study

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Objective: To investigate the liver parenchymal changes on MRI in patients with extrahepatic portal venous obstruction (EHPVO).

Methods: This was a retrospective evaluation of the MRI studies in patients with EHPVO between January 2016 and April 2018. The diagnosis of EHPVO in each case had been established on the basis of clinical and Doppler parameters. Following findings were recorded on MRI: liver size; outline; overall volume redistribution; volume redistribution of caudate, right and left lobes; signal heterogeneity, intrahepatic biliary radicle dilatation, focal liver lesions, gallstones and ascites.

Results: A total of 164 MRI studies were evaluated. Median age was 27 years (range, 6–70). There were 90 (54.9%) males and 74 (45.1%) females. The median liver size was 14 cm (range 5–17). The median spleen size was 15.9 cm (range, 6–28). A spleen size ≥ 12 cm was seen in

136 (82.9%) patients. The liver outline was nodular in 32 (19.5%) patients. Volume redistribution was seen in 63 (38.4%) patients. Caudate lobe hypertrophy was seen in 49 (29.9%) patients. Right lobe atrophy and hypertrophy was seen in 4 (2.4%) and 1 (0.6%) patients respectively. Left lobe atrophy and hypertrophy was seen in 15 (9.1%) and 10 (6.1%) patients respectively. 30 MRI (18.3%) showed heterogeneous signal intensity. Focal lesions were seen in 22 (13.4%) patients. Intrahepatic biliary radicle dilatation, gallstones and ascites were seen in 120 (73.2%), 54 (32.9%) and 26 (15.9%) patients respectively.

Conclusion: Liver morphological changes are common in EHPVO.

Advances in knowledge: The morphological changes in liver in patients with EHPVO have not been described previously. This information will prevent misdiagnosis of this condition as cirrhosis.

INTRODUCTION

Extrahepatic portal venous obstruction (EHPVO) is one of the most common causes of non-cirrhotic portal hypertension (NCPH).¹ It accounts for portal hypertension in 40% of adults and 80–85% of children.¹ One of the important events secondary to EHPVO is development of portal cavernoma and portal cavernoma cholangiopathy (PCC).² PCC develops in 80–100% patients with EHPVO.² The vast majority of patients with PCC are asymptomatic. As EHPVO is a pre-hepatic phenomenon, the liver parenchymal morphology has been reported to be normal.³ However, altered portal venous and hepatic arterial perfusion leads to liver parenchymal volume redistribution.³ At routine ultrasound evaluation, these morphological changes may be misdiagnosed as cirrhosis, particularly when the color Doppler evaluation is not done. Moreover, it is not uncommon for the radiologists to diagnose

cirrhosis in patients with known EHPVO. However, even on long term follow-up, liver dysfunction and secondary biliary cirrhosis is a rare occurrence (2%–4%).⁴ There is an extensive literature on the vascular and biliary changes in EHPVO. However, no published studies have addressed the liver parenchymal changes in EHPVO. In the present study, we aim to evaluate the liver parenchymal changes on MRI in patients with EHPVO.

METHODS AND MATERIALS

We conducted a retrospective review of consecutive MRI studies of the abdomen performed between January 2016 and April 2018 in patients with EHPVO. The diagnosis of EHPVO in each case was based on Baveno VI consensus.⁵ Patients who presented with upper gastrointestinal bleeding and/or massive splenomegaly underwent Doppler evaluation. EHPVO was diagnosed when portal vein obstruction,

Figure 1. Axial post-contrast T_1 weight image (A) shows the method of calculation of modified caudate to right lobe ratio using the bifurcation of right portal vein as the landmark. Coronal T_2 weighted image shows the method of calculation of liver and spleen size. R, right lobe; C, caudate lobe; L, liver; S, spleen.

presence of solid intraluminal material or portal vein cavernoma was documented on Doppler. Liver biopsy and fibroscan was performed in selected cases to exclude cirrhosis (however, the data was not available for analysis). Hepatic venous pressure gradient is not performed in patients with EHPVO in our centre.

In our institute, MRI is performed in patients with EHPVO as a part of pre-operative work-up (for planning shunt surgery), follow up after surgical intervention to document shunt patency, and for planning follow up after endoscopic retrograde cholangiopancreatography (ERCP). The studies were performed on a 1.5 T MRI scanner (Magnetom Verio, Siemens, Erlangen, Germany). Following sequences have been performed: axial and coronal half-Fourier acquisition single-shot turbo spin-echo [repetition time (TR): 1300; echo time (TE): 102]; axial and coronal true fast imaging with steady-state free precession (TRUFI) (TR: 4.1; TE: 2); axial T_1 weighted volume interpolated breath-hold examination including in-phase and out of phase (TR: 6.9; TE: 4.8 and TR: 6.9 and TE: 2.4); dynamic post-gadolinium T_1 weighted volume interpolated breath-hold examination in axial plane (TR: 4.5; TE: 2.2); coronal post-gadolinium T_1 weighted (TR: 4.5; TE: 2.2); axial diffusion-weighted imaging ($b = 0, 400$ and 800) and MR cholangiopancreatography (thick

slab and three-dimensional). The studies were reviewed by three abdominal radiologists with an experience of 5, 10 and 13 years in reporting abdominal MRI. The radiologists were not blinded to the clinical data. The modified caudate to right lobe (C/RL) ratio was assessed to document caudate lobe enlargement (C/RL > 0.55)⁶ (Figure 1A). This method involved using the right portal vein as the landmark. Although, the portal veins are not opacified in EHPVO, the right portal vein bifurcation is still visible anatomically (Figure 1A) as branching hypointensity. The enlargement and atrophy of the right and left lobe was based on the relative size of each lobe by subjective assessment. No measurements were done in this regard. Liver volume redistribution was defined by the presence of caudate lobe enlargement with enlargement/atrophy of the right and left lobe in different combinations. Both the liver and spleen were measured on a coronal plane showing the maximum craniocaudal length (Figure 1B). The findings that were recorded included: liver size; liver outline (smooth or nodular); signal intensity on half-Fourier acquisition single-shot turbo spin-echo images (normal or heterogeneous); presence of volume redistribution; size of right and left lobe (categorized into normal, atrophy or hypertrophy) (Figure 2); size of caudate lobe (categorized into normal or hypertrophy); spleen size (Figure 3); intrahepatic biliary radicle dilatation, focal liver lesions (characterized based on features at MRI; no FNAC or biopsy was done),

Figure 2. Axial TRUFI image shows left lobe atrophy (arrow) with collaterals replacing the main portal vein at porta (short arrow). Also note the hypointense foci in spleen suggestive of Gamna Gandy bodies (arrowhead).

Figure 3. Axial T_2 weighted MR image shows caudate lobe hypertrophy (arrow). Also note the intrahepatic biliary radicle dilatation (short arrow).

gallstones and ascites. Demographic features and prior history of ERCP and surgery was also recorded.

Descriptive data were presented as mean, median and percentage. χ^2 Chi-square test was applied to test whether there was any significant association of surgery or ERCP and volume redistribution and nodular outline. *P* value < 0.05 was considered statistically significant.

RESULTS

A total of 164 MRI studies were evaluated. Median age was 27 years (range, 6–70). There were 90 (54.9) males and 74 (45.1%) females. Imaging was performed following ERCP in 21 (12.8%) patients and following surgery in 24 (14.6%) patients (proximal splenorenal shunt in 23 and mesoatrial shunt in 1). The median liver size was 14 cm (range 5–17). 73 patients (44.5%) had a liver size ≥ 15 cm. The median spleen size was 15.9 cm (range, 6–28). A spleen size ≥ 12 cm was seen in 136 (82.9%) patients. The liver outline was nodular in 32 (19.5%) patients. 30 MRI (18.3%) examinations showed heterogeneous signal intensity. Volume redistribution was seen in 63 (38.4%) patients. Caudate lobe hypertrophy was 49 (29.9%) patients. Right lobe atrophy and hypertrophy was seen in 4 (2.4%) and 1 (0.6%) patients respectively. Left lobe atrophy and hypertrophy was seen in 15 (9.1%) and 10 (6.1%) patients respectively. Focal lesions were seen in 22 (13.4%) patients. These included regenerative nodules in 10 patients, cholangitic abscesses in 8 patients and hemangiomas in 4 patients. Intrahepatic biliary radicle dilatation, gallstones and ascites were seen in 120 (73.2%), 54 (32.9%) and 26 (15.9%) patients respectively. None of the patients with ascites had a clinical presentation with liver decompensation. There was no significant difference in the frequency of nodular liver outline and volume redistribution between surgical and non-surgical as well as ERCP and non-ERCP groups. Table 1 highlights the important MRI features. Figure 4 shows the MR images from a patient with EHPVO and a patient with cirrhosis.

DISCUSSION

NCPH refers to vascular disorders that cause portal hypertension with preservation of synthetic function of the liver with normal or slight elevation of hepatic venous pressure gradient. EHPVO is one of the most common causes of NCPH.¹ In fact, EHPVO accounts for portal hypertension in 40% of adults and 80–85% of children.⁴ It is also the most common aetiology for gastrointestinal bleeding in children and young adults.¹ Predisposing factors are identified in more than two-thirds of adults with EHPVO.⁷ These are identified less frequently in children with EHPVO (38–74%). Local factors that predispose to EHPVO are trauma, tumor, and inflammation. Myeloproliferative disorders (MPD) are an important cause of EHPVO in adults. In a meta-analysis, the prevalence of MPD and JAK2 mutations was 31.5 and 27.7%, respectively, in adults.⁸ Both congenital causes (cardiovascular, urinary tract and chromosomal abnormalities) and perinatal events (omphalitis, neonatal enterocolitis, and neonatal sepsis) are important risk factors for EHPVO in children.⁷

One of the important events secondary to EHPVO is development of multiple collateral venous channels that aim at maintaining

the hepatopetal blood flow. These collaterals are referred to as portal cavernoma. As these channels are in close relationship with the biliary tree, they produce a variety of morphological changes in the biliary tree referred to as PCC.^{2,9,10} PCC develops in 80–100% patients with EHPVO over a variable period of time in the clinical course.^{2,9,10} The vast majority of patients with PCC are asymptomatic. When symptoms do develop in a small percentage of patients, they are a result of chronic cholestasis or acute cholangitis.¹⁰ As EHPVO is a pre-hepatic vascular insult, the liver parenchymal morphology (size, architecture, volume and echotexture) has been reported to be normal.³ However, there is a relative reduction in portal venous flow to the periphery of liver along with compensatory increase in arterial blood flow.³ These circulatory changes lead to better perfusion of the central liver. Thus, over time liver parenchymal volume redistribution, parenchymal extinction and smooth hepatic atrophy ensues.¹¹ At routine ultrasound evaluation, these morphological changes may be misdiagnosed as cirrhosis, particularly when the color Doppler evaluation is not done or in cases where the collateralization around the liver is subtle. Moreover, it is not uncommon for the radiologists to diagnose chronic liver parenchymal disease in patients with known EHPVO based on these changes. However, even on long term follow-up, liver dysfunction and secondary biliary cirrhosis is a rare occurrence (2–4%).⁴ In fact, liver biopsy is rarely employed in patients with EHPVO.¹ In a study by Sharma et al, liver biopsy was performed in 65 patients with EHPVO who also underwent liver stiffness (LS) and splenic stiffness (SS) measurement.⁹ There was no fibrosis in 57 patients, Grade one fibrosis in seven patients, and grade II fibrosis in one patient.¹² In another large series of children with EHPVO where biopsy was performed, none of the patients had cirrhosis.¹³ Several studies have discussed the imaging features of PCC focusing on the vascular component of the disease. However, no published studies have addressed the liver parenchymal changes in EHPVO. The importance of this evaluation is to differentiate the liver parenchymal changes of EHPVO from those of cirrhosis and to highlight the fact that despite morphological changes that may parallel those of cirrhosis, secondary biliary cirrhosis is a rare phenomenon in EHPVO.

In the study by Achar et al comprising 20 children with EHPVO, liver parenchymal volume redistribution and caudate lobe hypertrophy was reported in 7 (35%) patients on MRI and in 5 (25%) patients on ultrasonography.⁴ Our results also support that volume redistribution is a common finding on imaging. The pattern of volume redistribution is that of caudate lobe hypertrophy in almost 30% patients followed by atrophy of left lobe (9.1%), hypertrophy of left lobe (6.1%), atrophy of right lobe (2.4%) and hypertrophy of right lobe (0.6%). Intrahepatic biliary radicle dilatation is a common finding in patients with EHPVO and PCC. Jabeen et al reported intrahepatic biliary radicle dilatation in 73.8% patients with EHPVO.¹⁴ Our results confirm this finding. Cholangitis is an important complication related to biliary stasis occurring in the setting of PCC. This was reported in 40% patients, however, cholangitic abscesses have not reported in large patient cohorts.¹⁴ Cholangitic abscess in the setting of EHPVO has been reported as isolated reports. We reported cholangitic abscesses in 4.8% of the cases. This variation

Table 1. Salient MRI features in 164 patients with EHPVO

Findings	Number (total n = 164)
Liver	
· Nodular outline	32 (19.5%)
· Heterogeneous signal	30 (18.3%)
· Volume redistribution	63 (38.4%)
<i>Caudate lobe</i>	
· Hypertrophy	49 (29.9%)
<i>Right lobe</i>	
· Hypertrophy	1 (0.6%)
· Atrophy	4 (2.4%)
<i>Left lobe</i>	
· Hypertrophy	10 (6.1%)
· Atrophy	15 (9.1%)
<i>Focal lesions</i>	22 (13.4%)
<i>Biliary system</i>	
· IHBRD	120 (73.2%)
· Gallstones	54 (32.9%)
Splenomegaly	136 (82.9%)
Ascites	26 (15.9%)

Figure 4. Post-contrast MR images of two patients with EHPVO and cirrhosis. Axial images (A, B) in a patient with EHPVO show volume redistribution in the form of hypertrophy of caudate lobe and atrophy of left lobe (arrows, A, double arrow shows stomach). Portal cavernoma is shown in B (arrow). Axial images (C, D) in a patient with cirrhosis show similar changes (arrows, C). However, the portal vein is patent (D, arrow). Note that there is a greater heterogeneity of signal intensity in cirrhosis (C) compared with EHPVO (D). Also surface nodularity is well visualized in cirrhosis (C). EHPVO, extrahepatic portal venous obstruction.

may be related to the larger patient number in our series. Also, no previous series on MRI has dedicatedly evaluated this aspect of the disease. Moderate to massive splenomegaly is one of the hallmark clinical signs in patients with EHPVO and has been reported in 90–100% patients with EHPVO.⁷ Our results of 82.9% for splenomegaly appear to be less than the previously reported data. However, this must be interpreted in the light that 23 patients in our study had already undergone splenectomy. Peter et al reported ascites in 12.8% children with EHPVO.¹⁰ None of these children had ascites secondary to liver dysfunction. Liver biopsy in all these children revealed normal histology.¹³ Ascites in our study was reported in a marginally higher percentage of patients and may simply represent the study of a larger and more heterogeneous patient population. The incidence of gallstones in the setting of EHPVO has been variably reported ranging from 4 to 46%.^{9,14,15} Sarin et al reported gallstones in 4.3% patient.¹⁵

In the study by Jabeen et al cholelithiasis was reported in 14.3% cases.¹⁴ We observed gallstones in 32.9%.

There were a few limitations in the study. Liver biopsy correlation was not available. This did not allow detecting and grading fibrosis in patients who had morphological changes. However, liver biopsy in EHPVO may not be justifiable given the available body of evidence. LS and SS measurement is a non-invasive way of evaluating liver fibrosis. However, in the present study, neither LS nor SS was done. Follow up of the patients was not available. Moreover, the assessment of volume redistribution of right and left lobe was based on subjective assessment. The liver and spleen were measured only in terms of craniocaudal length. Volume was not calculated. However, length is the parameter that is most frequently assessed in routine clinical practice and this is the also the practice followed in our institute.

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