Comparison of Gd-EOB-DTPA enhanced liver MRI findings of atypical hypervascular mass-forming intrahepatic cholangiocarcinoma (MICC) and typical MICC

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Purpose

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary hepatic tumor, originating from the epithelial cell lining of the intrahepatic bile ducts. ICC usually does not cause clinical symptoms in the early stage, therefore the disease is often advanced at the time of diagnosis, and the prognosis is known to be worse than that of extrahepatic cholangiocarcinoma. ICC can be divided into three subtypes, mass-forming, periductal infiltrating, and intraductal growth types, according to the morphologic classification system proposed by the Liver Cancer Study Group of Japan. Among the three subtypes, the mass-forming ICC (MICC) is the most common type of tumor, accounting for 60% of all ICC. The prognosis of ICC differs according to its subtypes. MICC and periductal-infiltrating cholangiocarcinomas are known to have poorer prognosis than intraductal-growing type. Therefore, the correct and precise diagnosis of ICC is crucial in the optimal treatment planning and prognosis prediction.

Contrast enhanced CT, MR and other imaging modalities are helpful in the diagnosis and in determining the extent of MICC. The most frequent findings of MICC in dynamic CT or MR include initial peripheral, rim-like enhancement with progressive centripetal enhancement in the delayed phase. However, several previous studies reported that small MICC in cirrhotic background may mimic the appearance of hepatocellular carcinomas (HCCs) in dynamic CT, MRI or contrast-enhanced ultrasonography. To our knowledge, most of previous studies focused on MRI findings with extracellular agents, and there has never been a report describing the imaging findings of hypervascular MICC using Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) enhanced liver MRI.

The purpose of this study is to define the imaging findings of MICC in Gd-EOB-DTPA-enhanced MR and to compare the imaging features of the typical MICC and hypervascular MICC and to evaluate imaging features assist in the differential diagnosis of hypervascular MICC.

Methods and Materials

Patient population

Retrospective study: from January 2008 to March 2011.

Twenty-two pathologically confirmed MICC patients who underwent Gd-EOB-DTPA enhanced MR.

Exclusion criteria: Hepatic nodules larger than 3.5cm or extensive intrahepatic metastasis
Surgical resection (n=9), US-guided liver biopsy (n=3)

Finally, 12 patients, 20 lesions were included in the study.

Image technique

3.0 T unit, Magnetom Trio a Trim ; Siemens, Erlangen, Germany

Parameters

- Fat suppressed respiratory triggered T2 weighted turbo spin-echo sequence
- T2-weighted HASTE sequence
- Breath-hold T1-weighted fast low-angle shot (FLASH) sequence
- Dynamic imaging with IV injection contrast 0.1 m/kg of Gd-EOB-DTPA (Primovist, Bayer Schering Pharma)

Arterial phase achieved using bolus tracking.

Portal 70 seconds, delayed 120 seconds, hepatobiliary 20 minutes after contrast injection.

Image Interpretation

Two radiologists retrospectively evaluated the liver MR.

On dynamic liver MRI with Gd-EOB-DTPA,

1. Enhancement pattern in the arterial dominant phase
   - Typical: rim or peripheral enhancement patterns.
   - Hypervascular: complete or near complete enhancement.

2. Dynamic enhancement patterns on portal and delayed phase
   - Progressive centripetal, stable, total washout, partial washout.

3. Appearance of Gd-EOB-DTPA uptake on hepatobiliary phase images
   - Defect: Homogeneous low SI
   - EOB Cloud: Cloud-like SI in center with peripheral low SI rim
- Heterogeneous reticular uptake

Image Analysis

- Size

- Signal Intensity Ratio: Intratumoral SI / normal liver parenchymal SI in hepatobiliary phase

- Intrahepatic metastasis

- Capsule retraction

- Bile duct dilatation

Clinical findings

- Chronic liver disease (HBV, HCV, LC)

- Tumor markers (AFP, CA19-9)

Results

Twenty MICC measuring less than 3.5cm, were found in twelve patients. The mean diameter of the twenty MICC was 2.055cm [range 0.7-3.4cm]. The nodules were further divided into typical MICC group [14/20, 70%] and hypervascular MICC group [6/20, 30%] according to its enhancement pattern in the dynamic study. The mean diameter of the nodule in the hypervascular MICC group was 1.72cm [range 0.7-2.6cm] and that of the typical MICC group was 2.2cm [range 1-3.4cm]. The tumor in hypervascular MICC group had the tendency to be smaller, but since the numbers were small, tumor size was not significantly different between the two groups (P=0.274).

The typical MICC group included 14 nodules with rim or peripheral enhancement patterns in the arterial dominant phase. All 14 nodules showed centripetal enhancement in the portal and delayed phase. (Figure 1, 2) The hypervascular MICC groups included six nodules with either complete [4/6, 67%] or partial [2/6, 33%] enhancement in the arterial dominant phase. Among the six nodules, five showed total washout in the portal and delayed phase, and one showed partial washout.

On the hepatobiliary phase, the residual enhancement in each nodule was evaluated. In the typical MICC group, 13 of the 14 lesions (93%) showed central hyperintense cloud-like
SI with a peripheral low SI rim, described as "EOB cloud", and one lesion (7%) showed heterogeneous reticular SI. In the hypervascular MICC group, two nodules (33%) showed "EOB cloud", and other four nodules (67%) appeared as a total "defect".

Other MR imaging findings, such as capsule retraction, bile duct dilatation, intrahepatic metastasis, and underlying liver disease, such as chronic hepatitis B, C or liver cirrhosis showed no significant difference between the two groups. Serum tumor markers (AFP, CA 19-9) were obtained from each patient at the time of diagnosis. The value of AFP ranged from 1 to 532.6, and CA 19-9 ranged from 1 to 2895.1. Among the twelve patients, four patients had elevated CA 19-9 levels (CA 19-9 > 36 U/mL), and three patients had elevated AFP levels (AFP > 11 ng/mL). In the hypervascular group, three nodules (50%) had elevated AFP levels, two nodules (33%) had elevated CA 19-9 levels, and in one nodule none of the tumor markers were elevated.

SI ratio, defined as tumor SI divided by nearby normal liver parenchyma SI on hepatobiliary phase, had a mean value of 0.70 [range 0.39-0.94]. The mean SI ratio of typical MICC group was 0.77 [range 0.39-0.94] and that of hypervascular MICC group was 0.59 [range 0.39-0.86]. The average SI ratio of hypervascular MICC group seemed to be lower, however the SI ratio difference between the two group was not significant (p=0.057).

Images for this section:
Fig. 1: Tables showing the comparison between typical and hypervascular MICC.
Fig. 2: Tables showing the dynamic enhancement pattern of typical and hypervascular MICC.

<table>
<thead>
<tr>
<th>Dynamic enhancement pattern</th>
<th>Typical MICC (n=14)</th>
<th>Hypervascular MICC (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive centripetal enhancement</td>
<td>14 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stable contrast enhancement</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Complete washout</td>
<td>0 (0)</td>
<td>5 (83)</td>
</tr>
<tr>
<td>Partial washout</td>
<td>0 (0)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Hepatobiliary phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Defect”</td>
<td>0 (0)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>“Target sign”</td>
<td>13 (93)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Heterogeneous reticular pattern</td>
<td>1 (7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrahepatic metastasis</td>
<td>8 (57)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Capsule retraction</td>
<td>8 (57)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Bile duct dilatation</td>
<td>6 (43)</td>
<td>2 (33)</td>
</tr>
</tbody>
</table>
Fig. 3: Hypervascular MICC characterization
**Fig. 4:** Typical MICC #1

**Fig. 1** Typical MICC in a 65-years old male patient
A. Arterial phase 3D MRI demonstrates a peripheral rim-like enhancing 2.7cm sized mass in S4 subcapsular area.
B, C. Portal and delayed phase 3D MRI shows centripetal enhancement pattern.
D. Hepatobiliary phase 3D MRI obtained after 20 minutes after Gd-EOB-DTPA administration shows EOB cloud, showing cloud-like SI in the center with peripheral rim defect.
F. Surgical specimen reveals mass-forming intrahepatic cholangiocarcinoma.
Fig. 2: Typical MICC in a 39 years old female patient
A. Arterial phase 3D MRI demonstrates a rim-like enhancing 1.9cm sized mass with lobulations in S7.
B. Portal phase 3D MRI shows mild progression of the enhancement into the mass.
C. Delayed phase 3D MRI taken 2 minutes after injection shows centripetal enhancement of the mass.
D. Hepatobiliary phase 3D MRI obtained after 20 minutes after Gd-EOB-DTPA administration shows EOB cloud with peripheral rim defect, corresponding with the area of enhancement in the arterial dominant phase.
E. Surgical specimen reveals mass-forming intrahepatic cholangiocarcinoma.

Fig. 5: Typical MICC #2
Results

Hypervascular MICC

**Fig. 3** Atypical hypervascular MICC in a 67-years old male patient with a history of HBV and LC.

A. Arterial phase 3D MRI demonstrates a well-enhancing mass measuring 2.3cm in the liver anterior segment.
B. Portal phase 3D MRI shows mild washout.
C. Delayed phase 3D MRI taken 2 minutes after contrast injection shows washout, and the mass appears hypointense compared to the normal liver parenchyma.
D. Hepatobiliary phase 3D MRI obtained after 20 minutes after Gd-EOB-DTPA administration shows EOB cloud with low SI peripheral rim.

**Fig. 6:** Hypervascular MICC #1
Fig. 4: Atypical hypervascular MICC in a 63 years old male patient with a history of HBV and LC.
A. Arterial phase 3D MRI demonstrates a well-enhancing mass measuring 1cm in the liver S8.
B. Portal phase 3D MRI shows washout.
C. Delayed phase 3D MRI taken 2 minutes after contrast injection shows washout, and the mass appears hypointense compared to the normal liver parenchyma.
D. Hepatobiliary phase 3D MRI obtained after 20 minutes after Gd-EOB-DTPA administration appears as a defect.

Fig. 7: Hypervascular MICC #2
Conclusion

Limitations

1. It was a retrospective study and the radiologists were aware of the pathologic diagnosis.

2. Number of lesions included in the study was small, limiting the statistical analysis.

3. Radiological and pathological correlation was not available for all lesions.

Conclusion

Gd-EOB-DTPA enhanced liver MR imaging features for typical MICC (70%) include peripheral or rim-enhancement in the arterial dominant phase, centripetal enhancement in portal and delayed phase, "EOB cloud" appearance in hepatobiliary phase with central cloud like opacity with low signal intensity (defect) peripheral rim. Histopathologically, periphery of tumor reveals active growth of tumor cells, and central portion is known to have plenty intercellular matrix.

Hypervascular MICC(30%) in Gd-EOB-DTPA enhanced MR imaging features include complete or nearly complete enhancement in the arterial dominant phase, complete or partial washout in portal and delayed phase, defect (67%) or "EOB cloud"(33) in hepatobiliary phase. This study was first to described that washout was present in all hypervascular MICC. Gd-EOB-DTPA amplified the sensitivity of detecting dynamic contrast enhancement and washout in MR. Histopathologically, hypervascular MICC has less central fibrosis, necrosis, and more frequent proportion of cellular area and cholangiocarcinoma component.

In conclusion, we evaluated the Gd-EOB-DTPA enhanced MR images of typical and atypical MICC. Typical MICC showed progressive centripetal enhancement in dynamic study and mostly appeared as an EOB cloud in hepatobiliary phase. Incidence of atypical MICC was 30% in our study, and during dynamic study arterial enhancement and complete / nearly complete washout was present. In the hepatobiliary phase, one third showed a total "EOB cloud" appearance with cloud like internal SI and peripheral defect, and two third appeared as a "defect", causing more difficulty in the differential diagnosis of HCC and MICC. In such cases, EOB cloud appearance, multiplicity(daughter nodules or intrahepatic metastasis), capsule retraction, and tumor markers such as CA19-9 may be helpful, but the differentiation of MICC from HCC remains challenging.
References


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