Cutaneous complication after transcatheter arterial chemoembolization for hepatocellular carcinoma with internal mammary artery: How to avoid this complication?

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Purpose

Introduction

Transcatheter arterial chemoembolization (TACE) is widely used in the management of hepatocellular carcinoma (HCC). HCC is a highly malignant tumor of liver cell origin and is known to be exclusively supplied by the hepatic artery. However, some condition conformed, for example, huge size of HCC or occlusion of the hepatic artery induced by repeat TACE or location of HCC, HCCs were supplied from extrahepatic collateral arteries, including the inferior phrenic artery, adrenal artery, intercostal artery, omental branch, and internal mammary artery (IMA). 1) Because extrahepatic collateral supplies can prohibit the effective control of tumor by TACE from the hepatic artery, we should treat the tumor via the extrahepatic collateral pathway.

IMA may develop as one of the extrahepatic collateral vessels when HCC is located in ventral hepatic areas, abutting diaphragm and anterior abdominal. 2) There have been several reports of transcatheter treatment from IMA. Although these reports have shown the relative safety of the treatment, cutaneous complications, such as skin lush, ulcer, and necrosis, have occurred in a few cases as a result of embolization of non-target branches. 3) 4) 5)

To our knowledge, there have been few reports describing the cutaneous complications from the aspects of chemoembolic methods and postoperative CT findings.

Purpose

The purpose of this study was to retrospectively evaluate cutaneous complications after transcatheter treatment for the HCC with IMA and to report how to avoid these complications.
Methods and Materials

Patients

Between April 2004 and August 2009, 13 sessions of transcatheter treatments from IMA were performed in 11 patients with 14 HCCs in Hiroshima University Hospital and National Hospital Organization Kure Medical Center. Two of the 11 patients received blood supply from the bilateral IMAs. One of the 11 patients had two HCCs received from ipsilateral IMA. These patients included 9 men and 2 women with ages ranging from 47 to 83 years (mean, 72 years). Five patients had recurrent HCCs post resection. The mean number of previous transcatheter treatments was 4.5 times (ranging from 1 to 5 times). Mean tumor size was 33 mm (ranging from 15 to 53 mm). Six HCCs were located on segment # and eight HCCs were on segments # or #, according to Couinaud’s liver segment classification.

Treatment Methods

Multiphase computed tomography (CT) imaging before transcatheter treatment had been obtained for all patients, which provided us with useful information.

Arteriograms of celiac and superior mesenteric arteries and CT during arterial portography (CTAP) and CT during hepatic arteriography (CTHA) were performed in all patients. Selective arteriograms of IMA and CT during internal mammary arteriography using a 5-F or 4-F catheter or a 3-F microcatheter (Microferret-18; William Cook Europe, Bjaeverskov, Denmark) through it were usually attempted when HCCs were located in the ventral hepatic area and furthermore, the tumor stains on CT during hepatic and inferior phrenic arteriography were not demonstrated corresponding to those depicted by CTAP. Transcatheter treatments were performed when an obvious blood supply to HCCs was shown on CT during internal mammary arteriography.

We attempted to insert a 3-F microcatheter into each of the tumor-feeding branches. If this was impossible, we advanced the microcatheter as close to these branches as possible. Treatment methods, which consisted of a choice between transcatheter arterial chemoembolization (TACE) or transcatheter arterial embolization (TAE) alone, were chosen by the procedural operators taking into consideration the drug amount in TACE. TACE was performed with gelatin sponge particles (Spongel; Yamanouchi, Tokyo, Japan or Gelpart; Nippon Kayaku, Tokyo, Japan) after injection of a mixture of 5.0 - 25 mg of cisplatin (IA-call; Nippon Kayaku, Tokyo, Japan) or epirubicin (Farmorubicin; Pfizer, Tokyo, Japan) and 0.5 - 2.5 ml of iodized oil (Lipiodol; Andre Guerbet, Aulnay-sous-Bois, France), as a ratio of 10 mg of anti-cancer agents to 1.0 ml of iodized oil. TAE was infused only with gelatin sponge particles. This suspension or emulsion and the embolic materials were injected until near-stasis was observed in tumor-feeding branches of the target vessel.
On the last procedure, we usually took a plain CT scan and checked two things; one is drug accumulation into the tumor and whether there was filling or not of iodized oil in subcutaneous vessels.

**Definition**

IMA gives four main branches around the liver, such as the phrenic branch, anterior intercostal artery, musculophrenic artery, and superior epigastric artery (Fig. 1) on page 6. The microcatheter catheterization techniques were classified into two groups; "selective" and "non-selective" groups. Selective and non-selective groups were defined as success of microcatheter insertion into the main branch or separate portion of distal two main branches and failure of these, respectively (Fig. 2) on page 6.
Fig. 0: The right IMA angiogram. This shows four main branches as tumor feeders supplying HCC.

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Fig. 0: The classifications of "selective" or "nonselective". On both angiograms, the arrow shows tumor staining and the arrow head is the head of the microcatheter. A. Selective group was defined as success of microcatheter insertion into the main branch or separate portion of distal two main branches. B. Nonselective was defined as failure of either those.

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Fig. 0: Postoperative CT findings. A. B. Filling and no filling groups of iodized oil in subcutaneous vessels. A. Subcutaneous vessels are filled with iodized oil (arrow head). B. High density area is accumulation of lipiodol at HCC after TACE with IMA(arrow).

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Results

Complications

Skin rash or ulceration as cutaneous complications occurred in 2 of 13 sessions (15.4%). Skin rash, which improved within several days by local subcutaneous steroid injection, occurred in one patient. Skin rash developed to refractory skin ulceration in another patient (Fig 4.) on page 10. The ulceration was sequential until the patient's death, which was 5 months later after transcatheter treatment, despite treatments.

Complications rates in the chemoembolization methods

Cutaneous complication rate was 0% (0/4 sessions) in the selective TACE group, 50% (2/4 sessions) in the nonselective TACE group and 0% (0/5 sessions) in the nonselective TAE group, respectively (Table 1). on page 10

Complications rates in the postoperative CT findings

Cutaneous complication rate was 66.7% (2/3 sessions) in the filling of iodized oil group and 0% (0/10 sessions) in the no filling group, respectively (Table 2) on page 11.

Complications in the chemoembolization methods and postoperative CT findings

All three sessions of filling of iodized oil were included in the nonselective TACE group. The larger amounts of infusion drug with complications tended to be used compared to those with no complications (Table 3) on page 12.
Images for this section:

![Image]

**Fig. 0:** Photograph at four months after nonselective TACE. Skin ulceration on the anterior right upper abdominal area where a superior epigastric artery distributed.

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<table>
<thead>
<tr>
<th>Method</th>
<th>Amount of infusion drug* (Mean ± SD)</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective TACE (n = 4)</td>
<td>9.5 ± 4.2</td>
<td>0 % (0/4)</td>
</tr>
<tr>
<td>Selective TAE (None)</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Nonselective TACE (n = 4)</td>
<td>18.5 ± 7.5</td>
<td>50 % (2/4)</td>
</tr>
<tr>
<td>Nonselective TAE (n = 5)</td>
<td>0</td>
<td>0 % (0/5)</td>
</tr>
</tbody>
</table>

TACE: transcatheter arterial chemoembolization; TAE: transcatheter arterial embolization; SD: standard deviation.
* A mixture of cisplatin or epirubicin (mg) and iodized oil (ml), as a ratio of 10 mg of anti-cancer agents to 1.0 ml of iodized oil.

**Fig. 0**: Complications in Chemoembolization Methods

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<table>
<thead>
<tr>
<th>Amount of infusion drug (Mean ± SD)</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filling of iodized oil in subcutaneous vessels (n = 3)</td>
<td>20 ± 8.6</td>
</tr>
<tr>
<td>No filling of iodized oil in subcutaneous vessels (n = 10)</td>
<td>5.1 ± 6.2</td>
</tr>
</tbody>
</table>

**Fig. 0:** Complications in Postoperative CT Findings

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<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Tumor size, (mm)</th>
<th>Amount of infusion drug (mg)</th>
<th>Filling of iodized oil in subcutaneous vessel</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>25</td>
<td>Yes</td>
<td>Skin ulcer</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>25</td>
<td>Yes</td>
<td>Skin rash</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>10</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>15</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**Fig. 0:** Details of Nonselective TACE Group

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Conclusion

Cutaneous complications were considered to be mainly caused by the therapeutic mixtures rather than the embolic materials into skin branches in this study. Filling of iodized oil containing anticancer drug in subcutaneous vessels may lead to skin injury.

IMA possess branches (ie, intercostal artery and superior epigastric artery) that feed the skin. When selective catheterization to the tumor-feeding branch is successful, TACE is acceptable. We need to address reflux into other branches and potential vessel communications. On the other hand, when unsuccessful reduction of therapeutic mixture or TAE alone without therapeutic mixture or TACE after change blood stream may be a less risky alternative.

A limitation of this study is its retrospective nature and exclusively described complications. A prospective study including the evaluation of tumor control and survival rates is needed to determine how best to treat.
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