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TRANSCATHETER CT HEPATIC ARTERIOGRAPHY-GUIDED PERCUTANEOUS ABLATION TO TREAT ABLATION SITE RECURRENCES OF COLORECTAL LIVER METASTASES: THE INCOMPLETE RING SIGN

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ABSTRACT

Transcatheter CT arterial portography (CTAP) guided percutaneous liver tumor ablation has proven feasible and accurate to treat liver metastases from colorectal origin that are obscure on ultrasound and unenhanced CT. However, distinguishing local recurrence from post-ablation scars can still be difficult. This report describes nine patients with post-ablation recurrences, in whom transcatheter CT hepatic arteriography (CTHA) allowed differentiation of recurring and residual tumor tissue (incomplete ring enhancing lesion) from tumor-free non-enhancing scars. Using CTHA it is possible to plan and guide percutaneous retreatment and confirm technical success without oversized re-ablations or jeopardizing patients renal function.
INTRODUCTION

For patients with technically unresectable liver-only malignancies, that are poorly or not visible on ultrasound (US) and unenhanced CT, single-session CT arterial portography (CTAP) guided percutaneous tumor ablation enables repeated contrast-enhanced imaging and real-time contrast enhanced CT (CE-CT) fluoroscopy. This technique improves lesion conspicuity, but adds risks related to catheter placement and leads to higher radiation exposure. Even with CTAP it remains difficult to distinguish site recurrences from scar tissue after ablation of colorectal liver metastases. This may lead to inaccurate or oversized re-ablations of the locally recurring tumor tissue.

Using the previously described CTAP technique to treat a local site recurrence (LSR) after thermal ablation of a colorectal liver metastasis (CRLM) in the right liver lobe, we coincidentally noted that the recurrence appeared as a hyperattenuating ring, directly adjacent to the non-enhancing ablation scar. It turned out that the patient had an aberrant right hepatic artery originating from the superior mesenteric artery. These findings led to the presumption that the visualization of local site recurrences required for retreatment, can be improved with CT hepatic arteriography (CTHA).

This brief report describes nine patients with LSR after previous ablation of CRLM in whom a transcatheter CTHA technique was successfully used for localization and retreatment of site recurrences.

MATERIALS AND METHODS

Between January 2013 and May 2014 nine consecutive patients with fluorine-18 (F-18) fluorodeoxyglucose (FDG) positron emission tomography (PET) avid marginal site recurrences after either radiofrequency ablation (RFA), microwave ablation (MWA) or irreversible electroporation (IRE) of CRLM were included. In all patients the liver lesions were occult or difficult to delineate from the ablation scar on both abdominal ultrasonography and unenhanced CT. Patient, lesion and treatment characteristics are displayed in Table 1. RFA was considered the technique of first choice. MWA was preferred for perivascular lesions and IRE was reserved for selected cases in which thermal ablation was considered unsafe due to the proximity of main bile ducts. The local review board waived approval for the catheter placement and for the retrospective analysis of patient data. All patients gave written informed consent for the catheter guided percutaneous tumor ablation.
The CTHA technique was similar to the previously described technique with the exception that the catheter was placed in the common hepatic artery proximal to the gastroduodenal artery and that a 40cc 1:1 mixed bolus contrast material (Xenetix300, Guerbet, Villepinte, France) with saline was injected at an injection rate of 4cc/sec (scan delay 6 sec and 22 sec). The procedures were performed on a 64-slice multidetector CT (Somatom Sensation, Siemens, Erlangen, Germany). Imaging parameters were 32x0.6mm collimation; 120kV; 100mAs; reconstructed slice width 3mm for the series and 30mAs; 120 kV; 5.4mm slice thickness for the CT fluoroscopy.

Complications due to either the catheter placement or the ablation were noted according to the common terminology reporting criteria (CTCAE version 3.0). Technique effectiveness was assessed according to standardization of terminology and reporting criteria as documented by the Society of Interventional Radiology (SIR) technology assessment committee and the International Working Group of Image-guided tumor ablation. Technical success was defined as the presence of a non-enhancing ablation zone completely surrounding the vital tumor tissue with at least a 5mm margin on CTHA, immediately after the procedure. To evaluate this margin in three dimensions, 3D image fusion, multiplanar reformatting and registration software with automated and manual rigid body shifting was used (Syngo Fusion, Siemens, Erlangen, Germany). Secondary technique effectiveness was analyzed using PET-CT at three months.

RESULTS

CTHA was successful in localizing the LSR in all 9 patients and the normal liver parenchyma showed typical arterial and portal-venous phase enhancement characteristics.

### Table 1: Patient, treatment and lesion characteristics

<table>
<thead>
<tr>
<th>#</th>
<th>Age</th>
<th>Sex</th>
<th>Segment</th>
<th>Size mm</th>
<th>CTHA</th>
<th>Initial treatment</th>
<th>Retreatment</th>
<th>Complications</th>
<th>Local site recurrence at 3 months</th>
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<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>F</td>
<td>IV</td>
<td>12x15</td>
<td>+</td>
<td>IRE</td>
<td>IRE</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>76</td>
<td>M</td>
<td>V</td>
<td>13x28</td>
<td>+</td>
<td>RFA</td>
<td>MWA</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>M</td>
<td>VII-VIII</td>
<td>14x17</td>
<td>+</td>
<td>RFA</td>
<td>RFA</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>81</td>
<td>F</td>
<td>VIII</td>
<td>8x11</td>
<td>+</td>
<td>RFA</td>
<td>MWA</td>
<td>+++</td>
<td>?</td>
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<tr>
<td>5</td>
<td>66</td>
<td>M</td>
<td>II-IV</td>
<td>16x25</td>
<td>+</td>
<td>RFA</td>
<td>RFA</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>69</td>
<td>M</td>
<td>V-VIII</td>
<td>9x19</td>
<td>+</td>
<td>IRE</td>
<td>IRE</td>
<td>-</td>
<td>?</td>
</tr>
<tr>
<td>7</td>
<td>49</td>
<td>F</td>
<td>VI</td>
<td>10x13</td>
<td>+</td>
<td>RFA</td>
<td>RFA</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>63</td>
<td>M</td>
<td>VII</td>
<td>28x32</td>
<td>+</td>
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<td>MWA</td>
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<td>-</td>
</tr>
<tr>
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<td>27</td>
<td>M</td>
<td>VII</td>
<td>8x18</td>
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<td>RFA</td>
<td>RFA</td>
<td>-</td>
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</table>
with densities comparable to or higher than on CECT. In 9/9 cases the LSR presented as a typical ring-enhancing lesion with an interruption at the interface with the abutting non-enhancing post-ablation scar, which will be referred to as the incomplete ring sign (Fig. 1). The recurring lesions were all successfully retreated using RFA (4 patients), MWA (3 patients) or IRE (2 patients). In one patient a new lesion, which was already detected on pre-procedural F18-FDG PET-CT, was also clearly visible using CTHA. Both the LSR and the new lesion were treated with RFA (Fig. 2; subject 9).

Technical success was 100% and no acute complications were seen. After the procedure, one major and two minor complications occurred: One patient (subject 4) developed a bilio-pleural fistula resulting in a biliary pleuritis requiring long-term chest drainage and hospital re-admission (CTCAE grade III; subject 4). One patient experienced pain lasting >4 days (CTCAE grade I; subject 8) and one patient developed reactive pleural effusion (CTCAE grade II; subject 7). There were no complications related to the femoral artery puncture site or catheter placement and no contrast induced renal impairment occurred.

At three months one IRE treated lesion showed residual F18-FDG tracer uptake. Differentiation between local site residue or IRE induced inflammatory change was
not possible (subject 6). The patient with the biliopleural fistula also showed F18-FDG tracer uptake, representing the fistula (subject 4). The other treated lesions did not show any tracer uptake at 3 months.

Fig. 2: Arterial phase (Fig. 2A) and mixed late-arterial to early-portal venous phase (LSR shown in white box and a new lesion detected in same session (*) Fig. 2B). CT hepatic arteriography (CTHA) images of a 27-year old male patient (subject 9) showing a typical incomplete ring lesion which represents a local site recurrence after previous RFA. Using transcathe ter contrast-enhanced CT fluoroscopy a 3.5cm LeVeen RFA needle ((Boston Scientific, Marlborough, MA, USA) is advanced and deployed into the lesion. Another CTHA series confirms the accurate position of the probe (Fig. 2C). After re-treatment the lesion including a non-enhancing tumor free margin of at least 5mm seems completely ablated (White box, Fig. 2D). A new segment VII CRLM, which was detected on pre-procedural F18-FDG PET-CT, was ablated within the same session (*).

DISCUSSION

Percutaneous re-ablation of local recurrence from post-ablation scars of CRLM is established as guideline treatment worldwide. A recent study evaluating the efficacy of re-ablations showed no difference in oncological outcome between patients with lesions requiring retreatment and patients with a primary successful thermal ablation. In the optimal ablation procedure, the obtained ablation zone is large enough to cover
all vital tumor cells, but does not risk damage to the surrounding vulnerable structures. Optimizing conspicuity of the lesion, the needle trajectory and the ablation zone will lead to less complications and more precise targeting which will result in a decreased number of patients requiring re-treatment. Imaging modalities and techniques used for targeting local tumor recurrence after previous ablation are largely chosen based on operator preference and local availability. Contrast-enhanced US for hypervascular lesions and real-time CT and -US fusion techniques have shown promising results in literature. No data exist in the treatment of typically hypovascular LSR after previous ablation. With these techniques misregistration pitfalls due to physiologic motion and the non-rigid nature of the organs remain problematic. CTHA enables repeated and real-time liver tumor visualization before, during and after placement of the probes and may therefore prove more accurate.

This report describes the feasibility of CTHA to differentiate the post ablation scar tissue from the vital recurring tumor tissue. This allows repeated contrast enhanced scanning to (1) plan treatment, (2) guide needle advancements, (3) verify probe position relative to the tumor and surrounding structures in 3 dimensions and (4) evaluate procedure related complications and technical success directly after the ablation, all without jeopardizing renal function.

The typical incomplete ring sign was clearly present in all 9 cases and matched the F18-FDG PET-CT avidity. Because the majority of CRLM are hypoattenuating on CE-CT compared to normal liver parenchyma, the use of CTAP seems ideal for repetitive visualization and localization of new CRLM during percutaneous ablation. Pitfalls are overestimation of the lesion size and the presence of perfusion heterogeneities. Placing the catheter in the common hepatic artery proximal to the gastroduodenal artery combines the hepatic arterial ring enhancement with an arterial portography, since contrast will also flow into the gastroduodenal artery and hence, after passing the duodenal, pancreatic and gastro-epiploic circulation, into the portal vein. Scanning twice at 6 and 22 seconds after contrast injection allows visualization of a pure arterial phase and a mixed late arterial - early portovenous phase. Lesions will appear as ring lesions on both series, with the ring best discerned on the arterial phase and best sited in the background of normal attenuating liver parenchyma and larger blood vessels during the second phase. Although this needs further validation, CTHA may even prove superior to CTAP in guiding percutaneous ablations for new CRLM as well.

The higher ratio of hepatic arterial flow over portal venous flow in the rim regions surrounding nearly all colorectal liver metastases is a well known phenomenon. There has been quite some debate whether this rim enhancement represents vital tumor tissue or reactively altered surrounding tissue. For determination of actual ablation zone size and therefore treatment accuracy, this is of crucial importance. The etiology behind these actions is not completely elucidated and most likely multifactorial. Firstly,
the proliferation of neoplastic blood vessels (neo-angiogenesis) favors the recruitment of hepatic artery branches over portal veins \(^5\). These alterations can also be found within a certain region surrounding the tumor, presumably due to the local spread of tumoral cytokines. Secondly, mechanical tumor compression and/or peritumoral vessel lumen-narrowing secondary to fixed leukocyte adherence will result in reduced portal flow \(^6\). Although under debate, decreased portal supply in the compressed hepatic parenchyma has been suggested to evoke a compensatory increase in arterial blood supply \(^7\). Hepatic artery perfusion in these areas is probably overestimated due to the decreased dilution within the hepatic sinusoids of the highly dense contrasted arterial blood with the not-yet-contrasted portal venous blood \(^8\). Thirdly, the drainage of blood flow from the tumor to the surrounding hepatic parenchyma in hypervascular metastases or by increased arteriportal shunts surrounding the tumor in hypovascular metastases may cause rim-like enhancement \(^9\). Finally, perilesional enhancement has been reported to correlate with histopathologic hepatic parenchymal changes, such as inflammatory cell infiltration, hyperemia and the presence of a desmoplastic reaction \(^10\). The arterial hyperattenuation of vital tumor tissue versus the hypattenuating non-vital scar tissue after thermal ablation has been previously turned to good account in a study using total liver volume perfusion for early detection and localization of treatment-site recurrences after RFA \(^11\). The interruption in the ring enhancement at the interface with the ablation scar suggests that either vital tumor tissue does not invade scar tissue or that the ring represents reactive surrounding liver parenchyma which is by definition not present at the margin of residual or recurring tumor tissue.

Limitations of the CTHA technique are possible complications related to sheath and catheter placement. The additional burden for the patient, costs and physician-time can only prove worthwhile, if it reduces the number of necessary re-treatments. The presence of arterial anatomy variants needs to be assessed prior to the procedure. Limitations of the study were the relatively small group and the heterogeneity of included patients and ablative methods.

In conclusion, CTHA enables repeated contrast-enhanced imaging with distinction of recurring/residual tumor tissue versus post ablation scar tissue requiring minimal amounts of contrast during treatment of recurring CRLM. A remarkable incomplete ring enhancing lesion directly adjacent to the post ablation scar was observed in all nine patients. Using CTHA, it was possible to plan and guide percutaneous re-ablation and confirm technical success without jeopardizing patients renal function. It is hoped that future work will show whether CTHA can also improve accuracy for percutaneous ablation of previously untreated CRLM.
REFERENCES