

Selective internal radiotherapy using Yttrium-90 labelled resin microspheres in a patient with relapsing liver metastases of adrenocortical carcinoma after previous microwave ablation

L.M. Hernandez MD, W. Noordzij MD, PhD

Department of Nuclear Medicine & Molecular Imaging, Universitair Medisch Centrum Groningen

Abstract

A forty-year-old female patient was referred with liver metastasis from adrenocortical carcinoma after routinely oncologic follow up, at nine months after resection of the primary tumour. Microwave ablation was performed, but six months post ablation there were diffuse liver metastases. Percutaneous radiofrequent ablation was considered unsuitable because of the extensiveness of the disease and the location of the metastases. Due to the arterial enhancement of the liver metastases on CT and MRI, and the fact that there was no conventional treatment line available anymore, the patient was considered suitable for selective internal radiotherapy (SIRT) of the right liver lobe with Yttrium-90 resin microspheres in compassionate use. Unfortunately, liver-MRI four months later showed growth of the liver metastasis in both the right as the left liver lobe.

Case

This case report details on a forty-year-old female patient with relapsing liver metastasis of adrenocortical carcinoma after previous microwave ablation. She was treated with ^{90}Y resin microspheres but showed progressive

disease after three months. At the age of 38 she was referred to our department of hepatobiliary surgery with a large right sided adrenocortical tumour of approximately eighteen cm in maximal diameter. There were no lymphogenic or distant metastasis. The tumour was radically resected and classified as a stage two, T2N0M0 adrenocortical carcinoma. The operation was complicated by massive bleeding caused by iatrogenic damage of the vena cava inferior. Routine oncologic follow-up CT performed three and six months after surgery didn't show a local recurrence or signs of metastases. However, at nine months post-surgery CT revealed multiple new hypodense liver lesions suggesting liver metastases. MRI of the liver confirmed the presence of multiple metastases, and a few weeks later microwave ablation (MWA) was performed of six liver metastases. Routinely performed CT

at one week and two months after MWA didn't show evidence of local recurrence, residual liver disease or new metastases. However, the CT-scan six months later demonstrated new liver lesions in segment VII and IVb. Liver MRI confirmed diffuse liver metastases (figure 1). After a multidisciplinary consultation, percutaneous radiofrequent ablation was considered unsuitable because of the extensiveness of the disease and the location of the metastases. Due to the arterial enhancement of the liver metastases on CT and MRI, and the fact that there was no conventional treatment line available anymore, the patient was considered suitable for SIRT with ^{90}Y resin microspheres in compassionate use. Because the tumour burden was predominantly in the right liver lobe and in segment I, it was decided to perform SIRT of the right lobe and segment I, and initially leave the left lobe untreated.

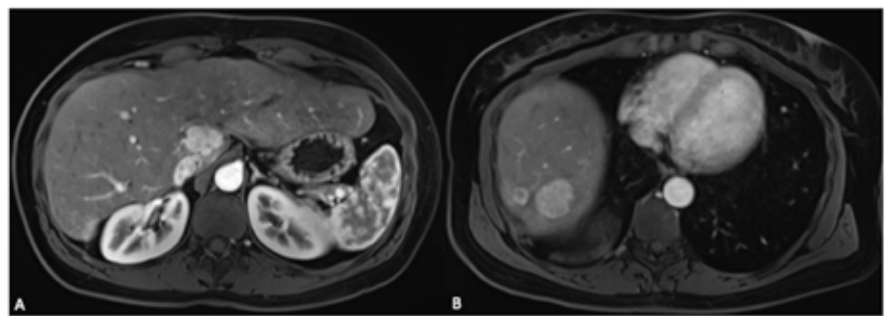


Figure 1. Transversal slices of liver MRI six months after microwave ablation, showing new enhancing liver lesions in segment I (image A) and in segment VII and VIII (image B).

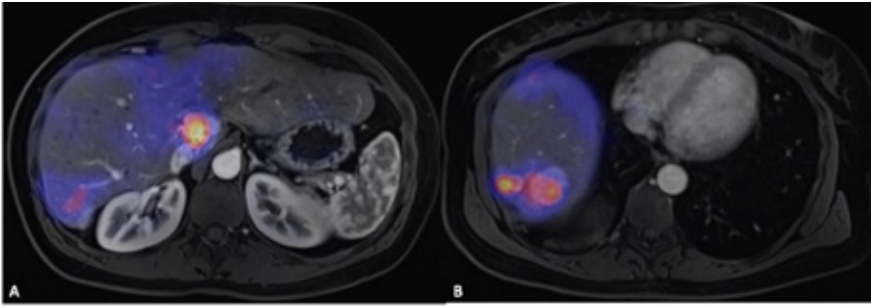


Figure 2. Fused images of liver MRI and SPECT-scan after injection with [^{99m}Tc]Tc-MAA injection. There is adequate targeting of liver metastases in segment I (image A) and metastases in segment VII and VIII (image B).

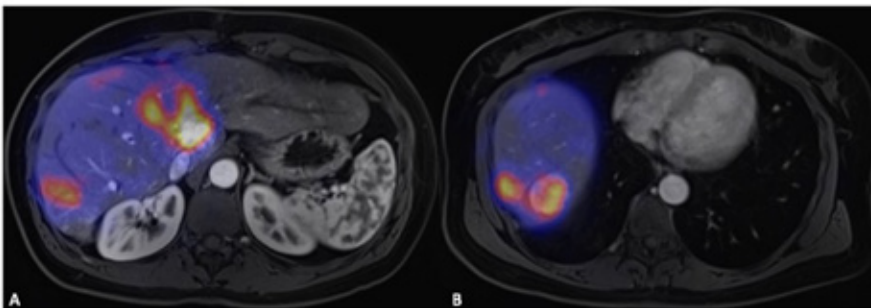


Figure 3. Fused transversal slice of liver MRI and PET after treatment with SIRT, showing an adequate targeting of resin microspheres on the liver metastases in segment I (image A) and in segment VII and VIII (image B).

Pre-therapy evaluation using Technetium-99m labelled macro-aggregated albumin ([^{99m}Tc]Tc-MAA) SPECT revealed adequate targeting of the metastasis in the right liver lobe and also of the metastases in segment I and III (figure 2). There was no significant extra-hepatic [^{99m}Tc]Tc-MAA accumulation, and pulmonary shunting was limited to 3.7%. The perfused liver volume was approximately 1700ml, including the right liver lobe and segment I and IV, whereas the tumour volume was estimated to be only 27ml. The remaining volume of the untreated left liver lobe is 340ml. The proposed treatment dose was 1650MBq, which should result in at least 130Gy on the liver metastases and approximately 40Gy on the non-affected liver. Through a very selective positioned microcatheter in the right hepatic

artery the treatment with ^{90}Y resin spheres was given in a slow and fractionated manner (figure 3). Beforehand the gastroduodenal artery was temporarily occluded to prevent spread of ^{90}Y spheres in other parts of the body, in particular the intestines. It was an uncomplicated procedure, and the patient was discharged the day after the treatment.

After the treatment, the patient complained of nausea and fatigue till about eight weeks after treatment. Metoclopramide was not effective enough. Other than that, the treatment was well tolerated. Liver MRI four months later showed growth of the liver metastasis in both the right as the left liver lobe and also new liver and lung metastases (figure 4).

Discussion

Adrenocortical carcinoma (ACC) is a rare and aggressive malignancy, with a poor prognosis. The five-year survival after complete resection is 16-50% and almost no survivors after an incomplete resection (1). It has an overall incidence of 0.5-2 per one million cases (2). There are two peaks of incidence: the first occurs between the ages of one and six, and the second between the ages of forty and fifty. Women tend to have a higher incidence compared to men with a ratio of 2:1, due to a proliferative effect of estrogen levels on ACC-cells (3). Patients often present with extra adrenal disease, because of the absence of specific cancer related early symptoms. They present with non-specific symptoms due to excess hormone secretion or symptoms secondary to mass effect. Up to 70% of patients are diagnosed with stage III and IV at presentation (4) or they present with distant metastases (17.8 - 39%) (1,5,6). Lungs (66%), liver (57%) and bone (17%) are the most common sites of ACC metastases (4). Some studies even show that the liver is the most common site of metastases (1,5,6).

In patients with metastatic disease surgery is an important treatment option when complete resection of the primary tumour and all its metastases is feasible. However even after aggressive surgery local recurrence is frequent. Salvage resections may be considered, particularly when more than twelve months have passed after the initial treatment (7,8). Local therapies such as radiofrequency ablation (RFA) have also been used as an alternative to surgery to reduce tumour burden (9). But RFA has limited efficacy in patients with bilobar lesions, multiple lesions, highly vascularized metastases, or metastases in proximity to large vessels due to the heat-sink effect (10-12) Systematic therapies (including adrenolytics, chemotherapy and

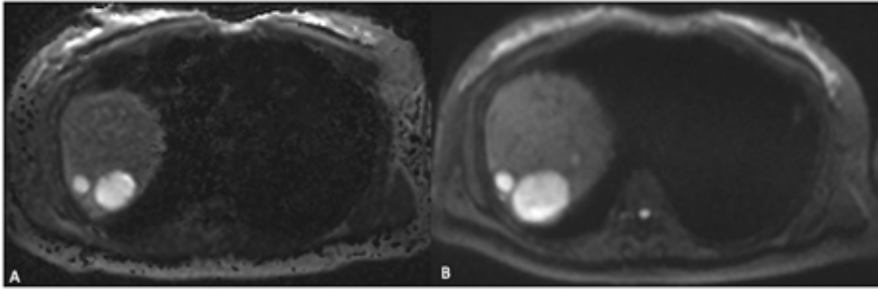


Figure 4. Transversal slice of MRI diffusion weighted imaging before (image A) and after SIRT (image B), demonstrating growth of liver metastases in segment 7 and 8. There are also new liver metastases visible.

targeted therapy) as single therapy or as a combined therapy, have proven not to be beneficial for overall survival (13). There were different first-line agents included in the study such as mitotane, cisplatin, etoposide, streptozocin, doxorubicin, paclitaxel, gemcitabine, cyclophosphamide and ifosfamide.

SIRT is a targeted treatment of liver malignancies using ^{90}Y labelled microspheres. It is approved for the treatment of hepatocellular cancer and colorectal liver metastases. For other pathologies, its use is considered off-label. In this case SIRT was also deployed as an off-label treatment without any hard evidence of efficacy.

Studies with SIRT in patients with ACC and liver metastasis are non-existent, due to the low prevalence of the disease. But there are a few case reports with good outcomes. Sen Lu presented a case where SIRT was surgically proven to be an effective treatment for isolated hepatic cortical adrenal carcinoma seven months post radioembolization (14). The estimated dose on the tumour was approximately 105Gy. After the procedure, the patient had an adrenal crisis. This was treated with dexamethasone and hydrocortisone. He was discharged on day three post procedure. Another case report also showed

successful treatment of the primary adrenal tumor and bilobar liver metastasis by combining SIRT, chemotherapy and surgery (15). The estimated dose that was given on liver metastases was about 120Gy in each lobe. There was management of disease for at least 12 months. The treatment was well tolerated with only low-grade fevers for 24 hours and upper quadrant pain, which resolved in two to three weeks.

A third case report showed a complete radiological response two years after bilobar SIRT on chemotherapy-resistant liver metastases of ACC (16). The dose on the tumor is not mentioned in the report.

This case report displays a patient in which SIRT showed not to be beneficial in the treatment of liver metastases of ACC. Because of the small volume of the untreated left liver lobe, the dose to the metastases in the right liver lobe was limited to 130Gy. In the mentioned case reports dosage differed from 105 to 120 Gy. Literature suggests that a normal dose varies between 120 and 150 Gy. Therefore, it is not likely that the dosage was too low. It could be that these metastases were radiation resistant.

Conclusion

Although some case reports show that selective internal radiotherapy is feasible in patients with adrenocortical carcinoma, our case demonstrates that SIRT was not as effective in the

treatment of liver metastases of ACC. This case report shows that arterial enhancement of liver metastases alone is not a good predictor of effectivity of SIRT. Due to the lack of research, it is not clear why in this patient SIRT was proven not effective. Further prospective study is needed to better establish efficacy, safety and patient selection.♦

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