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Transarterial Radioembolization Treatment of Advanced Hepatocellular Carcinoma Invading the Right Atrium

Kabalane Yammine, MD*[1], Sarah Khalife, B.Sc[2], Jihad Daher, M.D[3] and Feras Chehade, M.D, Ph.D[4].

[1]Radiology Department, Clémenceau Medical Center, Beirut, Lebanon

[2]Radiology Department, American University of Beirut, Beirut, Lebanon

[3]Radiology Department, Clémenceau Medical Center, Beirut, Lebanon

[4]Nuclear Medicine Unit Clémenceau Medical Center, Beirut, Lebanon

ABSTRACT

Tumor thrombus infiltration of hepatocellular carcinoma (HCC) into the inferior vena cava and right atrium is rare and is associated with a poor prognosis due to the critical location of the tumor and the limited efficiency of the available treatment strategies. In this study, we report the case of a patient with advanced HCC and tumor thrombus in the inferior vena cava and right atrium who demonstrated complete response with mass retraction upon Yttrium-90 trans-arterial radioembolization (90Y- TARE) therapy. Throughout the 16 months follow-ups after the radioembolization, the patient was free of any complications, revealing no occurrence of radiation-induced pneumonitis or tumor recurrence.

***Corresponding author**

Kabalane Yammine, Radiology Department, Clémenceau Medical Center, Beirut, Lebanon. Tel No: (+961) 03-936343, Email: kabalaneyammine.md@gmail.com

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Introduction

HCC is the most common primary liver cancer and the second most common cause of cancer death worldwide [1]. It is a highly aggressive malignancy in which the tumor thrombus (TT) is known to infiltrate portal and hepatic veins in the advanced stages [2]. Intravascular TT can further progress and extend into the inferior vena cava (IVC) and the right atrium (RA). Prognosis in such cases is extremely poor, with a median survival of about 2–5 months without treatment [3]. Although there are various possible treatments proposed (surgery, radio ablation, trans-arterial radioembolization (TARE), and combination treatments), there is still no optimal one established for TT infiltration of the RA [4]. In this study, we report the case of a patient with HCC and TT in the IVC and RA that showed a complete response to TARE. We discuss the risks and reasoning behind favoring 90Y- TARE therapy for our patient and how this treatment gives promising results compared to other treatments.

Case Presentation

A 65-year-old male with a known history of alcoholic cirrhosis (Child-Pugh A5) demonstrated a right hepatic lesion on routine screening ultrasound (US) of the abdomen. The tumor, of size 5 x 3 cm in segment VII of the liver, was abutting the middle hepatic vein. Pre-operative Magnetic Resonance Imaging (MRI) revealed two additional nodules in segments IV B and III, with maximal diameters measuring 1.5 and 0.8 cm respectively. Prior to the tissue sampling, the patient underwent upper gastrointestinal endoscopy that revealed an incidental distal esophageal tumor staged T2, N0, M0 (based on the 7th International Union Against Cancer TNM staging system) [5].

The patient underwent an ultrasound-guided core biopsy of the main hepatic lesion, and the resulting histopathologic report revealed a moderately differentiated HCC. Based on the Barcelona Clinic Liver Cancer (BCLC) staging system, the patient was stage B [6]. Locoregional treatment of the main hepatic lesion was performed by transarterial chemoembolization (TACE) with doxorubicin-loaded drug-eluting beads (BTG, London, UK) [7,8]. Follow-up imaging showed a good response, with a focal area of liquefaction at the site of the mass, and a minimal peripheral residual enhancement suggesting partial response. After that, a distal esophagectomy was done to resect the neoplastic mass of esophagus.

4 months after the TACE, follow-up computed tomography (CT) imaging exhibited near complete necrosis of the TACE-d hepatic tumor, with an appearance of a new mass medial to the previously embolized tumor. The mass infiltrated the intrahepatic IVC and RA and slightly extended to a branch of the right hepatic vein. The new tumor thrombus measured 6 x 3 cm and extended 3 cm into the RA. Due to the macrovascular invasion of the TT into

the IVC and RA, the patient was BCLC stage C [6]. The patient was asymptomatic at the time of the examination.

In an attempt to stop further tumor growth and infiltration, an emergency single session 90Y-TARE took place. Y-TARE treatment was favored in this patient as surgical resection of the thrombus was deemed perilous. Likewise, TACE was contraindicated due to the increased risk of tumor rupture, cardiopulmonary embolism/collapse, and hepatic necrosis [9,10]. Sorafenib was not administered to the patient. Pre-planning of TARE with 99mTechnetium-macroaggregated albumin (99mTc-MAA) scintigraphy imaging was not done for expediency. However, digital subtraction angiography (DSA) (Figure.1 a-b), and cone-beam CT (CBCT) (Figure.1 c-f) were both used to determine the volume and arterial supply to the tumor.

These modalities also assessed the presence of any extrahepatic arterial communications that could increase the risk of shunting and deposition of the 90Y-spheres outside the liver. Using the images from the CB-CT scan, the volume of the treatment area measured around 100 cc. Before the injection of 90Y, selective arteriography revealed exclusive tumor supply through the right inferior phrenic artery (rIPA) and not from the hepatic arteries. Consequently, a 2.7 Fr microcatheter was advanced beyond the posterior branch of the IPA to avoid radiation to the posterior half of the right hemidiaphragm. CB-CT imaging, with contrast administered through the microcatheter in place for treatment, demonstrated good uptake by the tumor and its extension into the intrahepatic IVC and the right RA.

There was no hepatoportal shunting on either of the DSA and CBCT images. After confirming the adequacy of the injection position, preparation for injection of the 90Y SIR-spheres was done. In regard to the exclusive tumor supply through selected rIPA, exclusion of significant participation of liver tissue, and absence of hepato-portal shunt, the mono-compartmental equation of the medical internal radiation dose (MIRD) was chosen to calculate the desired curative activity to be administered. The total calculated activity of the injection was 0.5 GBq. Radioembolization was performed injecting the calculated activity of SIRS-spheres (Sirtex Medical Inc.) through the rIPA under fluoroscopic observation.

Post-administration 90Y-PET/CT (Figure.1 g-h) exhibited adequate locoregional coverage of the TT and, to a lesser extent, the diaphragm, without significant uptake in the remainder of the liver and lungs. According to the locoregional 90Y-SIR PET distribution, the calculated absorbed doses were 225 Gy, 21.25 Gy and 5 Gy to the tumor, the diaphragm, and lungs respectively. Over the short- and medium-term follow-ups post 90Y-TARE, the patient did not exhibit any respiratory symptoms, as radiological imaging did not demonstrate any signs of organizing pneumonia or evidence of radiation-induced lung disease. Additionally, the patient did not develop liver toxicity following the treatment.

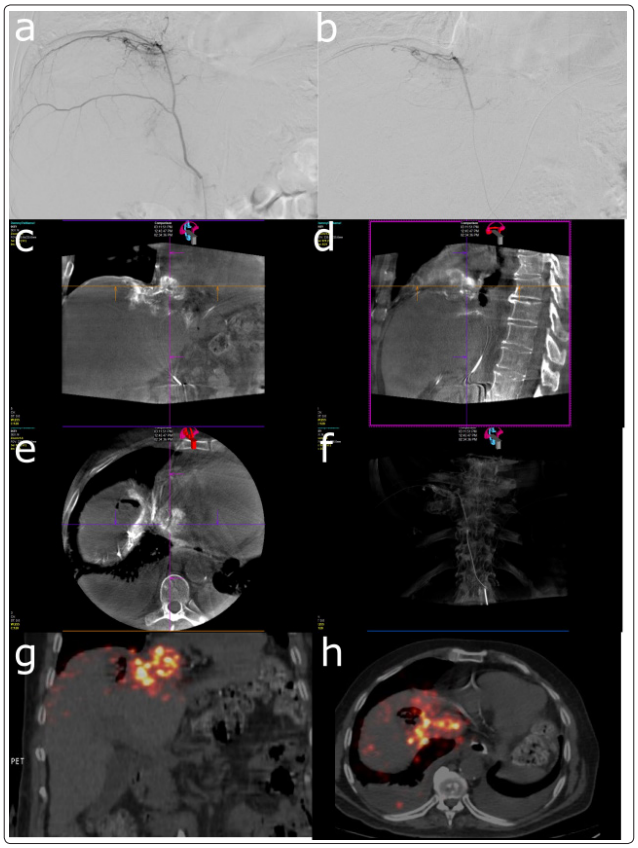

Figure 1: Pre-injection DSA (a-b) and Cone-beam CT c-f) show contrast uptake of the tumor and diaphragm through Right inferior phrenic artery (rIPA). Contrast media was injected through a 2.7 Fr microcatheter advanced beyond the posterior branch of the IPA to avoid radiation to the posterior half of the right hemidiaphragm. Dose uptake in the tumor and diaphragm was evaluated on post-treatment 90Y-PET-CT images (g-h).

After 4 months, follow-up CT imaging revealed a retraction of the mass from the inferior vena cava and RA, with a non-enhancing residual occlusion of the right hepatic vein branch. The patient is still alive and has maintained a healthy condition for 16 months since the treatment (Figure.2). CT images showed a minimal calcification at the site of the previous radio embolized mass, suggesting a complete response. At 16-month follow-up CT imaging, the patient showed progression of HCC in other parts of the liver. He underwent chemoembolization for the progressions in segments VIII and VII.

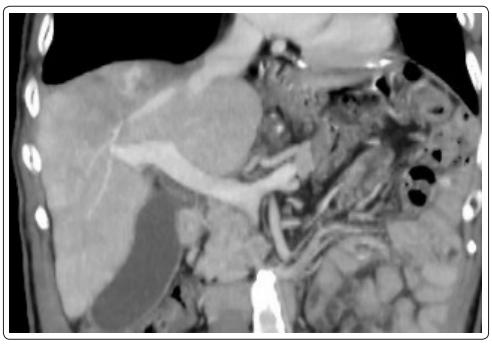

Figure 2: Contrast-enhanced axial CT images at 16 months post-90Y-TARE indicate complete mass retraction from the RA.

Discussion

HCC is a highly aggressive malignant hepatic tumor that progresses into the portal and hepatic veins, IVC, and RA in its advanced stages. HCC infiltration into the RA is rare and has a poor prognosis, with a median survival time of 2–5 months if untreated [10]. While there are several proposed treatment strategies for managing the progression of the TT into RA, there is no consensus as to which treatment method gives the best results. The current BCLC staging system suggests the administration of sorafenib as the standard of care for managing advanced HCC (BCLC-C stage) [11]. However, many other treatment strategies have been attempted with varying response efficiencies. These therapies include surgical treatments such as TT resection and non-surgical options such as external beam therapy, Transarterial Chemoembolization (TACE), and TARE [3].

Surgical resection has the most favorable treatment results due to the decreased risk of recurrence upon the successful and complete removal of the TT [6]. However, due to the risk of circulatory failure and the poor general status of patients with HCC RA TT, this approach is not compatible with all patients. Likewise, External beam radiation therapy is also not suitable for all patients due to the associated severe adverse effects and liver toxicity that may result from radiation doses exceeding 35 Gy [3,4,12].

Conventional TACE is the most commonly used locoregional treatment for the management of HCC and is the recommended standard therapy for intermediate-stage HCC [12]. However, TACE is generally contraindicated for cases of HCC with IVC and RA TT due to the high number of associated complications which include: high-risk ischemic hepatic necrosis, pulmonary embolization, and metastasis [10]. TARE, unlike TACE, is not an absolute contraindication for advanced-stage HCC and has demonstrated better outcomes in patients [4].

According to two meta-analyses by Yang & Si and Zhang et al., TARE compared to TACE gives better overall survival rates (OS) (median OS of 12 months compared to 9 months for TARE and TACE, respectively), and 3-year OS rates (20.3% compared to 9.7% for TARE and TACE, respectively) [13,14]. They also found TARE to be associated with longer time to tumor progression (TTP), significantly lower toxicity profile, and fewer adverse effects post-treatment. On the whole, 90Y -TARE treatment was favored in our case of advanced HCC for its promising efficiency.

The success and safety of radioembolization therapy are highly contingent upon appropriate radiation dose administration to the targeted hepatic tumor and its surrounding parenchyma. A key concern in radioembolization therapy for advanced-staged HCC is the possible radiation-induced pneumonitis ensued by the hepatopulmonary shunting and deposition of 90Y microspheres in the lungs [15]. Based on data from external beam radiation therapy studies, the maximum lung absorbed dose of 30 Gy per radioembolization is advised for the prevention of radiation-induced lung injury [16].

Our doses were well below this threshold, and measured 5 Gy on the post-TARE 90Y-PET/CT images. Furthermore, in an attempt to limit the radiation dose given to the diaphragm and surrounding parenchyma, dose administration was given into the rIPA, after microcatheter advancement beyond the posterior branch of the IPA. Although the administration of 90Y microspheres into the IPA is generally contraindicated due to the possible risks of extrahepatic shunting and nontarget radiation induced injury recent literature has showed the feasibility and safety of catheter-directed, dose administration through the rIPA under the guidance of CBCT and DSA imaging [17-20].

Even though it is customary to use 99m Tc-MAA imaging as a pre-planning step for TARE to reflect the extent of the hepatopulmonary shunting and safety of the treatment, we did not use it for expediency. Therefore, we have relied on DSA, multiphasic CT, and CBCT imaging to assess the extent of hepatopulmonary shunting. This method, in particular, was employed based on a recent study that indicated comparable detection efficiencies of hepatopulmonary shunting when 99m Tc-MAA imaging, DSA, and CBCT are used [21].

Post-imaging results confirmed the success of the procedure, which, in turn, indicates the appropriateness of our risk calculation decisions. The patient did not report any pulmonary complaints and did not show any signs of pneumonitis even after 6 months of treatment. One additional aspect that might have been advantageous in our case was the patient's continuous follow-up that allowed us to treat him without the TT infiltrating further into the heart. Since most patients with IVC and RA TT infiltration are asymptomatic and due to the highly aggressive nature of HCC, constant monitoring of patients is essential [22-24].

Conclusion

To conclude, the use of 90Y-TARE in cases with advanced-stage HCC extending to the RA is a safe and effective palliative treatment option. The risk of an increased hepatopulmonary shunting in advanced cases not lead to the automatic exclusion of TARE treatment. Instead, an analysis of risk versus benefit should be performed on a case-by-case basis for and a personalized interventional radiology approach and administered 90Y microspheres dose. The success of 90Y-TARE therapy case of advanced HCC is attributed to the constant follow-up and good pre-planning using the different interventional radiology modalities.

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Authors' Contributions:

The study was designed by Kabalane Yammine. Material preparation and data collection were performed by Sarah Khalife. The first draft of the manuscript was written by Sarah Khalife, Kabalane Yammine and Feras Chehade and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. D Gomez-Puerto, O Mirallas, J Vidal-González, V Vargas, (2020) Hepatocellular carcinoma with tumor thrombus extends to the right atrium and portal vein: A case report. World J Hepatol 12: 1128-1135.
2. W Li, Y Wang, W Gao, J Zheng (2017) HCC with tumor thrombus entering the right atrium and inferior vena cava treated by percutaneous ablation. BMC Surg 17: 21-21.
3. A Mavroudis, E Cholongitas (2020) Long-Term Survival under Arterial Chemoembolization and Sorafenib of a Patient with Hepatocellular Carcinoma and Tumor Atrial Thrombus: A Case Report and Literature Review. Gastrointest. Tumors 7: 156-162.
4. A Cappelli, C Pettinato, R Golfieri (2014) Transarterial radioembolization using yttrium-90 microspheres in the treatment of hepatocellular carcinoma: a review on clinical utility and developments. J. Hepatocell. Carcinoma 1: 163-182.

5. S B Edge, C C Compton (2010) The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 17: 1471-1474.
6. K Sakamoto, H Nagano (2018) Outcomes of surgery for hepatocellular carcinoma with tumor thrombus in the inferior vena cava or right atrium. Surg Today 48: 819-824.
7. S Mafeld, J French, D Tiniakos, B Haugk, D Manas, et al. (2018) Fibrolamellar Hepatocellular Carcinoma: Treatment with Yttrium-90 and Subsequent Surgical Resection. Cardiovasc. Intervent. Radiol 41: 816-820.
8. S Murata, Takahiko Mine, Fumie Sugihara, Daisuke Yasui, Hidenori Yamaguchi, et al. (2014) Interventional treatment for unresectable hepatocellular carcinoma. World J Gastroenterol 20: 13453-13465.
9. R Girardet, Sarah Boughdad, Antonia Digklia, Catherine Beigelman, Marie Meyer, et al. (2020) Transarterial Radioembolization for the Treatment of Advanced Hepatocellular Carcinoma Invading the Right Atrium. Cardiovasc. Intervent. Radiol 43: 1712-1715.
10. Y Xia, J Zhang, X Ni (2020) Diagnosis, treatment and prognosis of hepatocellular carcinoma with inferior vena cava/right atrium tumor thrombus (Review). Oncol Lett 20: 101.
11. L Cerrito, B E Annicchiarico, R Iezzi, A Gasbarrini, M Pompili, et al. (2019) Treatment of hepatocellular carcinoma in patients with portal vein tumor thrombosis: Beyond the known frontiers. World J Gastroenterol 25: 4360-4382.
12. H A Lee, C H Rim (2020) Efficacy of Local Treatments for Hepatocellular Carcinoma Involving the Inferior Vena Cava and/or Right Atrium. J Hepatocell. Carcinoma 7: 435-446.
13. Y Yang, T Si (2018) Yttrium-90 transarterial radioembolization versus conventional transarterial chemoembolization for patients with hepatocellular carcinoma: a systematic review and meta-analysis. Cancer Biol. Med 15: 299-310.
14. Z Zhang, Eric C H Lai, Chong Zhang, Hong-wei Yu, Zhuo Liu, et al. (2015) The strategies for treating primary hepatocellular carcinoma with portal vein tumor thrombus, Int J Surg 20: 8-16.
15. J D Allred, J Niedbala, J K Mikell, D Owen, K A Frey, et al. (2018) The value of (99m)Tc-MAA SPECT/CT for lung shunt estimation in (90)Y radioembolization: a phantom and patient study. EJNMMI Res 8: 50.
16. A Das, Ahsun Riaz, Ahmed Gabr, Rehan Ali, Ronald Mora, et al. (2020) Safety and efficacy of radioembolization with glass microspheres in hepatocellular carcinoma patients with elevated lung shunt fraction: analysis of a 103-patient cohort. Eur J Nucl Med Mol Imaging 47: 807-815.
17. M H K Abdelmaksoud, John D Louie, Nishita Kothary, Gloria L Hwang, William T Kuo, et al. (2011) Embolization of parasitized extrahepatic arteries to reestablish intrahepatic arterial supply to tumors before yttrium-90 radioembolization. J Vasc Interv Radiol JVIR 22: 1355-1362.
18. M C Burgmans, Yung Hsiang Kao, Farah Gillan Irani, Erin Leslee Dames, Terence Kiat Beng Teo, et al. (2012) Radioembolization with infusion of yttrium-90 microspheres into a right inferior phrenic artery with hepatic tumor supply is feasible and safe. J Vasc Interv Radiol JVIR 23: 1294-1301.
19. H C Kim, Y J Kim, J C Paeng, J W Chung (2018) Yttrium-90 Radioembolization of the Right Inferior Phrenic Artery in 20 Patients with Hepatocellular Carcinoma. J Vasc Interv Radiol JVIR 29: 556-563.
20. G Roche, T K B Teo, A E H Tan, F G Irani (2012) Intra-arterial CT angiography visualization of arterial supply to inferior vena cava tumor thrombus prior to radioembolization of hepatocellular carcinoma, Saudi J. Gastroenterol. Off J Saudi Gastroenterol. Assoc 18: 384:387.
21. V L Gates, K G Marshall, K Salzig, M Williams, R J Lewandowski, et al. (2014) Outpatient single-session yttrium-90 glass microsphere radioembolization. J Vasc Interv Radiol JVIR 25: 266-270.
22. H B Albackr (2014) A large Right atrial mass in a patient with hepatocellular carcinoma: Case report and literature review, J Saudi Heart Assoc 26: 174-178.
23. J Liu, Y Wang, D Zhang, B Liu, Q Ou (2012) Comparison of survival and quality of life of hepatectomy and thrombectomy using total hepatic vascular exclusion and chemotherapy alone in patients with hepatocellular carcinoma and tumor thrombi in the inferior vena cava and hepatic vein. Eur. J. Gastroenterol. Hepatol 24: 186-194.
24. T Sempokuya, D T Bolger Jr (2018) Right Atrium Invasion of Tumor Thrombus from Hepatocellular Carcinoma Incidentally Found on Transthoracic Echocardiogram. Hawaii J Med Public Health J Asia Pac Med Public Health 77: 131-134.