Journal of Hepatocellular Carcinoma

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

A Case of Microwave Ablation Activating Immune Response in Pulmonary Metastases from Hepatocellular Carcinoma

Juncheng Wan[1–4], Chaoqiao Jin[1–3], Changyu Li[1–3], Wei Zhang[1–3], Yongjie Zhou[1–3], Caihong Yu[1–3], Zhuoyang Fan[1–3], Xudong Qu[1–3]

[1]Department of Interventional Radiology, Zhongshan Hospital, Fudan University, Shanghai, People's Republic of China; [2]Shanghai Institute of Medical Imaging, Fudan University, Shanghai, People's Republic of China; [3]National Clinical Research Center of Interventional Medicine, Zhongshan Hospital, Fudan University, Shanghai, People's Republic of China; [4]Department of Radiology, Zhongshan Hospital, Fudan University, Shanghai, People's Republic of China

Correspondence: Xudong Qu, Department of Interventional Radiology, Zhongshan Hospital, Fudan University, Shanghai, 200032, People's Republic of China, Tel +86 13621858134, Email qu.xudong@zs-hospital.sh.cn

Abstract: Immune checkpoint inhibitors have significantly transformed the treatment of advanced solid tumors, revolutionizing the therapeutic landscape. However, drug resistance is a key clinical obstacle to the application of immune checkpoint inhibitors in patients. We describe a patient who developed pulmonary metastases from hepatocellular carcinoma 5 years after hepatectomy. After continuous targeted therapy and immunotherapy, the lesion still progressed slowly, but after ablation of one lesion, the other lesions were significantly reduced when immunotherapy was used again. This case might provide insight into to the current low response rate to immunotherapy, providing a new direction for further exploration.

Keywords: case report, immunotherapy, ablation, pulmonary metastases, hepatocellular carcinoma

Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide, with a relative 5-year survival rate of approximately 18%.[1] Immune checkpoint inhibitors (ICIs) have recently shown significant efficacy in the treatment of HCC, greatly improving patient survival rates and becoming a standard therapeutic approach.[2,3] Additionally, immunotherapy has become a critical treatment method for many other types of tumors. However, for patients with advanced tumors, particularly after first- and second-line treatments have failed, many drugs used subsequently often prove to be less effective. This limited efficacy leaves doctors and patients with few options, and they often resort to palliative care. Therefore, it is crucial to find new treatment options. This article reports a case in which a metastatic tumor's response to immunotherapy was suddenly enhanced following microwave ablation. This observation suggests that, in addition to developing new drugs, finding suitable synergistic treatment methods to enhance the efficacy of existing drugs is also of paramount importance.

Case

An adult patient who presented with symptoms of abdominal pain, abdominal distension, and elevated alpha-fetoprotein levels was diagnosed with massive hepatocarcinoma, with a tumor measuring 14×12 cm, which was confirmed by enhanced magnetic resonance imaging (MRI) on March 28, 2018. Four rounds of transcatheter arterial chemoembolization (TACE) were performed between April 2018 and July 2018 because the tumor was too large. Hepatectomy was subsequently performed in August 2018 (Figure 1), and postoperative pathologic examination revealed Grade III hepatocellular carcinoma. Three rounds of prophylactic TACE were performed after hepatectomy between October 2018 and July 2019. No recurrence has been reported in the liver thus far.

https://doi.org/10.2147/JHC.S532524
Received: 5 April 2025
Accepted: 15 January 2026
Published: 17 March 2026

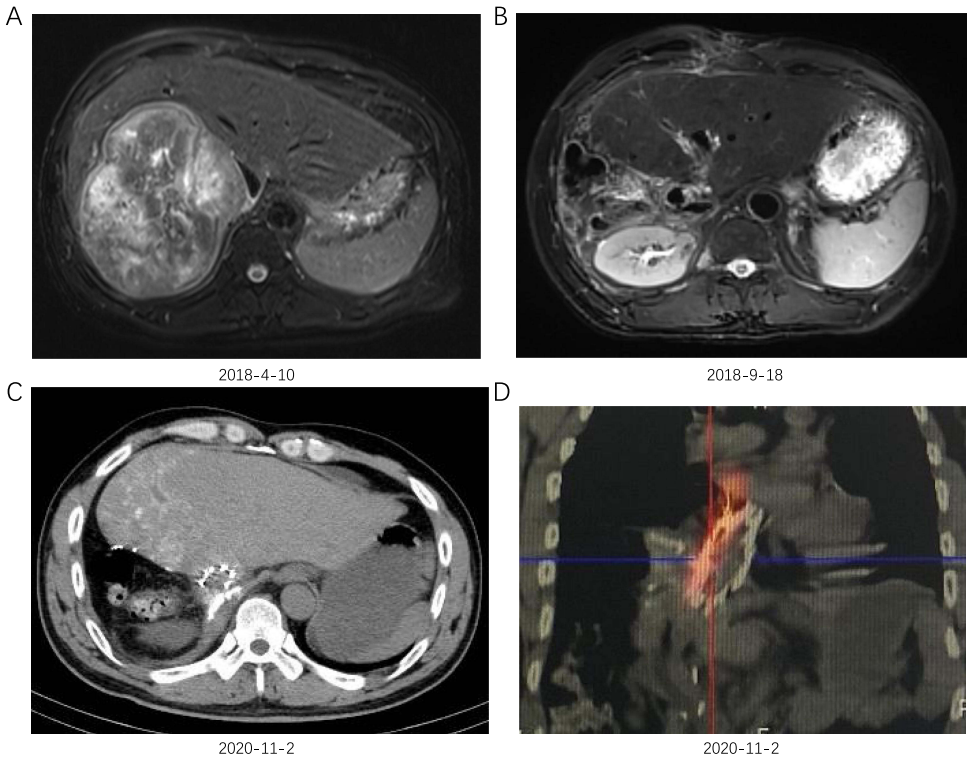

Figure 1 Changes in abdominal lesions. (**A**) Intrahepatic lesion after TACE. (**B**) Post-hepatectomy liver status. (**C**) Peritoneal metastasis after stent and iodine-125 particle implantation. (**D**) Radiation after iodine-125 particle implantation. Red and blue crosshairs indicate reference lines in the multiplanar reconstruction images; they mark the intersection of different planes to localize the iodine-125 particles. Different colors are used to distinguish the respective planes and improve visual clarity.

However, 2 years later, peritoneal metastasis was found in October 2020. The inferior vena cava was affected. Therefore, a stent and iodine-125 particles were implanted adjacent to the inferior vena cava (Figure 1), and three rounds of TACE were performed. Since then, the patient started targeted therapy (lenvatinib 8 mg orally every day). During the follow-up period, PET-CT revealed that the activity of the metastasis was reduced.

Regrettably, multiple pulmonary metastases have been identified in the patient since August 2022. Despite various treatments, including chemotherapy with oxaliplatin combined with 5-fluorouracil, a change in medication from lenvatinib (8 mg daily) to regorafenib (80 mg daily), and immunotherapy (tislelizumab 200 mg every three weeks), the pulmonary metastases continued to grow slowly. Owing to the lack of significant improvement, chemotherapy was discontinued, but the patient continued to use regorafenib and tislelizumab.

Under the guidance of cone beam computed tomography, the doctors performed a puncture and conducted microwave ablation on the largest lesion in the left lung (30 W for 2 minutes, 40 W for 2 minutes, and 60 W for 2 minutes) (Figure 2). During follow-up, the metastases were significantly reduced in size. Systemic therapy was not changed before or after ablation, and when immunotherapy was used again, the nonablated metastases in the lung shrank significantly. In the subsequent follow-up, regorafenib 80 mg every day and tislelizumab 200 mg every three weeks were maintained. There was no significant change in pulmonary metastases during the 1-year follow-up (Figures 3 and 4).

Given the dispersed nature of the patient's metastases, it is not sufficient to evaluate the changes only via images. Hence, we employed volume measurement software (uAI-ChestCare R001) to assess the ten largest lesions in both lungs, offering a more nuanced view of the volumetric changes before and after ablation (Figure 5).

Unfortunately, owing to the rarity of this phenomenon and the patient's financial considerations, tumor immunity-related blood markers were not part of our routine follow-up. As a result, we were unable to test these markers in a timely manner when the phenomenon occurred, preventing us from exploring the relationship between this rare event and the patient's tumor immunity-related markers.

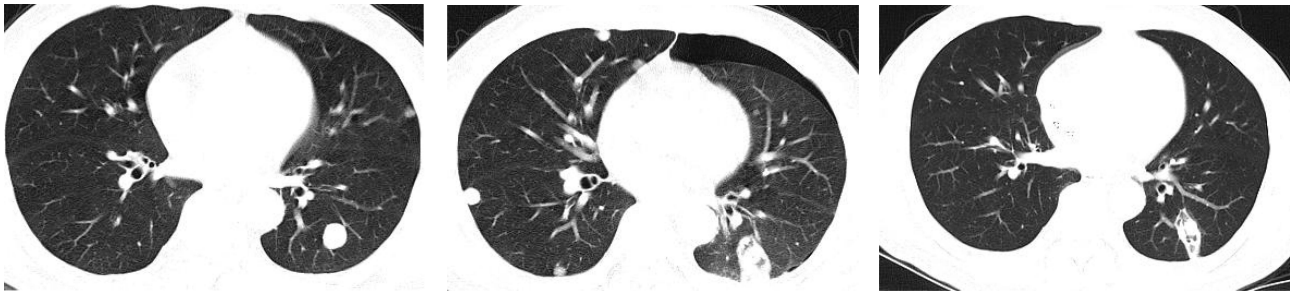

Figure 2 Lesions before and after ablation.

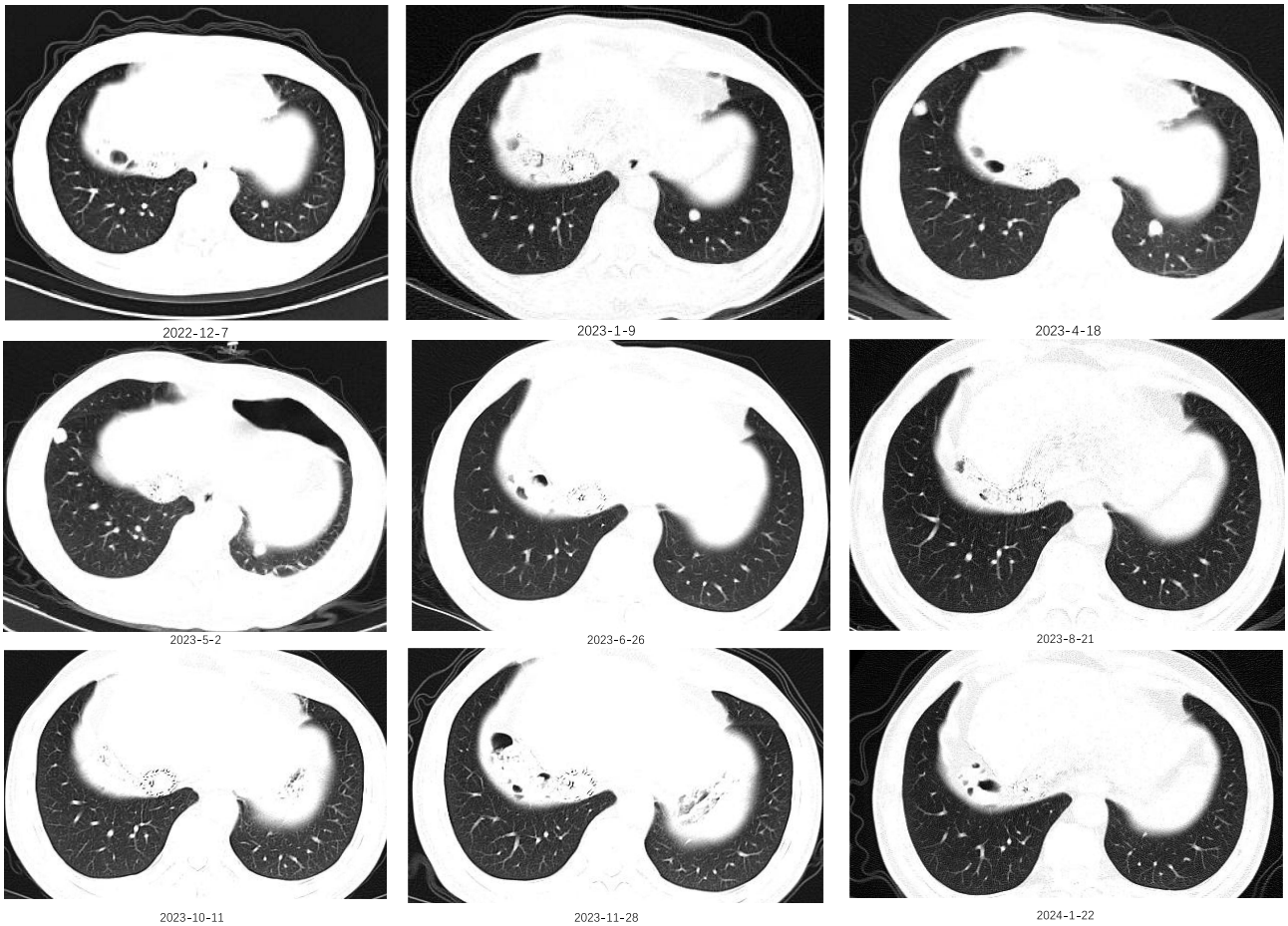

Figure 3 Changes in nonablated lesions.

While previous studies have documented the abscopal effect, our observations suggest a complex interplay beyond conventional understanding. Our main consideration is that the metastases still showed progression at 2 weeks after ablation, at which time the patient had not begun to receive immunotherapy after ablation. After the application of immunotherapy, the metastases began to shrink. This is a rarely reported phenomenon: when targeted therapy and immunotherapy remain unchanged, the response of other metastases to immunotherapy is suddenly activated after topical therapy.

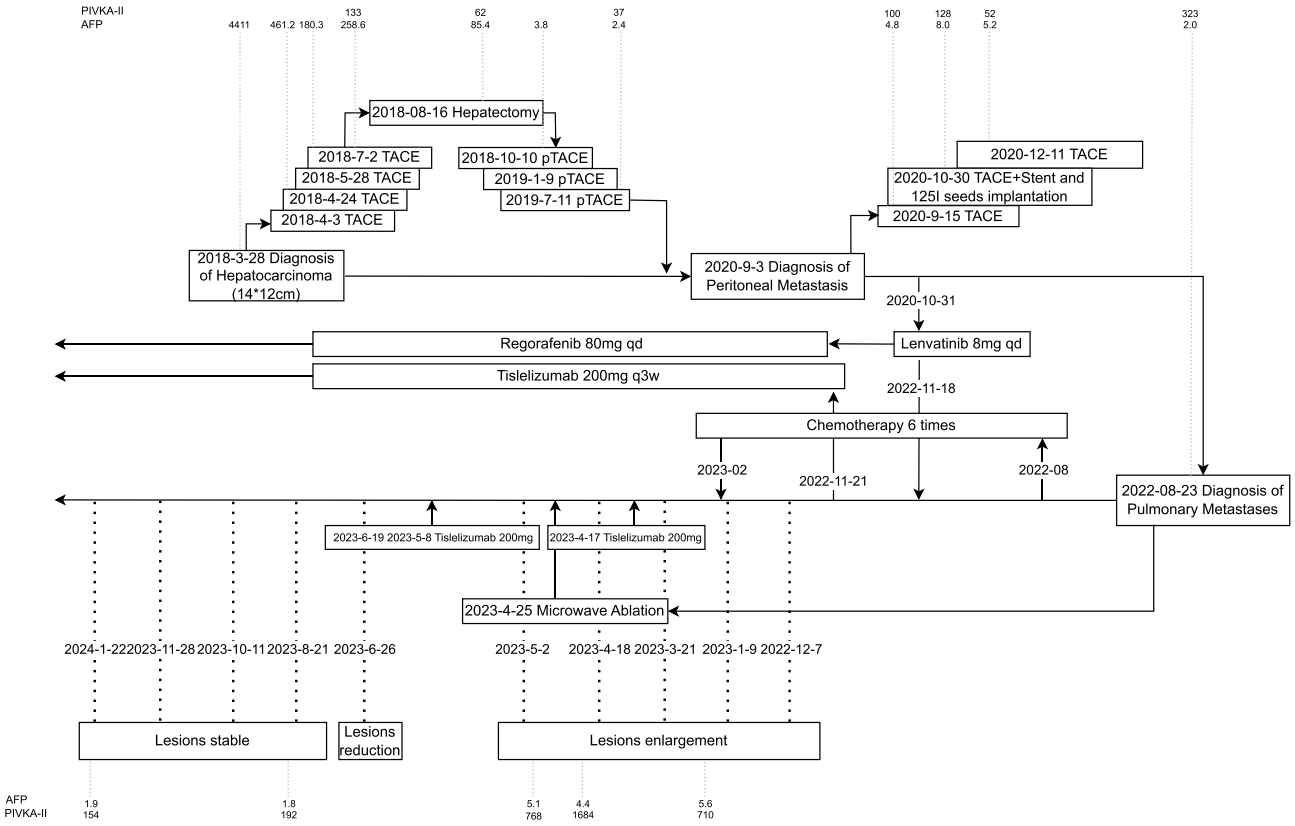

Figure 4 Course of treatment and changes in pulmonary metastases.
Abbreviations: TACE, Transarterial Chemoembolization; pTACE, Prophylactic Transarterial Chemoembolization; AFP, Alpha-Fetoprotein; PIVKA-II, Protein Induced by Vitamin K Absence or Antagonist-II.

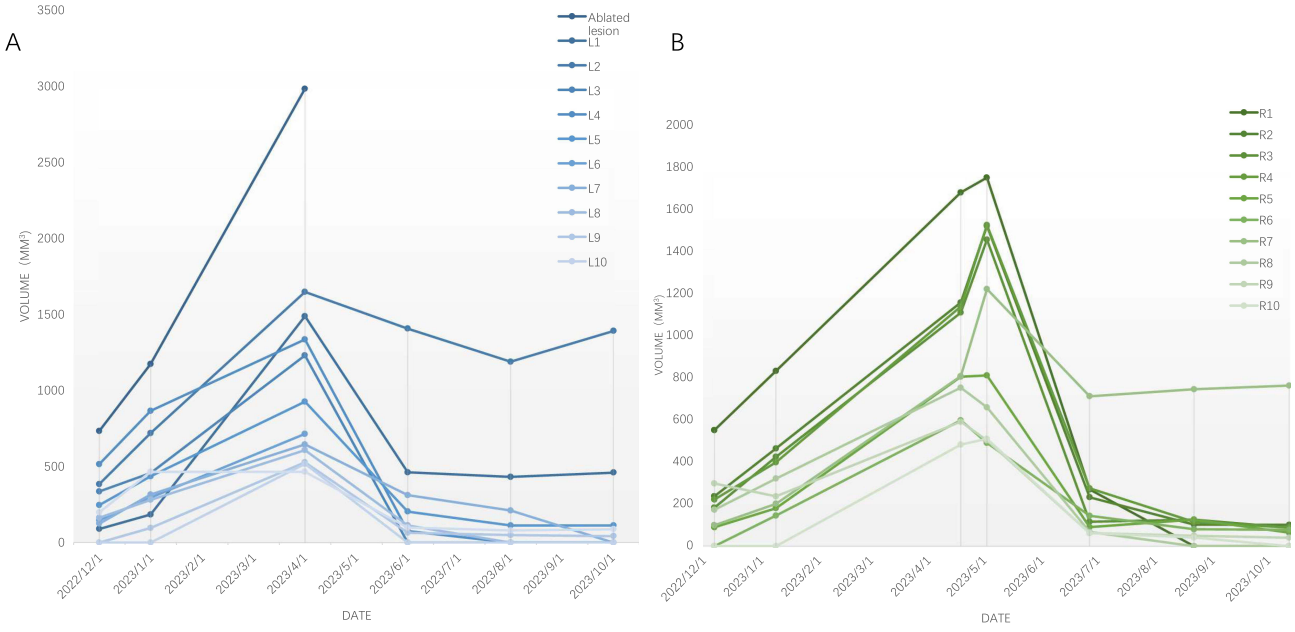

Figure 5 Volumes of lesions before and after ablation. (**A**) The 10 largest measurable lesions in the left lung. We did not calculate the volume of the left lung lesions scanned on 2023-5-2 because there was pneumothorax on the left side after ablation. (L6 could not be measured after ablation because it was too close to the ablated lesion) (**B**) The 10 largest measurable lesions in the right lung.

https://doi.org/10.2147/JHC.S532524

Discussion

Mole[4] proposed the concept of the abscopal effect over 70 years ago. The abscopal effect resulting from ablation[5] was introduced in 1970 for the treatment of prostate tumors. This effect is rare because established immune tolerance mechanisms during treatment may hinder the development of a sufficiently strong abscopal response. In recent years, many studies have reported the occurrence of the abscopal effect in radiotherapy,[6,7] cryoablation,[5,8] radiofrequency ablation,[9,10] and microwave ablation.[11] Several researchers have also experimentally demonstrated the mechanisms underlying the abscopal effect, suggesting that it is related to the immune system.[12,13] With the rise of immunotherapy,[14–18] numerous studies have shown that the abscopal effect seems to have a synergistic relationship with immunotherapy.[19–21] Our observations and proposed mechanisms align with the abscopal effect. However, in our case the nonablated tumors did not spontaneously shrink shortly after ablation. Shrinkage occurred only when ICIs were administered; therefore it could not be attributed to the abscopal effect. Thus, we classified it as "the response to immunotherapy activated by microwave ablation."

Many previous articles[22–25] have explained the principles of ablation-activated immunotherapy from different perspectives, providing a theoretical foundation for the synergistic effects of ablation and immunotherapy. Many animal experiments have also demonstrated ablation-activated immunotherapy.[26,27] Concurrently, numerous clinical studies are underway.[23] However, upon reviewing the literature, we found that most reports show therapeutic effects of combined ablation and immunotherapy on the basis of hematological changes,[28] animal experiments, or patient survival.[29–31] There has never been a case report as clear as ours that directly and distinctly demonstrates this phenomenon. Our case provides a more intuitive and clearer clinical basis for this viewpoint than previous studies do. For patients who do not respond or respond poorly to ICIs, this case clearly demonstrates an approach to enhancing treatment efficacy. Additionally, because immunotherapy was administered at least 13 days after ablation in this patient, we observed that the stimulatory components produced by the tumor after ablation seemed to persist for a long period of time. This challenges our previous understanding, as few studies have investigated the appropriate timing for immunotherapy following ablation. However, Den[32] demonstrated an increase in tumor-specific T cells 10 days after both cryotherapy and radiofrequency/ablation combination treatment by identifying OVA kb tetramer-positive CD8b + T cells. Therefore, we are considering whether the optimal timing for immunotherapy after ablation might be a factor influencing the efficacy of immunotherapy. Additionally, some articles[33] suggest that a high tumor burden has a negative effect on anticancer immunity. Therefore, we believe that the relatively low overall tumor burden in this patient might also be a contributing factor to this phenomenon.

Owing to the effective control of the patient's primary lesion, the impact of this immunotherapy after ablation on other lesions was not observed. Many studies[34–40] have demonstrated the heterogeneity of metastatic tumors compared with that of primary tumors. Research[34] suggests that metastatic tumors can acquire new (epi)genetic mutations, preventing T-cell recognition and potentially altering the immune response to metastatic lesions. Additionally, some studies[38,39] have shown that radiotherapy of metastatic organs can enhance their antitumor effects. Although we initially considered whether this phenomenon might be related to ablation altering the acquired resistance of metastatic tumors, previous clinical studies have shown that the response rate of lung metastases of patients with primary liver cancer to ICIs is greater than that of intrahepatic lesions.[41–43] Therefore, we have temporarily abandoned this hypothesis.

In recent years, the emergence of immunotherapy has greatly prolonged the survival of many patients, but the response to immunotherapy often varies greatly from individual to individual. For some patients with distant organ metastases, systemic therapies are not effective enough to inhibit tumor progression, as topical therapy cannot be performed. Our findings suggest that microwave ablation may serve as a potent catalyst for immunotherapy. Although numerous studies have suggested the synergistic potential of ablation with immunotherapy, direct clinical evidence remains scarce. This case not only sheds light on this synergy but also underscores the need for comprehensive studies to explore the underlying mechanisms and broader applicability of this approach. We hope that our findings will inspire further research, potentially leading to more effective treatment strategies for patients with cancer. We will also conduct further review and research on past cases of lung metastases treated with ablation to identify additional cases of this rare phenomenon in our existing database.

Conclusion

This case highlights a rare phenomenon in which microwave ablation appeared to enhance the efficacy of immunotherapy, despite no changes in systemic treatment. Unlike the classical abscopal effect, the response was only observed after immunotherapy resumed, suggesting a distinct mechanism of ablation-activated immune re-sensitization. These findings underscore the potential of combining local and systemic therapies to overcome resistance and warrant further investigation into optimal treatment strategies.

Ethics Statement

Details of the case reported in the article were approved by the Ethics Committee of Zhongshan Hospital, Fudan University, Shanghai, China (Approval No. B2025-018).

Consent for Publication

Written informed consent was obtained from the patient for the publication of all the data and images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was funded by the Shanghai Innovative Pharmaceutical and Medical Device Product Application Demonstration Project (24SF1905500, 25SF1908600), Shanghai Innovation Medical Device Application Demonstration Project (23SHS03900-09) and National Key R&D Program (2023YFC2411404).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Vogel A, Meyer T, Sapisochin G, Salem R, Saborowski A. Hepatocellular carcinoma. *The Lancet*. 2022;S0140673622012004.
2. Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. *J Hepatol*. 2022;76(3):681–693. doi:10.1016/j.jhep.2021.11.018
3. Zhou J, Sun H, Wang Z, et al. Guidelines for the diagnosis and treatment of primary liver cancer (2022 edition). *Liver Cancer*. 2023;12(5):405–444. doi:10.1159/000530495
4. Mole RH. Whole body irradiation; radiobiology or medicine? *Br J Radiol*. 1953;26(305):234–241. doi:10.1259/0007-1285-26-305-234
5. Soanes WA, Ablin RJ, Gonder MJ. Remission of metastatic lesions following cryosurgery in prostatic cancer: immunologic considerations. *J Urol*. 1970;104(1):154–159. doi:10.1016/S0022-5347(17)61690-2
6. Powerski M, Drewes R, Omari J, Relja B, Surov A, Pech M. Intra-hepatic abscopal effect following radioembolization of hepatic metastases. *Cardiovasc Intervent Radiol*. 2020;43(11):1641–1649. doi:10.1007/s00270-020-02612-4
7. Yano R, Hirooka M, Morita M, et al. Hepatocellular carcinoma showing tumor shrinkage due to an abscopal effect. *Intern Med*. 2024;63(2):241–246. doi:10.2169/internalmedicine.1844-23
8. Kaplan JL, Turker I, Chumsri S, Gabriel E. Abscopal effect following cryoablation in a patient with metastatic breast cancer. *Front Biosci*. 2023;15(1):2. doi:10.31083/j.fbs1501002
9. Sánchez-Ortiz RF, Tannir N, Ahrar K, Wood CG. Spontaneous regression of pulmonary metastases from renal cell carcinoma after radio frequency ablation of primary tumor: an in situ tumor vaccine? *J Urol*. 2003;170(1):178–179. doi:10.1097/01.ju.0000070823.38336.7b
10. Kim H, Park BK, Kim CK. Spontaneous regression of pulmonary and adrenal metastases following percutaneous radiofrequency ablation of a recurrent renal cell carcinoma. *Korean J Radiol*. 2008;9(5):470–472. doi:10.3348/kjr.2008.9.5.470
11. Xu H, Sun W, Kong Y, et al. Immune abscopal effect of microwave ablation for lung metastases of endometrial carcinoma. *J Cancer Res Ther*. 2020;16(7):1718–1721. doi:10.4103/jcrt.JCRT_1399_20
12. Mehta A, Oklu R, Sheth RA. Thermal ablative therapies and immune checkpoint modulation: can locoregional approaches effect a systemic response? *Gastroent Res Pract*. 2016;2016:9251375. doi:10.1155/2016/9251375
13. Leuchte K, Staib E, Thelen M, et al. Microwave ablation enhances tumor-specific immune response in patients with hepatocellular carcinoma. *Cancer Immunol Immunother*. 2021;70(4):893–907. doi:10.1007/s00262-020-02734-1

14. Guven DC, Erul E, Kaygusuz Y, et al. Immune checkpoint inhibitor-related hearing loss: a systematic review and analysis of individual patient data. *Support Care Cancer*. 2023;31(12):624. doi:10.1007/s00520-023-08083-w
15. Guven DC, Sahin TK, Erul E, et al. The association between albumin levels and survival in patients treated with immune checkpoint inhibitors: a systematic review and meta-analysis. *Front Mol Biosci*. 2022;9:1039121. doi:10.3389/fmolb.2022.1039121
16. Sahin TK, Ayasun R, Rizzo A, Guven DC. Prognostic value of neutrophil-to-eosinophil ratio (NER) in cancer: a systematic review and meta-analysis. *Cancers (Basel)*. 2024;16(21):3689. doi:10.3390/cancers16213689
17. Sahin TK, Rizzo A, Aksoy S, Guven DC. Prognostic significance of the royal marsden hospital (RMH) score in patients with cancer: a systematic review and meta-analysis. *Cancers (Basel)*. 2024;16(10):1835. doi:10.3390/cancers16101835
18. Vitale E, Rizzo A, Maistrello L, et al. Sex differences in adverse events among cancer patients receiving immune checkpoint inhibitors: the MOUSEION-07 systematic review and meta-analysis. *Sci Rep*. 2024;14(1):28309. doi:10.1038/s41598-024-71746-z
19. Lucas AP, Lewis AR, Kasi PM, Toskich BB, Paz-Fumagalli R. Abscopal downstaging of intermediate stage hepatocellular via combination cryoablation and immunotherapy with complete pathologic response. *Radiol Case Rep*. 2024;19(3):910–914. doi:10.1016/j.radcr.2023.11.062
20. Yang X, Gao M, Xu R, et al. Hyperthermia combined with immune checkpoint inhibitor therapy in the treatment of primary and metastatic tumors. *Front Immunol*. 2022;13:969447. doi:10.3389/fimmu.2022.969447
21. Nelson BE, Adashek JJ, Lin SH, Subbiah V. The abscopal effect in patients with cancer receiving immunotherapy. *Med*. 2023;4(4):233–244. doi:10.1016/j.medj.2023.02.003
22. Slovak R, Ludwig JM, Gettinger SN, Herbst RS, Kim HS. Immuno-thermal ablations – boosting the anticancer immune response. *J Immunother Cancer*. 2017;5:78. doi:10.1186/s40425-017-0284-8
23. Kim NJ, Yoon JH, Tuomi AC, Lee J, Kim D. In-situ tumor vaccination by percutaneous ablative therapy and its synergy with immunotherapeutics: an update on combination therapy. *Front Immunol*. 2023;14:1118845. doi:10.3389/fimmu.2023.1118845
24. Galati F, Marra A, Cicciarelli F, et al. Cryoablation for the treatment of breast cancer: immunological implications and future perspectives. Utopia or reality? *Radiol Med*. 2024;129(2):222–228. doi:10.1007/s11547-024-01769-z
25. Adnan A, Muñoz NM, Prakash P, Habibollahi P, Cressman ENK, Sheth RA. Hyperthermia and tumor immunity. *Cancers*. 2021;13(11):2507. doi:10.3390/cancers13112507
26. Guo RQ, Peng JZ, Li YM, Li XG. Microwave ablation combined with anti-PD-1/CTLA-4 therapy induces an antitumor immune response to renal cell carcinoma in a murine model. *Cell Cycle*. 2023;22(2):242–254. doi:10.1080/15384101.2022.2112007
27. Mandt T, Bangar A, Sauceda C, et al. Stimulating antitumoral immunity by percutaneous cryoablation and combination immunoadjuvant therapy in a murine model of hepatocellular carcinoma. *J Vasc Interv Radiol*. 2023;34(9):1516–1527.e6. doi:10.1016/j.jvir.2023.05.008
28. Machlenkin A, Goldberger O, Tirosh B, et al. Combined dendritic cell cryotherapy of tumor induces systemic antimetastatic immunity. *Clin Cancer Res*. 2005;11(13):4955–4961. doi:10.1158/1078-0432.CCR-04-2422
29. Xie C, Duffy AG, Mabry-Hrones D, et al. Tremelimumab in combination with microwave ablation in patients with refractory biliary tract cancer. *Hepatology*. 2019;69(5):2048–2060. doi:10.1002/hep.30482
30. Duffy AG, Ulahannan SV, Makorova-Rusher O, et al. Tremelimumab in combination with ablation in patients with advanced hepatocellular carcinoma. *J Hepatol*. 2017;66(3):545–551. doi:10.1016/j.jhep.2016.10.029
31. Wang X, Liu G, Chen S, et al. Combination therapy with PD-1 blockade and radiofrequency ablation for recurrent hepatocellular carcinoma: a propensity score matching analysis. *Int J Hyperthermia*. 2021;38(1):1519–1528. doi:10.1080/02656736.2021.1991011
32. den BMHMGM, Sutmuller RPM, Nierkens S, et al. Efficient loading of dendritic cells following cryo and radiofrequency ablation in combination with immune modulation induces anti-tumour immunity. *British Journal of Cancer*. 2006;95(7):896. doi:10.1038/sj.bjc.6603341
33. Fg D, M A, C C, et al. Tumour burden and efficacy of immune-checkpoint inhibitors. *Nature Reviews Clinical Oncology*. 2022;19(2).
34. Edwards SC, Hoevenaar WHM, Coffelt SB. Emerging immunotherapies for metastasis. *Brit J Cancer*. 2021;124(1):37–48. doi:10.1038/s41416-020-01160-5
35. Jiao S, Subudhi SK, Aparicio A, et al. Differences in tumor microenvironment dictate T helper lineage polarization and response to immune checkpoint therapy. *Cell*. 2019;179(5):1177–1190.e13. doi:10.1016/j.cell.2019.10.029
36. Sun L, Kienzler JC, Reynoso JG, et al. Immune checkpoint blockade induces distinct alterations in the microenvironments of primary and metastatic brain tumors. *J Clin Invest*. 2023;133(17):e169314. doi:10.1172/JCI169314
37. Deng JY, Gou Q, Yang L, et al. Immune suppressive microenvironment in liver metastases contributes to organ-specific response of immunotherapy in advanced non-small cell lung cancer. *J Immunother Cancer*. 2023;11(7):e007218. doi:10.1136/jitc-2023-007218
38. Yu J, Green MD, Li S, et al. Liver metastasis restrains immunotherapy efficacy via macrophage-mediated T cell elimination. *Nat Med*. 2021;27(1):152–164. doi:10.1038/s41591-020-1131-x
39. Gide TN, Wilmott JS, Scolyer RA, Long GV. Primary and acquired resistance to immune checkpoint inhibitors in metastatic melanoma. *Clin Cancer Res*. 2018;24(6):1260–1270. doi:10.1158/1078-0432.CCR-17-2267
40. Conway JW, Braden J, Wilmott JS, Scolyer RA, Long GV, Pires da Silva I. The effect of organ-specific tumor microenvironments on response patterns to immunotherapy. *Front Immunol*. 2022;13:1030147. doi:10.3389/fimmu.2022.1030147
41. Lu LC, Hsu C, Shao YY, et al. Differential organ-specific tumor response to immune checkpoint inhibitors in hepatocellular carcinoma. *Liver Cancer*. 2019;8(6):480–490. doi:10.1159/000501275
42. Huang C, Zhu XD, Shen YH, et al. Organ specific responses to first-line lenvatinib plus anti-PD-1 antibodies in patients with unresectable hepatocellular carcinoma: a retrospective analysis. *Biomark Res*. 2021;9(1):19. doi:10.1186/s40364-021-00274-z
43. Kim HD, Park YG, Kim S, et al. Organ-specific response with first-line atezolizumab-bevacizumab versus lenvatinib for patients with advanced hepatocellular carcinoma. *Hepatol Int*. 2024;18(3):973–983. doi:10.1007/s12072-023-10626-6