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A Case of Target Immunotherapy Combined with Interventional Therapy for Massive Liver Cancer

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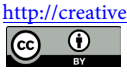

Abstract

This article reports a case of massive hepatocellular carcinoma. After intervention combined with targeted and immunotherapy, it was successfully cured by surgical resection, which provides some experience for the comprehensive treatment of liver cancer, and also improves the understanding of systematic treatment of liver cancer, so as to improve the understanding and diagnosis of the disease.

Keywords

Hepatocellular Carcinoma, Targeted Therapy, Immunotherapy, Interventional Therapy

1. Introduction

Hepatocellular carcinoma (HCC) is a type of primary liver cancer, accounting for 75% - 85% of the classification of primary liver cancer. Its incidence rate ranks third in malignant tumors and second in mortality in China [1]. Liver cancer has a high mortality and recurrence rate, and a single treatment method is no longer applicable; Early diagnosis and early treatment is the main aspect to improve the 5-year survival rate of liver cancer. For advanced liver cancer, comprehensive treatment under the guidance of multidisciplinary treatment mode is the first choice. We report a case of massive hepatocellular carcinoma (HCC). After intervention combined with targeted and immunotherapy, it was successfully cured by surgical resection, providing some experience for comprehensive treatment of liver cancer, and also improving the understanding of systematic treatment of liver cancer. Informed consent was obtained from the patient himself and his family for this study.

2. Case Presentation

A 55-year-old male patient was admitted to the hospital on March 14, 2021 due to "right upper abdominal pain for one week". One week ago, the patient had no obvious inducement to develop right upper abdominal pain, which was persistent distension and pain. Later, he went to other hospitals to see a doctor. The abdominal ultrasound examination showed that there was a single mass in the right lobe of the liver, with a size of 12 cm × 8 cm, only symptomatic treatment for pain relief was accepted in this hospital. He had a history of hepatitis B virus for more than 30 years and did not receive antiviral treatment. Have a history of smoking and drinking for more than 40 years, and have not quit smoking and drinking. The mother died of ascites due to cirrhosis, details unknown; the father died of lung disease, details unknown. Physical examination on admission: there is no yellow stain on the skin and mucous membrane of the whole body, and the superficial lymph nodes are not swollen. The abdomen is flat and soft, no gastrointestinal type and gastrointestinal peristalsis wave are found, 3 cm below the liver rib is accessible, the spleen is not large, and it is not accessible under the rib. No tenderness, rebound pain and percussion pain were found in the whole abdomen. The mobility dullness is negative, and the bowel sounds are 5 times/minute. Laboratory examination: blood routine examination, liver and kidney function, and blood coagulation function are all within normal range. Leucocyte count: 5.87×10^9/L. Platelet count: 164×10^9/L. Alanine transaminase: 45 U/L. Asparchyl aminotransferase: 35 U/L. Creatinine: 60 μmoI/L. Prothrombin time: 11.8 s. Child Pugh grading of liver function: 5 points, A level. Hepatitis B surface antigen, hepatitis B E antibody and hepatitis B core antibody are all positive. hepatitis B virus DNA quantitative: 2.39×10^4 IU/mL. Tumor markers: alpha fetoprotein 7.9 ng/mL, abnormal prothrombin 66,887.00 mAU/mL. Imaging data at the first admission: CT enhancement of the upper abdomen suggested that the right lobe of the liver was huge, considering malignant tumor, and the possibility of hepatocellular carcinoma was high (**Figure 1**). The enhanced MR imaging of the upper abdomen showed that the right lobe of the liver had a huge blood-rich lesion with slight bleeding. The malignant tumor lesion (liver cancer) was considered, involving the right posterior branch of the portal vein and forming a tumor thrombus in the right posterior inferior vein of the liver (**Figure 2**).

After the Multi-disciplinary Treatment (MDT) of liver cancer in our hospital, considering that the diagnosis of massive liver cancer in patients is clear, considering that the tumor is huge, its portal vein branch and right hepatic vein have tumor thrombus invasion, it is suggested that hepatic artery embolization combined with targeted and immunotherapy should be the first choice; For hepatitis B, use propofol tenofovir 25 mg once a day.

After the first admission to the hospital, the first transarterial chemoembolization (TACE) was performed on March 18, 2021. During the operation, large tumor staining was seen in the right lobe of the liver (**Figure 3**). During the operation,

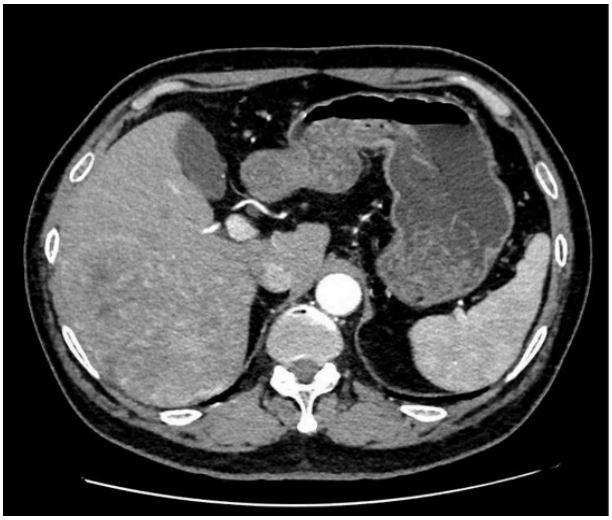

Figure 1. First admission to CT: The tumor was significantly enhanced in the right hepatic lobe artery stage.

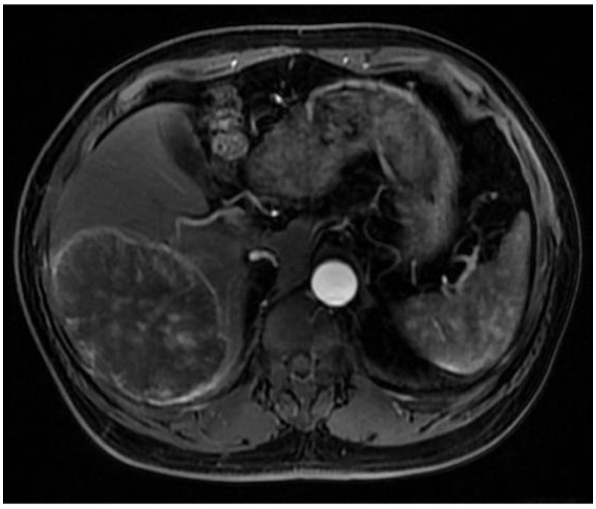

Figure 2. First admission to MR: The arterial stage tumor was significantly enhanced with involvement of the right branch of the portal vein and the hepatic vein.

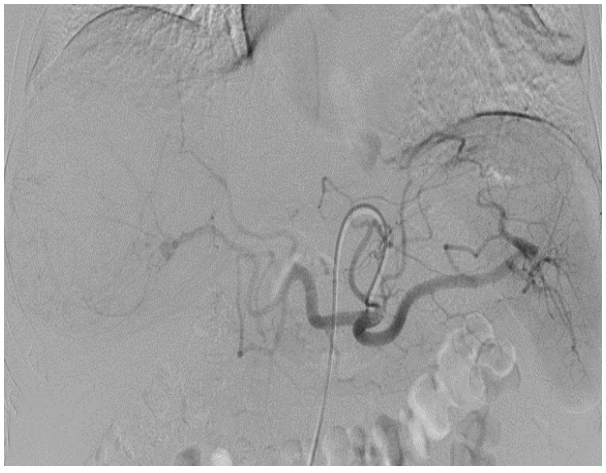

Figure 3. The first TACE showed that tumor was supplied by the right hepatic artery.

a drug-loaded microsphere + pirarubicin 50 mg and iodol 12 mL were used to embolize the right hepatic artery branch. After the embolization, the tumor staining was reduced.

On April 20, 2021, he was admitted to the hospital for the second time. The modified response evaluation criteria in solid tumor (mRECIST) were used to evaluate partial remission. On April 23, 2021, he underwent the second hepatic arterial chemoembolization. In addition to the right hepatic artery branch, two branches of the right phrenic artery were seen to have intrahepatic tumor blood supply (**Figure 4**). During the operation, 1 drug-loaded microsphere + 50 mg of pirarubicin and 20 mL of lipiodol were used for embolization respectively.

On May 26, 2021, he was admitted for the third time and evaluated as partial remission with mRECIST. On May 31, 2021, he underwent the third transcatheter hepatic arterial chemoembolization. During the operation, it was found that the tumor blood supply artery originated from the right hepatic artery, the right phrenic artery, and the branches of the right intercostal artery. During the operation, 1 bottle of embolic pellets + 50 mg of pirarubicin and 20 mL of lipiodol were used for embolization respectively. After discharge from the hospital this time, the targeted treatment of Remvastinib Mesylate (Leweima) was 12 mg, once a day, and the immunotherapy of Karelizumab (Ereka) was 200 mg, once a week.

On June 27, 2021, for the fourth time, the enhancement of upper abdominal MRI showed that the enhancement of cancer focus had been significantly reduced and the size of the focus had been reduced. From August 2021 to February 2022, there were four regular reexaminations, and the upper abdominal MRI was enhanced. No enhancement was found in the cancer focus, and no new cancer focus was found (**Figure 5**). The tumor indicators were reduced to the normal range. The improved solid tumor evaluation standard was evaluated as complete remission.

In April 2022, the patient again accepted MDT discussion. Considering that the tumor was inactive and the tumor was smaller than that at the initial diagnosis,

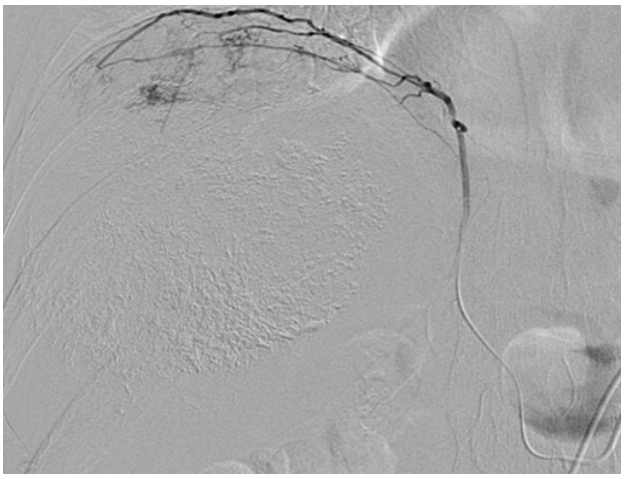

Figure 4. The second TACE showed that tumor was supplied by the phrenic artery.

surgical resection was feasible. On May 7, 2022, laparoscopic liver lesion resection + laparoscopic cholecystectomy was performed. During the operation, S6 and S7 segments of the right lobe of the liver were seen, with a size of about 10 cm. The tumor protruded from the surface of the liver, with unclear boundary and soft texture. Postoperative pathology: the focus was extensively necrotic, accompanied by fibrous tissue hyperplasia, collagenization and foam like cell aggregation, and no clear tumor tissue was found (Figure 6). The patient underwent three times of transcatheter hepatic artery embolization, during which he regularly took anti hepatitis B virus drugs, targeted drugs, lenvartinib, and immune drug, karelizumab. The tumor was completely necrotic, which was evaluated as CR according to mRECIST patients.

3. Discussion

Most primary liver cancer is occult. Most Chinese patients with liver cancer have

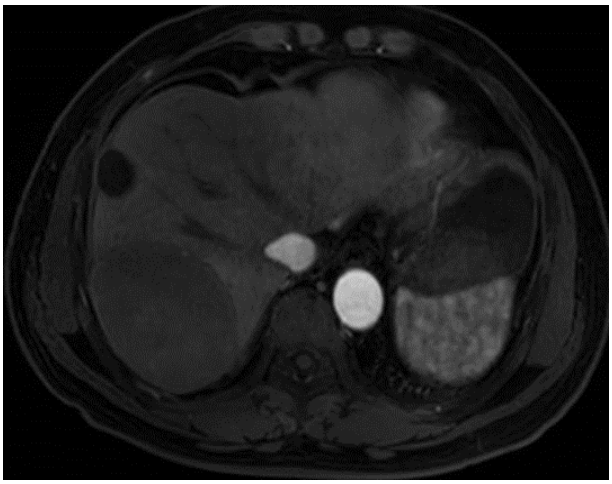

Figure 5. MR before surgery: The tumor was completely necrotic and was no enhancement in the arterial phase.

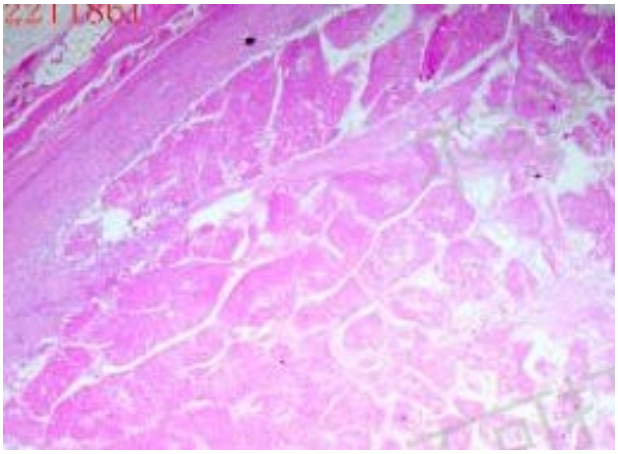

Figure 6. Pathology after resection: The lesion showed extensive necrosis, with fibrotissue hyperplasia, collagenization and foam-like tissue cell aggregation, no clear tumor tissue, met the change after embolization.

the background of liver cirrhosis caused by hepatitis. When the diagnosis is found, most of them are already advanced liver cancer. For a single surgical resection, the liver tolerance is insufficient, the recurrence rate is high, and the treatment effect is not ideal [2]. This patient is middle and late stage liver cancer. After comprehensive anti-tumor treatment, the tumor in the liver was completely necrotic, the tumor indicators returned to normal, and finally reached the tumor descending stage. There is a chance to further carry out radical surgical resection to achieve clinical cure.

In this case, the experience summarized by the author mainly includes two points. The first is the importance of MDT treatment mode for middle and late stage liver cancer. The main discussion points of MDT for liver cancer include but are not limited to the diagnosis and staging of tumor, the first choice of treatment, the comprehensive treatment of middle and late stage liver cancer, the replacement of follow-up plan for tumor progression, whether the tumor can be degraded into treatment, and the supportive treatment of end-stage liver disease; We discussed MDT after the first diagnosis of the patient and the reduction of the tumor, so as to control the treatment means and timing of the patient. Second, hepatic artery chemoembolization is still an important treatment method for advanced liver cancer at present [3] [4]. According to the study, TACE mainly induced microbial-related molecular patterns (Microbe-associated molecular patterns, MAMPs), damage-related molecular patterns (damage-associated molecules, DAMPs), and tumor-associated antigen (tumor-associated antigen, TAA), which thus affected the anti-tumor effect of CD8 T cells [5]. Each operation requires the operator to comprehensively evaluate the blood supply vessels of the tumor, not only satisfy the angiography and embolization of the hepatic artery. The patient needed multiple embolization due to the huge tumor during the first TACE operation; in the follow-up TACE operation, the tumor blood supply artery was re-evaluated, and the septal artery and intercostal artery were also involved in blood supply. At the same time, regular medical examination and timely detection of recurrent and surviving lesions are also the key to the whole standardized treatment of liver cancer [6]. This patient complied with the doctor's advice, reviewed the tumor indicators and abdominal MR regularly, and adjusted the treatment plan in time. Finally, this patient with massive middle and late stage liver cancer was clinically cured, and we will continue to follow up the patient's condition.

Finally, the occurrence of liver cancer has been proven to be a malignant tumor caused by the imbalance of the immune environment of the body. For its treatment, it has entered the targeted combined immune drugs or even "double immune" drug treatment [7]. The result of good prognosis of this case also lies in the fact that the patient regularly takes the targeted combination of ranvastinib mesylate and karelizumab. As a multi-target tyrosine kinase inhibitor (TKI), ranvastinib can inhibit the signal pathways such as VEGF and FGF in the metabolism of tumor cells, thus showing a strong anti-tumor angiogenesis effect [8], Karelizumab is a humanized anti-programmed death protein 1 (PD1) monoc-

lonal antibody, which can block the combination of PD1 and PD-L1, restore the activity of $CD8^+$ T cells and $CD4^+$ T cells, enhance the immune response, and achieve the anti-tumor effect [9].

4. Conclusion

The treatment concept of liver cancer has moved from simple surgical resection to multidisciplinary comprehensive treatment. In the future, it is believed that the treatment of liver cancer will become more and more standardized, and the cooperation among disciplines will become closer. Targeted combined immunotherapy and even "double immunotherapy" drug therapy have begun a new chapter.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Giraud, J., Chalopin, D., Blanc, J.F. and Saleh, M. (2021) Hepatocellular Carcinoma Immune Landscape and the Potential of Immunotherapies. *Frontiers in Immunology*, **12**, 655697. https://doi.org/10.3389/fimmu.2021.655697

[2] He, J., Chen, W.Q. and Shen, H.B. (2022) Guidelines for Liver Cancer Screening in Chinese Population (2022, Beijing). *China Cancer*, **31**, 587-631.

[3] Llovet, J.M. and Bruix, J. (2003) Systematic Review of Randomized Trials for Unresectable Hepatocellular Carcinoma: Chemoembolization Improves Survival. *Hepatology*, **37**, 429-442. https://doi.org/10.1053/jhep.2003.50047

[4] Lencioni, R., De Baere, T., Soulen, M.C., *et al.* (2016) Lipiodol Transarterial Chemoembolization for hepaTocellular Carcinoma: A Systematic Review of Efficacy and Safety Data. *Hepatology*, **64**, 106-116. https://doi.org/10.1002/hep.28453

[5] Ringelhan, M., Pfister, D., O'Connor, T., Pikarsky, E. and Heikenwalder, M. (2018) The Immunology of Hepatocellular Carcinoma. *Nature Immunology*, **19**, 222-232. https://doi.org/10.1038/s41590-018-0044-z

[6] Chen, M.S. (2022) Chinese Guidelines for Integrated Cancer Diagnosis and Treatment (CACA)—Liver Cancer. *Journal of Comprehensive Cancer Treatment*, **8**, 31-63

[7] Singh, P., Toom, S., Avula, A., Kumar, V. and Rahma, O.E. (2022) The Immune Modulation Effect of Locoregional Therapies and Its Potential Synergy with Immunotherapy in Hepatocellular Carcinoma. *Journal of Hepatocellular Carcinoma*, **2020**, 11-17. https://doi.org/10.2147/JHC.S187121

[8] Wang, F. and Qin, S.K. (2022) Research Progress on the Mechanism of Synergistic Effect of Renvartinib Combined with Immunosuppressant in the Treatment of Malignant Tumors. *Journal of Clinical Oncology*, **27**, 165-171.

[9] Huang, J., Xu, J.M., Chen, Y., *et al.* (2020) Camrelizumab Versus Investigator's Choice of Chemotherapy as Second-Line Therapy for Advanced or Metastatic Oesophageal Squamous Cell Carcinoma (ESCORT): A Multicentre, Randomised, Open-Label, Phase 3 Study. *The Lancet Oncology*, **21**, 832-842. https://doi.org/10.1016/S1470-2045(20)30110-8