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Immunotherapy in Hepatocellular Carcinoma: A Case Report

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Abstract

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world, with a global incidence of over 600,000 new cases per year. Once diagnosed, hepatocellular carcinoma has a dismal prognosis. Small, localized tumors are potentially curable with surgery (resection and liver transplantation) or radio frequency ablation (RFA) in well-selected cases. Unfortunately, less than 20% of HCC patients are eligible for these procedures because most patients have advanced disease at the time of diagnosis, have liver dysfunction limiting aggressive treatment, or have recurrent disease. In these cases, therapy is largely palliative and includes transarterial chemo embolization (TACE) (1). However, the recurrence rate remains quite high despite potentially curative treatment. Immunotherapy for HCC represents an attractive approach to supplement the current therapies, based on the sensitivity, specificity, and memory capacity of the immune system (2, 3).

Case Report

We present the case of a 68-year old man who was diagnosed with cirrhosis in 2010. The origin of his cirrhosis was NASH/ASH (diabetes type 2, hyperlipemia, alcohol consumption in the past). He underwent an abdominal CT scan and a lesion less than 2 cm was discovered in segment 4 of the liver. His alpha-fetoprotein (AFP) was elevated and we decided to treat him with radio frequency ablation (RFA) with a 3 monthly follow up by CT scan. 20 Months later we found a new lesion in segment 5. This time the lesion measured 5 cm and a laparoscopic resection was performed. Histology of the tumor showed a moderately differentiated adenocarcinoma grade 3 with lymfovascularinvasion. In the following years we see the recurrence of the HCC 3 more times, always treated by RFA. We proposed liver transplantation several times since the first time we diagnosed his hepatocellular carcinoma but this was refused by the patient every time.

In January 2014 we started a phase 1 study to evaluate the feasibility and safety of 4 doses of mRNA immunotherapy in combination with RFA. We document the time to tumor response and immunological response to the vaccine antigens. We believe that intranodalinjection of naked mRNA will lead to an immunological response which will reduce tumor recurrence after treatment with RFA. Immunotherapy will be most effective during or shortly after ablative therapy, when tumor cells are dying and an active immune response has commenced. This first 'priming' by the ablative therapy should be sustained by 'booster' immunizationstomaintain immune control over the tumor. A difficulty is the immune tolerance of the liver, and the immunosuppressive environment of cancer, which makes in situ activation of immune calls problematic. This problem can be overcome by ex vivoactivation of DCs or by in vivo activation of DCs in the skin or lymph nodes.

The patient we report was included in this study and received his first intranodal injection in March 2014. The injection consists of 300 µg Trimix mRNA + 200 µg mRNA per antigen. This was repeated for a total of 4 doses (week 0, 2, 4 and 6). These injections were performed under ultrasound guidance with a 22 Gauche needle. No local or systemic side effects were reported (4). At week 12 we performed a CT scan which showed recurrence of a few small lesions. We treated him with chemo-embolisation. The disease was stable for 2 years after his first injection. In March 2016 we saw the recurrence of multiple lesions and he was treated again by chemo-embolisation. Unfortunately another few months later there was progressive disease and treatment with sorafenib 800 mg daily was started. Despite this treatment, the patient deceased 7 years after his first diagnosis of HCC and more than 3 years after his first mRNA injection.

Conclusion

HCC is frequent cancer with a high mortality rate. Treatment options are limited and the patient often has a dismal prognosis if he cannot be listed for liver transplantation. Recurrence of tumor and development of new cancer after treatment is frequent. Immunotherapy is an interesting treatment option since it does not only treat the existing tumor but it also has the potential to prevent the development of new lesions in the liver.

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