



LOCOREGIONAL TREATMENT APPROACHES FOR HEPATOCELLULAR CARCINOMA – A CASE REPORT

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Summary

A hepatocellular carcinoma (HCC) is a primary liver malignancy, often arising in the setting of chronic liver disease. Incidence of this carcinoma is increasing at a great rate. Disease often manifests asymptotically and to make the final diagnosis is often challenging. Screening of patients at risk is based on ultrasound (US) examinations, which in the setting of suspicion lesion findings often converts to multiphasic computed tomography (CT) and magnetic resonance imaging (MRI) procedures for advanced disease evaluation. The selection of treatment modality depends on tumor size and location, extrahepatic spread and subsequent liver disease. For years the first line of treatment was liver resection and transplantation. Locoregional therapy is a novel approach to diverse stages of HCC with good response and higher overall survival rates, especially in early stages. Transarterial chemoembolization (TACE) is the method of choice in patients with multifocal HCC and maintained liver function, unsuitable for surgical treatment. We present a patient with HCC in the setting of hepatitis C virus (HCV) infection, treated with combined methods of locoregional therapy.

KEYWORDS: *Hepatocellular carcinoma, locoregional therapy, hepatitis C virus, liver cirrhosis*

INTRODUCTION

Hepatocellular carcinoma (HCC) represents the most common and aggressive primary liver malignancy with approximately 80% of cases developing in the setting of chronic liver disease(1). It is fourth leading cause of cancer related deaths in the world(2). Risk factors include hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, non-alcoholic fatty liver disease (NAFLD), cirrhosis, diabetes and lifestyle choices (obesity, smoking, alcohol)(3,4). *Bridging therapy* refers to local treatment option in order to prevent patients from

being excluded from the Milan criteria while awaiting liver transplantation(5). For a long period of time surgery and liver transplantation have provided favorable results and were only available treatment option. However, in recent years minimally invasive techniques have become very promising therapeutic methods for selected stages of HCC with the intent of improving overall patient survival(5). List of available minimally invasive techniques is increasing at a great rate, including various percutaneous, image-guided locoregional therapies like local ablation therapy for patients with solitary tumor or up to 3 tumors smaller than 3 cm each (6). Moreover, many studies have analyzed efficacy of combining both ablative techniques and transarterial chemoembolization (TACE) while showing significant benefits for

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patients(7,8). In our hospital, approach is to use minimally invasive techniques best suited for the lesion and patient status, but not in a combine matter. Therefore, we present a patient with HCC in the setting of HCV infection, treated with microwave ablation (MWA) and TACE intermittently for recurrence of disease.

CASE REPORT

We present a case report of a 72 year-old female diagnosed with HCV infection in her past medical history. Until now, she was treated with pegylated interferon (peg-IFN)+ribavirin (RV), unfortunately with no response to therapy. In 2016, she was diagnosed with HCC in underlying liver cirrhosis in another hospital and underwent segmental liver resection. Since then, she was annually followed-up undergoing list of imaging examinations such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission computed tomography (PET/CT) and ultrasound (US) outside our clinic, with showing no signs of HCC recurrence. During that period only the alpha-fetoprotein (AFP) tumor marker was noted higher than expected. In 2018, she came to our clinic for disease reevaluation, with a question of disease recurrence and antiviral therapy. Abdominal US displayed segmental hypertrophy of the left liver lobe and hyperechoic lesion (9 mm in diameter) in the right liver lobe that needed to be further characterized using MRI and liver specific contrast. MRI examination with Primovist® also showed enlarged liver and surface nodularity corresponding to liver cirrhosis with one lesion suspicious for HCC recurrence. Lesion was in near proximity to post-operative scarring, showing T2 hyperintense signal, post-contrast arterial hyperenhancement followed by a washout on the portal venous and delayed phase. After further clinical workup, the interdisciplinary team introduced her with currently available treatment modalities for HCC, including liver transplantation that was the optimal treatment for her. Unfortunately, due to her socioeconomic status and living alone, after her husband has passed away and son moved from home, she refused liver transplantation, being unable to look after herself. She did accept locoregional therapy and was keen to carry out antiviral therapy in a hospital near her place of living. On the interdisciplinary meeting, consisting of

gastroenterologists and interventional radiologists, it was decided to treat the lesion with microwave ablation (MWA). After patient preparation, small amount of local anesthetic was applied and the needle-like probe (14G, 15 cm in length) was guided using CT into the lesion that was situated in the fifth liver segment. During three-minute time period, 80W of current were used for the lesion treatment. The procedure was done under supervision of anesthesiologist. Immediate post-MWA follow-up CT scans showed, in the region surrounding what was the probe active tip position during the ablation, hypodense zone without vascular complications (bleeding and thrombosis). Postprocedural hospital stay was unremarkable and patient was discharged in good overall condition. To assess the effectiveness of treatment, an enhanced CT scan was routinely performed one month after the patient was treated, together with serum AFP levels. Abdominal US was performed every three months and MRI was performed four months after the procedure. There were no signs of residual tumor or recurrence. Enhanced CT scan, approximately ten months after the treatment, displayed one lesion in the sixth liver segment, measuring 23 mm, characteristics of HCC and the diagnosis of intrahepatic HCC recurrence was made. Interventional radiologist was consulted, and the patient was thought to be a good candidate for TACE, because of the solitary lesion greater than 2 cm in diameter with suspected adjacent satellite lesions, without macrovascular and bile duct invasion. Through a 5F right common femoral artery access, aorta and visceral vessels were found patent with conventional anatomy of celiac and superior mesenteric angiograms. The right hepatic artery was selected and arteriography showed hypervascular lesion in the right liver lobe. Using microcatheter Progreate®, segmental hepatic artery supplying the lesion was accessed and chemoembolised with Hepha-Sphera®, drug-loadable microsphere bound with doxorubicin. Post-embolization angiography revealed stasis in the segment six vessels. Hemostasis was achieved with FemoSeal™. After the procedure, the patient had an uneventful recovery and was discharged home. She was advised to undergo follow-up CT scan in one month interval. Instead, the patient underwent MRI in another clinic showing no signs of disease recurrence. However, PET/CT performed nine months after

the procedure showed recurrence in the right liver lobe. Again, interventional radiologist was advised by gastroenterologist during the interdisciplinary meeting, and the patient was found to be appropriate for TACE, because lesions were located superficial, under the liver capsule, in near proximity of gallbladder. Via a 5F right common femoral artery access, after application of local anesthetic, right artery was selected. Angiograms showed two hypervascular lesions, 10 mm in diameter in the sixth liver segment. Using Progreat® microcatheter, segmental hepatic artery supplying lesions was embolized with 15×25 ml HephaSphere® bound with doxorubicin. Control angiograms showed no opacification of mentioned lesions. Hemostasis was achieved with closure device FemoSeal™. There were no complications following procedure and she was discharged home in good condition. One month after TACE procedure, CT scan revealed no disease recurrence or new lesions. Considering good response (no recurrence or newly formed HCC lesions), sequential exposure to locoregional therapy and patient's negative response for liver transplantation, oncologist will be consulted as a part of multidisciplinary team for systemic therapy approach.

DISCUSSION

The prognosis of patients with HCC remains poor, as HCC usually does not produce symptoms early in disease onset(3). Therefore, it is critical to detect HCC early in its development. Patients at a high risk for developing HCC, due to cirrhosis or chronic viral hepatitis are candidates for US surveillance(1). Once US detects the abnormal lesion, more definitive imaging is required with multiphase CT and MRI(1). Treatment options are determined by tumor mass and patient's hepatic reserve(5). If HCC is diagnosed early, in favorable surgical candidates, resection and orthotopic liver transplantation is advisable curative option(3). Nonsurgical therapy, also known as locoregional therapy, is for patients with HCC limited to the liver, that are not candidates for surgery. It includes radiofrequency ablation (RFA), MWA, percutaneous ethanol injection (PEI), cryoablation, irreversible electroporation, transarterial embolization (bland embolization, chemoembolization and radioembolization), radiation therapy and

systemic therapy(5). MWA has been used as *bridging* option for cirrhotic patients with the Child-Turcotte-Pugh class A or B(9). As initial treatment MWA provides high effectiveness rate, low morbidity, few complications and can be used repeatedly for recurrence(9,10). TACE is the treatment method for patients with large unresectable HCC that are not transplant candidate, but possess adequate remaining liver function without macrovascular invasion or obstruction(9). Exceptional results are provided using combined treatment with ablation techniques and TACE(5). MWA can give better tumor necrosis and can treat some hypovascular HCC tumors that don't respond to TACE. Thermal injury can cause a heat sensitizing effect. On the other side, TACE can treat undetected satellite lesion adjacent to the main lesion, and may reduce the blood flow of the tumor and thus reduce heat loss of MWA. Chemotherapy agent can cause a heat sensitizing effect(11,12). This approach is being used in cases with good liver function, multiple tumors <5 cm in diameter or any >5 cm in diameter but with no vascular and extrahepatic spread. Zaitoun et al. have concluded that combined therapy was safe, well tolerated and had significantly higher overall survival rate and low recurrence rate after 12 months than TACE or MWA alone for >3-<5 cm HCC lesions(13). In both approaches, considering risk for disease recurrence, post-treatment surveillance advises imaging every three to six months for two years(14).

CONFLICT OF INTEREST

The authors report no conflict of interest.

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Sažetak

LOKOREGIONALNA TERAPIJA U LIJEČENJU HEPATOCELULARNOG KARCINOMA – PRIKAZ SLUČAJA

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Hepatoceleularni karcinom (HCC) je primarna maligna bolest jetre. Uslijed porasta broja oboljelih od kroničnog hepatitisa koji u konačnici dovodi do stadija ciroze jetre, incidencija ovog karcinoma je u porastu. U svom početnom stadiju bolest je najčešće asimptomatska, a postavljanje konačne dijagnoze je zahtjevno i s odgodom. Probir visoko rizične populacije zasniva se na ultrazvučnoj dijagnostici koja se, u slučaju pronalaska sumnjive lezije, nadopunjuje multifaznim CT i MR pregledom radi daljnje evaluacije bolesti. Odabir terapijske metode ovisi o veličini i lokaciji tumora, ekstraheptalnom širenju i priležnoj bolesti jetre. Prema svim dosadašnjim smjernicama, liječenje je uključivalo kiruršku resekciju i transplantaciju jetre. U pacijenata s određenim stadijem bolesti danas je metoda odabira lokoregionalna terapija. Tehnike ablacije pogodne su za pacijente u vrlo ranoj fazi bolesti. Transarterijska embolizacija (TACE) je metoda odabira kod pacijenata s multifokalnim HCC-om održane jetrene funkcije, nepodobnih za operaciju. Primjena lokoregionalne terapije s kombinacijom ostalih tehnika pridonosi boljoj rezoluciji bolesti s boljim ishodima preživljenja. U prikazanom slučaju, pratimo pacijenticu s HCC-om u podlozi hepatitis C virusne (HCV) infekcije kod koje se, odlukom multidisciplinarnog tima, odlučilo na lokoregionalnu terapiju naizmjeničnom kombinacijom mikrovalne ablacije i TACE kod recidivirajućeg HCC-a.

KLJUČNE RIJEČI: *Hepatoceleularni karcinom, lokoregionalna terapija, hepatitis C virus, ciroza jetre*