Considerations Upon a Case of Hepatocellular Carcinoma Treated with Magnetic Resonance Imaging - Guided Percutaneous Cryotherapy Guidance

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Hepatocellular carcinoma represents 5 % of the cases of death in the world. The recent epidemiological data show a major increase of its incidence in the western countries and USA, the explanation being through the growth in the incidence of viral hepatopathies, especially with hepatitis C virus.
Of the patients diagnosed with hepatocarcinoma, 70 % benefit from palliative treatment only. The curative treatment in the case of hepatocarcinoma includes surgical resection, liver transplant, radiofrequency.
Magnetic Resonance Imaging-guided percutaneous cryotherapy, the method in progress of evaluation, seems to give spectacular results in the case of small size, non resectable situated very close to the hepatic hylum.
The evolution of a patient with viral cyrrhosis C complicated with a hepatocarcinoma and the problems related to hepatocarcinoma treatment while waiting for liver transplantation was the object of an analysis that allowed the emphasis of the lack of tumoral progress and the reduction of tumoral volume until its disappearing from an imagistic point of view.

Keywords: hepatocarcinoma, viral hepatitis, cryotherapy, radiofrequency

Introduction

Hepatocellular carcinoma (HCC) represents 5% of the cases of cancer in the world, the worldwide incidence is from 560.000 to 1.000.000 new cases per year [1].

Recent epidemiological data show a major increase of HCC incidence in Western european countries and the USA [2]. This can be partly explained by a more effective and early diagnosis due to new imaging techniques. A French study reports an increase in mortality in the HCC C viral cirrhosis of 150% in men and 200% in women in 2020 [3, 4].

The prognosis is bad and variable depending on the period when it is found (average survival of 5.6 months in the symptomatic stage and up to 40 months in the absence of symptoms, metastases and vascular invasion) [5].

Curative treatment for HCC includes surgical resection, transplantation and more recently radiofrequency has demonstrated its efficacy in the small lesions, few in number and nonresectable [6]. Hepatocarcinomas are resectable in 15–20% of cases [7].

Cryotherapy is a very recent technique and is currently reserved for patients with tumors for whom another treatment is hard to do [8, 9].

Material and method

We studied the evolution of a patient diagnosed with hepatocellular carcinoma (HCC) developed on a viral cirrhosis C from June 2009 up to the present, the patient being currently listed on the national waiting list for liver transplantation.

Male (M.J.), 49 years old, known with history of 1988, surgical treatment for an occlusive syndrome in 1984, appendicectomy, chronical hepatitis C virus (HCV) discovered in 2006, active smoking.

The patient first shows up in our service in June 2009 accusing abdominal pain and bowel movement troubles.

A first assessment confirms the hepatitis C virus (ARN HCV = 6.17 log) and upon echography a cyrrhotic looking liver is discovered with a nodule of 3.5 cm in the V segment.

In August 2009 a thoracic-abdominal-pelvian Tomographic Computer (TC) diagnozes a cyrrhotic liver, dismorphic with a nodule of 4 cm from the junction of segment V and VIII close to the junction of the right branch of the portal vein. The nodule is hypervascularised in arterial time with a phenomenon of „wash out" in late time, typical HCC aspect and for whom it is advisable to do the second imagistic examination through Magnetic Resonance Imaging(MRI) for the final HCC diagnosis (according to the criteria of Barcelona 2005). There is also in TC an area discreetly hypervascularised in arterial time in segment VI compatible with perfusion anomalies. The examination does not find other anomalies in the thorax-abdomen-pelvian stages.

In September 2009 a MRI with Gadolinium injection in the dynamics finds the 4.5 cm nodule at the junction of segments IV, V, VIII with the characteristics of a HCC, another nodule of 1.6 cm from segment IV suspect with late "wash out" and a beach of 6 cm in segment VI hypervascular in arterial time without "wash out" (Figure 1).

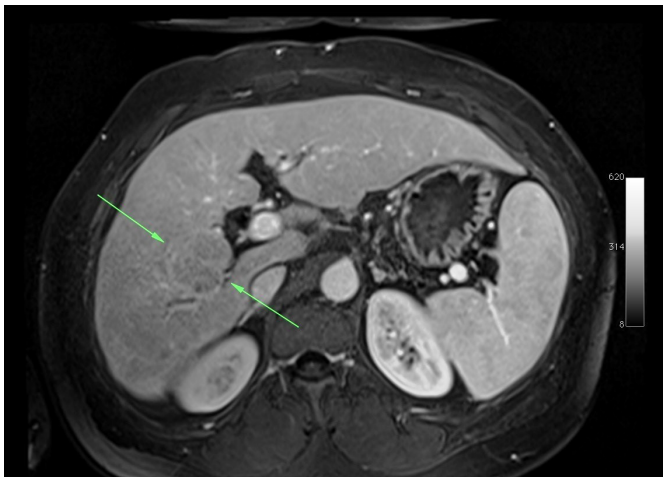

Fig. 1. Liver MRI – T1 with injection, portal phase. Hepatocarcinoma (arrows)

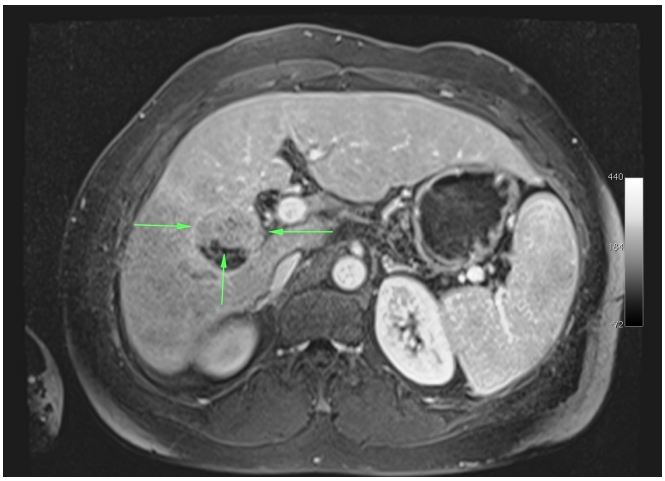

Fig. 2. Liver MRI – T1 with injection, portal phase, after lipiodol chemoembolization. Residual tumor (arrows).

One month later, liver biopsy was performed. We retrieved tissue originating from a 1.6 cm suspect nodule from segment IV and the hypervascular area from segment VI, the result being active chronical hepatitis and micronodular cirrhosis, Metavir score A3F4.

The tumoral markers are: AFP = 65, (VN < 7 µg/l), CA 19-9 = 69,5 (VN < 37 µg/l), and the scyntigraphy realized in November 2009 does not show bone metastases.

The hepatic arterial chemoembolisation with lipiodol was done in November 2009 for the nodule in segment V of 4 centimetres, and a control MRI done in December 2009 in order to appreciate the result of the chemoembolisation shows a partial tumor necrosis of approximately 30% from the tumoral volume and the 1.6 cm nodule known from segment IV (Figure 2).

In January 2010 a MRI-guided percutaneous cryotherapy is conducted in order to have a tumoral reduction in the view of a hepatic transplant.

As a technique we used: MRI Siemens of 1.5 Tesla, the cryotherapy system to which 6 cryotherapy probes of Ice Rod type are coupled, bottle with Argon gas for freezing and bottle with Helium gas for defrost (Figure 3).

Two 10 minute freezing cycles were conducted separated by a phase of 10 minutes passive freezing in order to realize the tumoral destruction. The post-procedural control shows a good coverage of the tumor with ice, the ice dimension reaching 5 cm (Figure 4).

Upon a week after cryoablation a postcryotherapy control TC shows the disappearing of the tumor, emphasizing a cryoablation scar without contrast charge.

The transplant assessment mulidisciplinary committee, based on the pre-graft, decides the patient's enlistment on the national waiting list for liver transplantation.

Control MRI conducted at one month after cryotherapy shows a complete cryoablation of the HCC without signs of residue or tumoral relapse (Figure 5).

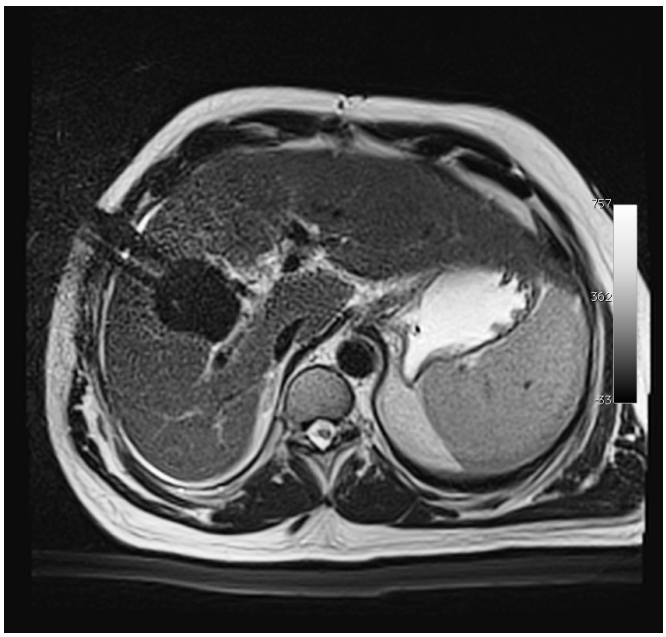

Fig. 3. Liver MRI – T2 axial plane. 2 cryotherapy probe.

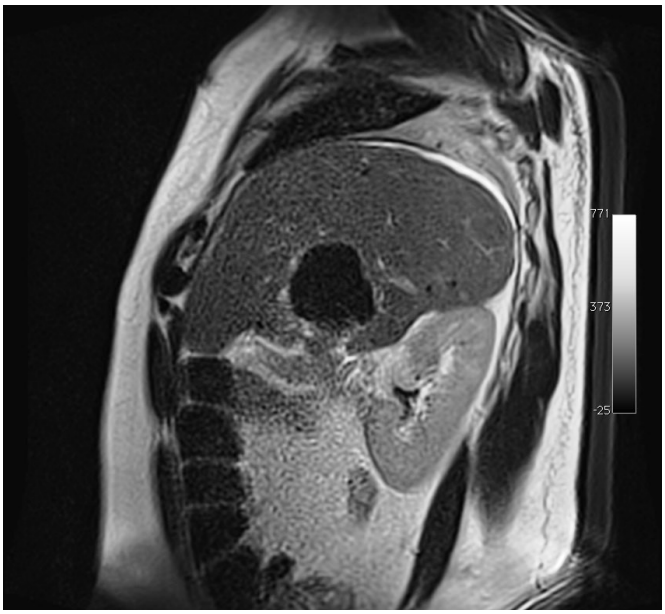

Fig. 4. Liver MRI – T2 sagital plane. Cryotherapy (ice ball-hypointense)

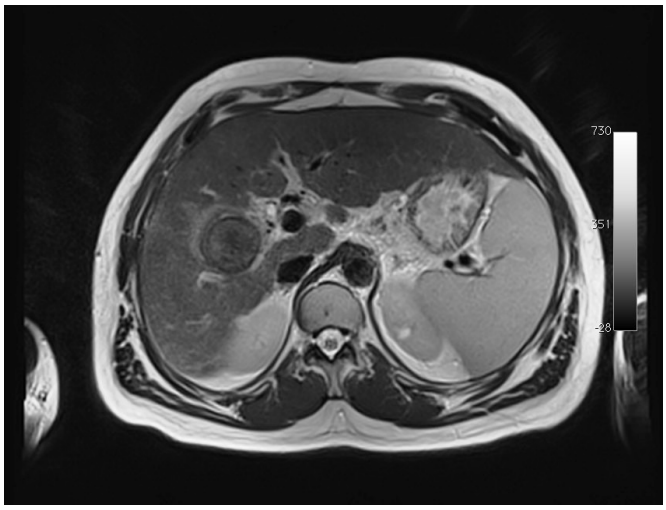

Fig. 5. Liver MRI – T2 axial plane. After cryotherapy.

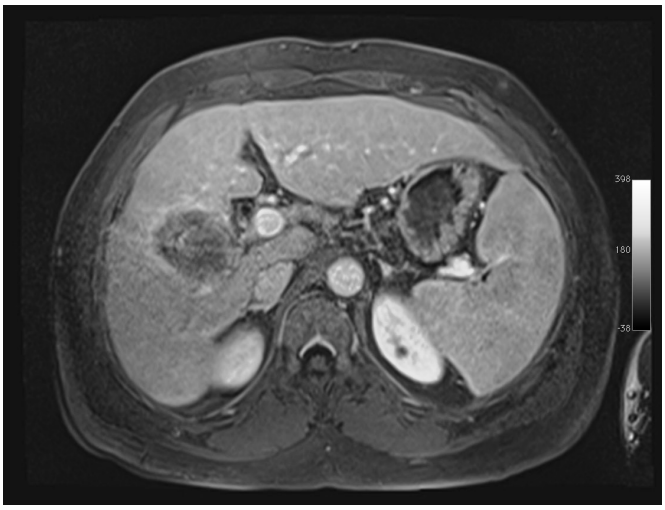

Fig. 6. Liver MRI – T1 with injection, portal phase. After cryotherapy (no more residual tumor).

An antiviral treatment in order to prevent the HCV after transplant began in March 2010 with Pegasys and Copegus, the viral NRA at the beginning of the treatment being of 317000 UI/ml, result which gives us the hope of a good antiviral answer. AFP does not exceed AFP = 36.4 µg/l.

At the last control MRI, realized at the end of April the same aspect of complete cryoablation of HCC is outlined without any presence of tumoral residue or local tumoral recidival (Figure 6).

Results

Magnetic Resonance Imaging-guided percutaneous cryotherapy is a promissing method as seen in the case of our patient, being in progress of evaluation for the HCC treatment while waiting for liver transplantation.

As in the case of our patient, this technique could be used in the case of small scale lesions, few in number, non resectable and that situated close to the hepatic hylum and for which a treatment though radiofrequency could induce an extended tumoral destruction being able to reach the right branch of the portal vein and/or the right hepatic channel.

Discussions

Cryotherapy is a very recent technique and is currently reserved for patients with tumors for whom another treatment is hard to do [8, 9].

Cryotherapy allows for tumoral distruction with the help of cryotherapy probes by realising cell lesions during the freezing and defrost phases.Cryotherapy realizes cell death though 2 pheomena: creation of direct cell lesions and vascular lesions. The direct cell lesions that appear immediately are worsened by the vascular lesions that will appear late (after a few hour) [10].

It seems that cancerous cells are much more sensible than the normal cells from the point of view of lesions induced by freezing [9].

With the help of present devices the freezing is obtained by Argon gas due to Joule-Thomson effect. The process starts and ends almost instantly. Two cycles of freezing/defrost as in the case of our patient, are necessary for a maximum of cell death at the periphery of the lesion to treat (where temperature is higher than -50 Centigrade degrees). The forming of intra and extracell ice brings with itself an alteration of cell structure and metabolism, responsible with cell death. For temperatures inferior to -50 C cell, death is safely and rapidly obtained though mechanical effect. For temperatures between -20 °C and -50 °C cell, death is mainly obtained through osmotic effect.

Defrost is obtained with the help of Helium gas due to the negative Joule-Thompson effect. In this phase cell death is mainly produced through rupture of cell membranes. The possibility of tissue recalescence using Helium is very useful also for the rapid probe extraction at the end of the freezing phase [9].

Cryotherapy provokes lesions of microcirculation vessels (capilaries, venules and arterioles), obtaining cell necrosis of ischemical origin. The cooling from the initial phase of freezing brings with itself a vasoconstriction inside the tissue treated, getting to the point when blood flow stops. Freezing itself generates direct lesions upon the blood cells and endotelial cells. The recalescence phase will bring a vasodilatation in the same vascular network, restoring blood flow.This transition from the state of vasoconstriction to vasodilatation provokes the rapid distention of vessels with the appearance of parietal breaches.The increased permeability of vascular walls allows a flow of plasma towards the interstitial environment having as consequence an increase in blood viscosity and finally the thrombosis of small vessels with cell ischemia and finally cell death [10]

The degree of tissue destruction induced by cryotherapy depends on 5 main parametres: the minimal temperature, freezing speed, defrost speed and the number of cycles of freezing/defrost. The more the temperature is superior to -50 °C and freezing is of a longer timespan, the more cell death is important. Defrost must be done slowly in order to favour at a maximum the phenomena

of recrystallization and water move towards the intracell environment [11].

The preliminary results of cryotherapy especially on kidneys are spectacular, but its development as a treatment technique requires on the one hand observation in the long term of the cohort of patients and on the other, a better understanding of assumed tissular effects, particularly in the tumoral context [9].

Cryotherapy when well used on bone, kidneys and more recently liver or lungs is of course promissing but is still considered an experiment technique [8].

MRI-guided percutaneous cryotherapy would be preferable due to the fact that gas or cold don't give artifacts as in the case of MRI-guided percutaneous radiofrequency [9].

Another indication would be in the case of a HCC that upon the TC examination with injection of contrast presents a dynamics in a fleeing (fugax) way or is not well visible. MRI, unlike CT, can be used to monitor cryoablation in close to real time in multiple planes, does not involve the use of ionizing radiation, and distinctly depicts both ice ball and tumor. Tumors typically have increased signal intensity on T2-weighted images, whereas ice balls cause a signal void. On CT, both tumor and ice ball are hypodense and often cannot be differentiated [8, 9].

The limits of the technique are the size of the lesion and the absence of histological control [10].

Conclusions

Magnetic Resonance Imaging-guided percutaneous cryotherapy is a promissing method as seen in the case of our patient, being in progress of evaluation for the HCC treatment while waiting for liver transplantation.

This technique could be used in the case of small scale lesions, few in number, non resectable and that situated close to the hepatic hylum and for which a treatment though radiofrequency could induce an extended tumoral destruction.

MR imaging–guided percutaneous cryotherapy of liver tumors is feasible and safe. MR imaging can be used to estimate cryotherapy effects and guide therapy intraprocedurally.

It is considered as a local treatment, it allows to treat a single location and cannot treat a cancer disseminated in other organs.

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