



TREATMENT OF HEPATOCELLULAR CARCINOMAS BY HEPATIC TRANSARTERIAL CHEMOEMBOLIZATION, CASE PRESENTATION AND REVIEW OF THE LITERATURE

ANDREI FLORIN BLOJ¹, IOANA HĂLMACIU², BOGDAN ANDREI SUCIU³,
LUCIAN MĂRGINEAN⁴

^{1,2,4}Țirgu Mureș County Emergency Clinical Hospital,

^{2,3}“George Emil Palade” University of Medicine, Pharmacy, Science and Technology, Țirgu Mureș

Keywords: hepatocellular carcinoma, hepatic transarterial chemoembolization

Abstract: Hepatocellular carcinoma is one of the most common liver tumours. At the time of diagnosis, only 20% of patients are suitable for liver resection for curative purposes. In patients who are not suitable for surgical resection, chemoembolization of the hepatic artery is a viable therapeutic option. We present the case of a 60-year-old male patient being admitted with a diagnosis of liver tumour in the right liver lobe. Abdominal angio-CT examination revealed the existence of a tumour formation of 9x10 cm in the liver segments IV, VIII. Given the large size of the tumour, as well as the patient's comorbidities, it was decided to practice hepatic chemoembolization with Irinotecan. The clinical evolution was favourable, the patient being discharged 48 hours after the intervention. Hepatic transarterial chemoembolization is a viable alternative in the treatment of patients with unresectable hepatocellular carcinomas, which may improve the prognosis of these patients.

INTRODUCTION

Among primary liver tumours, the most common histological type is hepatocellular carcinoma, which accounts for about 90% of most liver tumours.(1) The main therapeutic techniques with curative objective in these cases are represented by the surgical resection, respectively the liver transplant. Unfortunately, 75% of patients with hepatocellular carcinomas seek medical attention in advanced stages of the disease, which does not allow a curative treatment in these cases.(2,3)

In the past, the only therapeutic chance for patients with unresectable hepatocellular carcinomas was systemic chemotherapy and radiotherapy. In the last 10 years, due to the development of new interventional imaging techniques, there has been an increase in the importance of chemo-embolization of the hepatic artery (TACE), with its variant chemoembolization with drug-eluting beads (DEB-TACE).(4) Also, lately, in such cases, ablative techniques using radiofrequency or alcoholization, performed under percutaneous ultrasound guidance, are used more frequently.(5,6)

AIM

The purpose of this paper is to present the case of a patient with unresectable hepatocellular carcinoma where hepatic artery chemoembolization was performed and to conduct a literature review in this regard.

CASE REPORT

We present the case of a 60-year-old male patient admitted at the Surgery Clinic of the Țirgu Mureș County Emergency Clinical Hospital. At admittance, the patient presented asthenia, fatigue, weight loss, pain in the right hypochondrium. As for the laboratory findings, they were within

normal parameters. The abdominal angio-CT examination showed the existence of a tumour formation in the right hepatic lobe, in segments IV, VIII with a diameter of 9x10 cm (figures no.1,2).

Figure no. 1. Abdominal angio-CT examination, coronary section showing a space occupying lesion of 9x10 cm diameter with inhomogeneous iodophilia located in segments IV, VIII

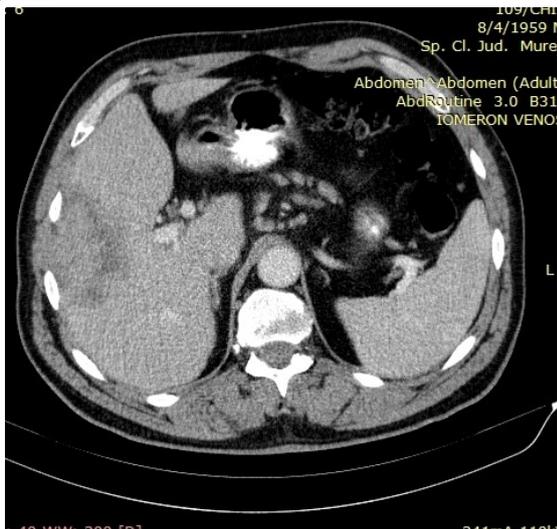


²Corresponding author: Ioana Hălmăciu, Str. Ghe. Marinescu, Nr. 50, Țirgu-Mureș, România, E-mail: anca_halmaciu@yahoo.com, Phone: +407400 91324

Article received on 09.06.2020 and accepted for publication on 10.08.2020

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Figure no. 2. Abdominal angio-CT examination, axial section that highlights a space occupying lesion of 9x10 cm diameter with inhomogeneous iodophilia located in segments IV, VIII



Given the large size of the tumour and the increased operative risk due to the associated cardiac comorbidities, it was decided to delay the surgical intervention in exchange for a chemoembolization of the hepatic artery. The intervention was performed under local anesthesia, practicing chemoembolization of arterial branches tributary to the tumour formation with embolization particles of Irinotecan (figure no. 3). The clinical evolution after the intervention was favourable, the patient presented in the first 24 hours a transient increase in serum values of transaminases that returned to normal after the introduction of hepatoprotective treatment.

Figure no. 3. Chemoembolization of hepatic artery with Irinotecan (angiographic aspect)



DISCUSSIONS

At the time of diagnosis, only about 20% of patients with hepatocellular carcinomas are suitable for curative treatment. This particularly low rate is due on the one hand to the tumour itself which is not suitable for curative resection, on the other hand due to the underlying condition of the patient's liver parenchyma (cirrhotic liver, alcoholic liver, chronic hepatitis C virus infection or B).(7-9)

Intra-arterial treatment for patients with hepatocellular

carcinoma is increasingly used. The motivation for practicing such therapeutic approach is based on the observation that the tumoral tissue is vascularised mainly by the hepatic artery, instead, the normal liver tissue has mainly a portal vascularization. Currently, both TACE and selective internal radiation therapy (SIRT) are used in clinical practice.(10,11) TACE is usually recommended in patients with multifocal tumours, without vascular invasion, without distant metastases, who have an acceptable clinical status and liver function within relatively normal parameters. SIRT, unlike TACE, is performed in patients with vascular invasion or after TACE failure.(12-14) SIRT is in fact a variant of loco-regional brachytherapy. Currently, there is no clear information in the literature to suggest the superiority of one of the two therapeutic approaches in terms of prognosis of these patients. Often, the option for one of the two therapeutic methods is based mainly on the experience of the medical centre where the therapeutic intervention is practiced. The main limiting factor of these therapeutic approaches is the obtaining of an incomplete tumour necrosis following these loco-regional therapies.(12)

Given that most patients with hepatocellular carcinomas seek medical attention in advanced stages of the disease when they are no longer suitable for surgical treatment, the practice of loco-regional therapies in such patients accompanied by a much lower morbidity is of real use. The application of loco-regional chemotherapy has the advantage that the introduction of chemotherapy in the hepatic artery increases its effectiveness on the liver tumour with the existence of lower systemic side effects. Also, during the practice of TACE, due to the embolization of the arterial branches tributary to the tumour, the contact time of the chemotherapeutic drug with the tumour cells increases. Usually, during TACE, chemotherapy is given in combination with lipiodol. Another advantage is represented by the fact that this technique can be performed under local anesthesia, it is not necessary to perform a general anesthesia. This aspect is of particular importance in clinical practice, because the vast majority of these patients have numerous comorbidities, the risks of general anesthesia in such cases being much higher.(15,16) Also, the ischemic effect produced on the tumour due to the occlusion of arterial sources that vascularise the tumour causes a partial necrosis of the tumour formation.(17)

In order to improve the prognosis of patients undergoing TACE, some authors recommend the association of embolization with microspheres. This method determines a superior efficacy in terms of decreasing the vascular flow at the level of the tumour formation. The cytotoxic effect of the chemotherapeutic agent in association with tumour tissue ischemia will ultimately lead to inhibition of the tumour growth.(18,19) At the level of the hepatic parenchyma, following the hypoxia, there is an increased cellular expression of vascular endothelial growth factor (VEGF).(20,21) This hyperexpression at the cellular level of VEGF will determine in time the appearance of neoformation vessels, proliferation of endothelial cells, as well as inhibition of apoptosis at the cellular level. These cellular processes resulting from increased cell secretion may ultimately lead to growth of the tumour formation, representing one of the main causes that may limit the clinical effects of TACE.(22-24)

In the case of SIRT, the use of Y90 microspheres does not cause a permanent occlusion of the arterial branches that are embolized, therefore hypoxia and tissue inflammatory response is smaller.(25) Unlike TACE, DEB-TACE uses non-biodegradable polymer microspheres, which results in irreversible vascular occlusion of the embolized vessel. This causes a much higher tissue concentration of the administered chemotherapy agent associated with a longer period of contact

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between it and the tumour tissue whilst maintaining a very low systemic concentration, which determines a much higher tolerability of the method for the patient.(26,27)

The main complications that can occur after practicing TACE are nausea, vomiting, fever, abdominal pain or local complications at the site of the arterial puncture.(28,29) In the literature, the so-called post-embolization syndrome is currently recognized, being characterized by the appearance of fever and a transient increase in serum transaminases in the first 72 hours after the practice of TACE. The pathogenesis of this syndrome relies in the appearance of tumour necrosis, as well as hypoxia, respectively ischemia of the healthy liver tissue.(30,31) Although the vast majority of patients have mild forms of this syndrome, there are a couple of cases mentioned in the literature where patients even developed liver failure. The occurrence of this syndrome varies in the literature between 45-80% of cases, its frequency depending on the experience of the medical staff where the intervention is practiced.(32-34)

Some authors have observed that the occurrence and the severity of post-embolization syndrome is not associated with a favourable therapeutic response, but is associated with a poor long-term prognosis and a higher long-term mortality of these patients.(35,36) Often, the occurrence of post-embolization syndrome in such patients is associated with increased serum levels of IL-6; being known in the literature the importance of IL-6 in regeneration, respectively hepatic homeostasis. In this regard, some authors consider that the increase in serum IL-6 levels is in fact a marker of the onset of post-embolization liver regeneration processes.(37,38)

In the treatment of post-embolization syndrome, the vast majority of authors recommend the administration of N-acetylcysteine due to its hepatoprotective and antioxidant role.(39)

In the long term, the survival of patients with unresectable hepatocellular carcinomas where TACE is practiced in combination with systemic chemotherapy varies between 26-47% at 3 years, these results varying depending on the experience of the centre where the procedure is performed. The outcome of TACE in these patients is particularly important, given that the 3-year survival rate in patients undergoing only systemic chemotherapy is around 3%. These results support the importance of the use of TACE in the therapeutic arsenal of patients with unresectable hepatocellular carcinomas.(40-43) On the other hand, regarding the prognosis of patients undergoing TACE and DEB-TACE there are contradictions in the literature on this subject. Some studies show a superiority of long-term survival after practicing DEB-TACE, but most studies show no differences in long-term survival between the two methods.(44)

CONCLUSIONS

Hepatic transarterial chemoembolization is a viable alternative in the treatment of patients with unresectable hepatocellular carcinomas, which may improve the prognosis of these patients.

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