

Downstaging case of hepatocellular carcinoma.

Anna Paula Aureliano¹, Danielle Mourão¹, Silas Romeres¹, Liliana Mendes¹, Marcos Carneiro¹, and Luiz de Freitas²

¹Hospital de Base do Distrito Federal

²UFBA

October 4, 2023

Downstaging case of hepatocellular carcinoma

“Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy”

ABSTRACT

Introduction: Transarterial chemoembolization (TACE) is the most used treatment option for patients with intermediate-stage hepatocellular carcinoma (HCC) who are not candidates for a curative approach. Through it, it is possible both to carry out palliative treatment and to reduce the size of the tumor so that the patient is eligible for a curative treatment such as a liver transplant. This modality of offering TACE to reduce the tumor stage and allow curative treatment is called “Downstaging”. Patients with HCC greater than 7 cm generally do not respond very well to chemoembolization to reduce tumor size, and generally this “downstaging” is not performed.

Objective: To disseminate information in the medical community about a case of a patient with a hepatocellular carcinoma larger than 7 cm, who underwent chemoembolization to reduce staging and who met eligibility criteria for liver transplantation.

Methods: Data were collected from notes in the medical records, after signing the informed consent form by the patient and approval by the Research Ethics Committee.

Results: This study presents a case report of a 55-year-old man with chronic liver disease and a history of infection by the hepatitis C virus and the human immunodeficiency virus, who evolved with non-invasive hepatocellular carcinoma in segment VI/VII of the liver out of Milan criteria for curative therapeutic proposal. The patient underwent two sessions of TACE, which were effective in reducing the size of the tumor, making him eligible for curative treatment – liver transplantation.

Conclusion: The case in question stands out for being a condition of atypical evolution, where often, due to the size of the tumor, the response to chemoembolization is not so significant. The case report is justified in order to provide information and enable downstaging attempts to be made in patients with similar profiles.

Keywords: Hepatocellular carcinoma. Transarterial chemoembolization. TACE. Hepatitis C

Introduction:

Hepatocellular cancer (HCC) is the sixth most common cancer worldwide and the third most common cause of cancer mortality. (KADALAYIL *et al*, 2013). Unfortunately, most patients have unresectable disease and liver transplantation is a curative and lifesaving treatment for these patients (SAN MIGUEL *et al.* , 2015).

Not all patients with HCC meet the eligibility criteria for liver transplantation. To reduce the tumor burden, *downstaging* through chemoembolization is used. Patients with HCC greater than 7 cm generally

do not respond very well to chemoembolization to reduce tumor size and generally this “downstaging” is not performed (KADALAYIL *et al*,2013).

In the reported case, we have a patient with a HCC measuring 9.1 cm, who underwent chemoembolization to reduce staging, which was successful and thus reached the eligibility criteria for liver transplantation.

METHODS:

This -is a descriptive study, with analysis of the medical records of a patient with liver cirrhosis secondary to hepatitis C and hepatocellular carcinoma measuring 9.1 cm, outside curative therapeutic possibilities, submitted to chemoembolization to reduce tumor size and thus being within the criteria of eligibility for liver transplantation.

This study is presented in the form of a case report, which consists of a detailed description of a clinical case with specific characteristics of the case in question, reporting the procedures studied.

Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

RESULTS AND DISCUSSION :

CASE REPORT

Male patient, 55 years old, with liver cirrhosis secondary to hepatitis C, co-infected with the human immunodeficiency virus. Previous decompensation with upper gastrointestinal bleeding due to esophageal varices in January/2021. Magnetic resonance imaging of the abdomen was performed at the same time as the first decompensation and evidence of a lesion with hyper-enhancement artery and late wash -out in segments VI and VII, compatible with hepatocarcinoma, measuring 9.1 x 5.8 cm. Laboratory tests: alpha-fetoprotein 345, total bilirubin 1.5.

In March/2021, the patient underwent the first TACE session, uneventfully, with a reduction of the lesion to 5.3x2.9cm. In May/21, a new TACE session was performed, after the procedure, the patient evolved with complications of upper digestive hemorrhage, atrial fibrillation and presented a reduction of the lesion to 1.8 cm in the control exam. Thus becoming eligible, according to the Milan criteria, for liver transplantation.

DISCUSSION

Most HCCs occur in patients with underlying liver disease, mainly as a result of hepatitis B or C virus (HBV or HCV) infection, alcohol abuse, and non-alcoholic fatty liver disease (NAFLD) (RAOUL *et al.*,2019) . It represents up to 90% of all primary liver malignancies, and its incidence continues to progressively increase in the world (CHEDID *et al.* , 2017).

Liver transplantation is a curative option for patients who are not candidates for tumor resection and the Milan criteria have been proposed, validated and widely used as eligibility criteria for consideration of transplantation in the treatment of HCC (PARIKH *et al.*,2015) . Studies have shown that tumor size consistently influences survival, with a larger tumor volume being associated with a greater risk of vascular invasion and distant metastasis. (KADALAYIL *et al*, 2013).

Unfortunately, only a minority of patients with HCC meet the Milan criteria (SAN MIGUEL *et al.* , 2015). It is necessary to fit the following criteria: 1 tumor with less than 5 cm or up to 3 tumors with less than 3 cm in size (PARIKH *et al.* , 2015) . If patients present outside these criteria, liver transplantation is generally not an option in many transplant centers and patients are left with no other curative options (ALTEKRUSE *et al.* , 2014) . For selected patients, downstaging is attempted to bring tumors within the Milan criteria using liver-targeted therapy (FACCIORUSSO *et al.* , 2015).

Options for downstaging include radiofrequency ablation (RFA), chemoembolization transarterial (TACE), radioembolization transarterial radiation (TARE), stereotactic body radiation (SBRT) or a combination of therapies (CHEDID *et al.* , 2017) .

The predominant blood supply for HCCs is through the hepatic artery, unlike the normal hepatic parenchyma, which obtains 75% of its blood supply from the portal vein (TOWNSEND *et al.* , 2019) . In patients undergoing conventional TACE, this selective arterial perfusion is taken advantage of by administering a chemotherapy drug such as doxorubicin or cisplatin locally into the tumor, subsequently followed by injection of an embolic agent. (HABIB *et al.* , 2015). The combination of direct cytotoxicity of chemotherapeutic agents and ischemia by selective embolization induces tumor necrosis and consequent size reduction. (LENCIONE, 2012), in addition to contributing to the control of alpha-fetoprotein serum levels and the patient's survival time.

Studies have shown that high values of bilirubin ($> 17\mu\text{mol/l}$) and alpha-fetoprotein (AFP) ($>400\text{ng/ml}$), in addition to large tumor size ($>7\text{cm}$) were associated with a two- to three-fold increase in the risk of death, and generally chemoembolization is discouraged. (KADALAYIL *et al.*, 2013).

Our patient in the clinical case has HCC measuring 9.1cm, but with normal bilirubin and alpha-fetoprotein , in addition to having his liver disease very well controlled. Aiming at curative therapy, chemoembolization was successfully performed to reduce staging, and thus the eligibility criteria for liver transplantation were met.

Conclusion:

The case in question stands out for being a condition of atypical evolution, where often, due to the size of the tumor, the response to chemoembolization is not so significant. The case report is justified in order to provide information and enable downstaging attempts to be made in patients with similar profiles.

Bibliographic references:

ALTEKRUSE, SF; HENLEY, SJ; CUCINELLI, JE; MCGLYNN, KA Changing hepatocellular carcinoma incidence and liver cancer mortality rates in the United States. *American Journal of Gastroenterology*. [SI], [2014], 542-553 p, v. 109, no. 4.

CHEDID, MF; KRUEL, CRP; PINTO, MA; GREZZANA-FILHO, TJM, LEIPNITZ, I.; KRUEL, CDP; *et al.* Hepatocellular carcinoma: diagnosis and surgical management. *Brazilian Archives of Digestive Surgery [São Paulo]*. [2017], 272-278 p, v. 30, no. 04.

FACCIORUSSO, A.; LICINIO, R.; MUSCATIELLO, N.; DI LEO, A.; BARONE, M. Transarterial chemoembolization: Evidences from the literature and applications in hepatocellular carcinoma patients. *World Journal of Hepatology*. [SI], [2015], 2009-2019 p, v. 7, no. 16.

HABIB, A.; DESAI, K.; HICKEY, R.; THORNBURG, B.; LEWANDOWSKI, R.; SALEM, R. Locoregional therapy of hepatocellular carcinoma. *Clin Liver Dis*. [SI], [2015], 401-420 p, v. 19, no. two.

LENCIONI, R. Chemoembolization for hepatocellular carcinoma. *Seminars of Oncology*. [Italy], [2012], 503-509 p, v. 39, no. 4.

PARIKH, ND; WALJEE, AK; SINGAL, AG Downstaging hepatocellular carcinoma: A systematic review and pooled analysis. *Liver Transplantation*. [Ps], [2015], 1142-1152 p, v. 21, no. 9.

RAOUL, JL; FORNER, A.; BOLONDI, L.; CHEUNG, TT; KLOECKNER, R.; DE BAERE, T. Updated use of TACE for hepatocellular carcinoma treatment: How and when to use it based on clinical evidence. *Cancer Treatment Reviews*. [Ps], [2019], 28-36 p.

SAN MIGUEL, C.; MUFFAK, K.; TRIGUERO, J.; BECERRA, A.; VILLEGAS, T.; NOGUERAS, F.; *et al.* Role of Transarterial Chemoembolization to Downstage Hepatocellular Carcinoma Within the Milan Criteria. *Transplantation Proceedings*. [Ps], [2015], 2631-2633 p, v. 47, no. 9.

TOWNSEND, CM; BEUCAMP, RD; EVERS, BM; MATTOX, KL *Sabiston Textbook of Surgery - The Biological Basis of Modern Surgical Practice*. 20. ed. Rio de Janeiro: Elsevier, 2019, 1457-1463 p.