Simultaneous surgical treatment of hepatocellular carcinoma with tumor thrombus in the inferior vena cava and ischemic heart disease – own research and literature review

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ABSTRACT:

Introduction: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide. Tumor penetration into the inferior vena cava/right atrium is rare, as it occurs only in 3–4% of HCC patients. There are no clear guidelines for the management of this stage of disease.

Aim: This is a case report of a patient with HCC and tumor thrombus in the inferior vena cava and with advanced coronary artery disease.

Materials and methods: The patient was qualified for a simultaneous cardiac surgery and liver resection with removal of the tumor thrombus from the inferior vena cava due to a high risk of sudden cardiac death. The first stage involved aortocoronary bypass followed by a right-sided hemihepatectomy with removal of the tumor thrombus from the inferior vena cava (this part of the operation was performed by extracorporeal circulation). The postoperative period was uneventful. Surgical treatment is one of the therapeutic options that offers a chance to radically remove the tumor and extend the patient’s life. From a standpoint, these operations are extremely difficult and carry a high risk of perioperative complications (up to 40%). At the same time, the patient is at risk of complications due to cancer, such as pulmonary embolism, tricuspid valve stenosis, and congestive heart failure, which should be considered when choosing a treatment method. A significant number of patients also suffer from chronic conditions that worsen the prognosis. Cardiac diseases combined with tumor thrombus in the inferior vena cava may cause sudden cardiac death.

Conclusions: Surgical treatment should be considered in patients with HCC and tumor thrombus in the inferior vena cava, especially in patients with cardiovascular disease burden, as it is not only a chance to prolong life, but also to protect them against life-threatening cardiac complications.

KEYWORDS: hepatocellular carcinoma, ischemic heart disease, tumor thrombus of inferior vena cava

INTRODUCTION

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide. A tumor located in the liver can spread as a tumor thrombus through the hepatic veins to the inferior vena cava, and even to the right atrium of the heart. Tumor thrombus in the inferior vena cava/right atrium of the heart during HCC is relatively rare, approximately 3–4% of the patient population. It significantly worsens the prognosis, which is associated with a high risk of metastasis and complications such as: pulmonary embolism, tricuspid valve stenosis, and congestive heart failure. The median survival time of patients after radical tumor resection and tumor thrombus removal ranges from 19 to 30.8 months [1]. There are 3 types of tumor thrombus depending on the location...
in the inferior vena cava. In type I, the head of the tumor thrombus is located below the diaphragm; in type II, it is above the diaphragm, and in type III, it enters the right atrium (Fig. 1.). In type I, a standard liver resection with transabdominal removal of the liver can be accessed from the abdominal cavity through liver mobilization and diaphragmatic incision. The greatest challenge is tumor thrombus in the right atrium and ventricle. In this case, it is necessary to completely cut off the hepatic vasculature, apply extracorporeal circulation, and open the heart.

**MATERIAL AND METHODS**

This is a case report of a 63-year-old man with a tumor thrombus of the right hepatic lobe (segments 7 and 8 and partially segments 5 and 6) of HCC type penetrating through the inferior vena cava to the right atrium (Fig. 2, 3.). Initially, the patient was not eligible for surgery due to the tumor size (162 x 130 mm). Radiochemoembolization was used and a selective tyrosine kinase inhibitor (Sorafenib) was added as part of the clinical trial. Control imaging studies showed a reduction in the size of the focal lesion to 144 x 123 mm, as well as hypertrophy of the left liver segments, in which no metastatic lesions were visible. The tumor thrombus was still visible in the inferior vena cava and extended to the right atrium. The AFP antigen was 17.9 ng/mL. The multidisciplinary council qualified the patient for surgery. Due to the history of coronary artery disease, hypertension, insulin-treated diabetes mellitus, preoperative diagnostics was extended to include coronary angiography, which showed a critical left main coronary artery stenosis (LM) and significant stenosis of the anterior descending branch and the circumflex left coronary artery.

Coronary artery bypass grafting (CABG) and extracorporeal circulation during removal of tumor thrombus from the inferior vena cava were necessary. Therefore, it was decided to perform a simultaneous liver tumor thrombus excision and cardiac surgery. The first stage involved myocardial revascularization without extracorporeal circulation, by implanting the left internal thoracic artery into the left anterior descending coronary artery. This was followed by a sequential bypass, implanting a fragment of the saphenous vein into the diagonal branch and the marginal branch of the left coronary artery. In the second stage, a laparotomy was performed, the arterial inflow to the right lobe of the liver was cut off, and the inferior vena cava was closed just below the liver and under the right atrium. In order to exclude the operated area from circulation, venovenous extracorporeal membrane oxygenation (ECMO) was used in the configuration of the femoral vein (collecting cannula) and right atrium (donating cannula). The rest of the operation was performed with extracorporeal circulation. After the Pringle maneuver, the wall of the inferior vena cava was incised, showing no signs of infiltration through the tumor thrombus which was removed in its entirety (Fig. 4, 5.). The circulation was then restored and a rightsided hemihepatectomy was performed without ischemia (Fig. 6.). The postoperative period was uneventful. There were no signs of hepatic failure and no abnormalities in the control echocardiogram. The patient was discharged home on the 6th post-operative day. Histopathological examination revealed a multifocal, moderately differentiated G2 hepatocellular carcinoma with infiltration of numerous venous vessels, including the inferior vena cava, in the absence of nerve infiltration, pT4N0R1 (AJCC 8th ed.). The patient was qualified for treatment with a tyrosine kinase inhibitor (Sorafenib) after oncological consultation.

**DISCUSSION**

Hepatocellular carcinoma is a highly malignant tumor with a high vascular invasion capacity through the formation of a tumor thrombus, most commonly located in the portal vein. Hepatic veins with penetration into the inferior vena cava/right atrium are less frequently involved. Unfortunately, the prognosis of HCC patients with a tumor thrombus in the inferior vena cava/right atrium is unfavorable. In the course of advanced HCC with vascular invasion, a high risk of complications such as pulmonary infarction, Budd-Chiari syndrome, thromboembolism, tricuspid valve closure or pulmonary embolism has been confirmed [1, 2–4]. Mean survival time without treatment is 2 to 5 months [1, 5, 6]. There are currently no clear guidelines available for the management of HCC with a tumor thrombus in the inferior vena cava/right atrium. The treatment includes tyrosine kinase inhibitors, transarterial chemoembolization (TACE), immunotherapy, radiotherapy, also combined with surgical treatment. There is no conclusive evidence in the literature (including randomized trials) to significantly increase survival rates after the use of these therapeutic methods. Surgical treatment (as an element of multimodal treatment), which is the only method that enables radical removal of the tumor lesion, offers a potential chance to improve the prognosis. At the same time, it should be emphasized that due to the involvement of vascular structures, the extent of the tumor thrombus, including its penetration into the right half of the heart, surgical removal of the tumor is technically extremely difficult. Right-sided hemihepatectomy with removal of the tumor thrombus, which was performed in the described case, is associated with the risk of perioperative complications in approx. 40% and death in approx. 15% [7]. The basic condition for qualification for surgery is respectability of the tumor and good hepatic reserve, which is particularly difficult to achieve in patients with cirrhosis of the liver. It should be emphasized that the use of temporary liver ischemia during surgery may temporarily or permanently affect the efficiency of the retained liver parenchyma. Therefore, only patients with the Child-Pugh score A are qualified for surgery [1, 8]. The described patient met the basic conditions of surgical treatment. At the same time, due to cardiological burden and the advancement of cancer, the patient was particularly prone to sudden cardiac death, which ultimately determined the qualification for simultaneous coronary aortic bypass surgery and liver resection with removal of the tumor thrombus. The surgery was key in the therapeutic process. However, it was only one of the stages of treatment. Initially, the patient received a selective tyrosine kinase inhibitor (Sorafenib) and underwent radiochemoembolization, which resulted in tumor shrinkage and left segment hypertrophy (improved hepatic reserve).
Therapeutic management was consistent with reports from the literature, which emphasize that neoadjuvant treatment in combination with surgery is a promising strategy for the treatment of patients with HCC and involvement of the inferior vena cava by the tumor thrombus. [9] According to the Barcelona Clinic Liver Cancer (BCLC) classification adopted by many scientific societies (including the American Association for the Study of Liver Diseases (AASLD), the European Association for the Study of the Liver (EASL) and the European Organization for Research and Treatment of Cancer (EORTC)) that asses the stage of HCC and assigning patients to appropriate treatment methods, it should be assumed that tumor thrombus in the inferior vena cava/right atrium corresponds to grade C due to the involvement of large vessels. Until recently, patients with such disease advancement were qualified for therapy with tyrosine kinase inhibitors – most often sorafenib. Currently, the first line of treatment is immunotherapy (atezolizumab in combination with bevacizumab), which is recommended by both the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) [10, 11]. Another method of palliative treatment that was previously contraindicated in HCC with a tumor thrombus penetrating the inferior vena cava/right atrium is TACE. The results of some studies indicate that patients treated with this method may achieve longer survival time than patients treated symptomatically. The mean survival rate for TACE in advanced HCC is now 4.2 to 10.9 months [12, 13]. On the other hand, this method is not free from complications such as pulmonary embolism and ischemic liver necrosis [14]. Radiotherapy is another important treatment method, and although its use in the treatment of HCC is controversial, some authors report that it can be safely employed in the treatment of HCC with invasion of the inferior vena cava. Both external and internal irradiation is approved for use at this stage of the disease. The meta-analysis (2018) assessed the effects of teleradiotherapy treatment in HCC with a tumor thrombus in the inferior vena cava/right atrium. The total irradiation dose was 48-60 Gy and the median survival time was 13.2 months [15]. Komatsu et al. compared proton radiotherapy (n = 21) with surgical treatment (n = 19). The median survival time was significantly longer in patients who received proton radiotherapy (748 days vs. 272 days) [16]. However, most authors emphasize that radiotherapy should be limited to small lesion located close to the tumor thrombus, and the effectiveness of radiotherapy is much greater in HCC with a tumor thrombus in the inferior vena cava than in the portal vein or other veins [14]. Radioembolization is a highly selective radiotherapy method that can also be used in the treatment of advanced HCC. A randomized trial published in 2017 in Lancet compared the effectiveness of this method with sorafenib. The median survival time was 8 and 9.9 months, respectively. The authors emphasize that radioembolization may be used to reduce regional disease progression. It is important to use a method that will be better tolerated by the patient and will ensure a better quality of life [17]. As mentioned above, the effectiveness of surgery in the treatment of HCC with a tumor thrombus in the inferior vena cava/right atrium has not been clearly confirmed. Earlier study results, with survival time being approximately 7–8 months, which is not much different to that of untreated patients, were unsatisfactory [18, 19]. Now, thanks to technical advances in surgery, a better understanding of HCC pathophysiology, and the possibility of using combination therapies, the survival time was significantly extended. Wang et al. and Wakayama et al. have reported that the average survival time of patients with HCC and tumor thrombus in the inferior vena cava was 19.0 and 30.8 months [6, 7]. In contrast, in the prospective cohort study of Kokudo et al. from 2017, covering the largest group of patients (n = 71) to date, the survival rate was 16.4 months [20]. The main goal of surgical treatment is radical excision of the tumor (R0). However, sometimes the indication for surgical intervention is the threatening complications related to the tumor, such as pulmonary embolism or occlusion of the tricuspid valve (as in the case of the described patient). It is not always possible to remove the tumor in its entirety (R+), and the priority is to protect the patient from sudden cardiac death in such a situation. In addition, tumor removal, even non-radical, offers a chance to extend survival. An important aspect of surgical treatment is selection of the appropriate surgical technique depending on the location of the tumor thrombus. Li et al. distinguished three possible positions in relation to the heart. In type I, the tumor thrombus is located below the diaphragm, in type II above the diaphragm, but does not reach the heart, and in type III, it penetrates the right atrium [21]. Standard surgery consists of two parts: removal of the tumor thrombus and liver resection. However, it is debatable whether the removal of the tumor thrombus should be performed first or only after liver resection. Some authors suggest its removal before hepatectomy, which is argued by the possibility of displacement of the tumor thrombus during maneuvers related to liver resection. In the
temporary block of the inferior vena cava flow and a venous bypass for extracorporeal circulation. As a result, it was possible to safely remove the entire tumor thrombus, without risking its detachment and further movement towards the heart. There was no penetration of the cancer into the right atrium and it was not necessary to open it. However, it was necessary to perform aortocoronary bypass due to critical narrowing of the coronary vessels before the main stage of surgery. Decisions regarding the treatment of a patient requiring both cardiac revascularization of the heart muscle and resection of malignant tumor are difficult due to the need for urgent intervention for each comorbid condition. Advanced coronary artery disease limits the possibilities of intensive oncological treatment [22]. The presence of coronary stenosis increases the risk of myocardial ischemia and hemodynamic instability during non-cardiac surgery [23]. Significant stenosis of the LM or three-vessel disease and associated blood flow limitation has been shown to be the cause of a fatal myocardial infarction in many cases in the presence of increased perioperative myocardial oxygen demand. On the other hand, the rehabilitation period after cardiac surgery can significantly delay the start of oncological treatment. However, it is worth emphasizing that the average 3-year survival rate for patients with at least 70% stenosis of the LM who did not undergo revascularization is only 37% [24]. The presence of comorbidities worsens the prognosis. Single reports from recent years highlight the benefits of simultaneous CABG and oncological surgery [25, 26]. Simultaneous surgical treatment does not significantly increase the surgical risk and it does not delay the oncological treatment. It is associated with a one-time stress and perioperative trauma, as well as lower consumption of anesthetics, shorter total hospitalization period, and lower treatment costs compared to two-stage treatment. However, it significantly prolongs the intervention time and increases the risk of intraoperative blood loss and perioperative bleeding due to heparinization [25, 26].

Inferior vena cava with tumor thrombus

Inferior vena cava with tumor thrombus

Ryc. 4. Inferior vena cava with tumour thrombus.

Inferior vena cava sewing line

Ryc. 5. Inferior vena cava sewing line.

Left hepatic lobe with hemostatic dressing

Ryc. 6. Left lobe of the liver with haemostat.
CONCLUSIONS

Despite the high risk of post-operative complications and mortality, surgical treatment should always be considered in the case of HCC with a tumor thrombus in the inferior vena cava/right atrium. According to the literature, surgery as the treatment method of advanced HCC in a selected group of patients increases the survival time as well as prevents complications related to a tumor thrombus in the vascular system. The choice of the surgical technique depends on the tumor thrombus location. Its penetration above the diaphragm or into the right atrium of the heart requires cardiac surgery support. When it is necessary to perform additional procedures, e.g., coronary aortic bypass, as in the case of the described patient, the risk of complications increases, however, the potential benefits of surgery should be an important argument when choosing a treatment method.

REFERENCES


