

## **A Giant Twenty Centimeters Hepatocellular Carcinoma within A Noncirrhotic, Nonfibrotic, Seronegative Liver: Surgical Approach and Outcome**

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### **Abstract**

Hepatocellular carcinoma in patients with noncirrhotic, nonfibrotic, seronegative liver also known as “normal” liver, is a rare pathological entity and data on surgical approach and outcome of these patients are limited. We present the case of a 75 years old man who came to us for abdominal right upper quadrant pain, progressively increasing in intensity during the last three months and a tumor mass felt at palpation. The CT scan showed a non-homogeneous tumor with central necrosis zones occupying the entire right lobe of the liver (18 cm/16 cm/12 cm), well defined, without macrovascular invasion, without venous thrombosis, with inferior vena cava compression. Hepatitis B and C serologies were negative. The alpha-fetoprotein was over 500 ng/ml. The patient had a small for size left hemiliver at volumetry. We performed right portal vein ligation (PVL) in the first instance. We record the success of PVL with compensatory hypertrophy at 7 weeks. The patient underwent planned laparotomy and right hepatectomy. Postoperative follow-up was uneventful and discharge in the ninth day. Functional liver reserve, more than the size of the lesion, is an important factor in the selection of patients for surgical resection. Liver resection for giant hepatocellular carcinoma can be a safe procedure in selected cases and the only curative procedure.

**Keywords:** *Liver Surgery, Hepatocellular Carcinoma, Portal Vein Ligation, Two-stage Hepatectomy, Compensatory Liver Hypertrophy*

### **Introduction**

Hepatocellular carcinoma (HCC) represents a common malignancy worldwide. It is well known that up to 90% of hepatocellular carcinomas develop on a background of cirrhosis or chronic liver inflammation [1]. The most common risk factors include chronic viral hepatitis (types B or C), aflatoxin exposure and alcohol intake. Hepatocellular carcinoma in patients with noncirrhotic, nonfibrotic, seronegative liver also known as „normal” liver, is a rare pathological entity and data on surgical approach and outcome of these patients are limited [2].

### **Case Report**

We present the case of a 75 years old man who came to us for abdominal right upper quadrant pain, progressively increasing in intensity during the last three months and a tumor mass felt at palpation. Regarding his pathological and personal antecedents, he is known to be hypertensive, had bilateral cataract surgery (2006) and a left femoral fracture in road accident (1976).

The blood tests were in normal range, except AST 104 U/L and ALT 146 U/L. Urea was 76 mg/dl, creatinine 1,26 mg/dl, INR 1,14. Abdominal ultrasound revealed a giant mass of the right lobe of the liver. Hepatitis B and C serologies were negative.

The CT scan showed a non-homogeneous tumor with central necrosis zones occupying the entire right lobe of the liver (18 cm/16 cm/12 cm), well defined, without macrovascular invasion, without venous thrombosis, with inferior vena cava compression (Figure 1).

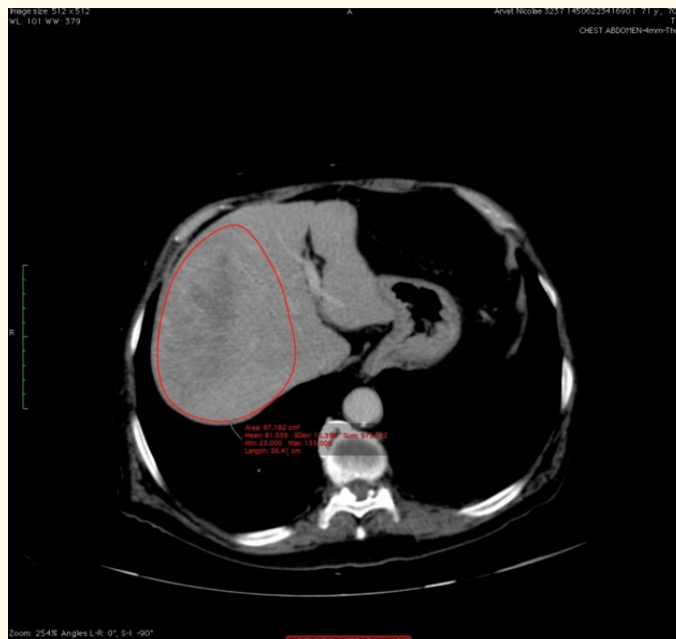


Figure 1: CT scan; tumor mass of the right lobe of the liver.

The alpha-fetoprotein was over 500 ng/ml.

The patient had a small for size left hemiliver at volumetry. The future liver remnant volume was 18,85% (Figure 2). Due to the insufficient future liver remnant, we performed right portal vein ligation (PVL) in the first instance, to convert the unresectable tumor to resectable for potential cure.

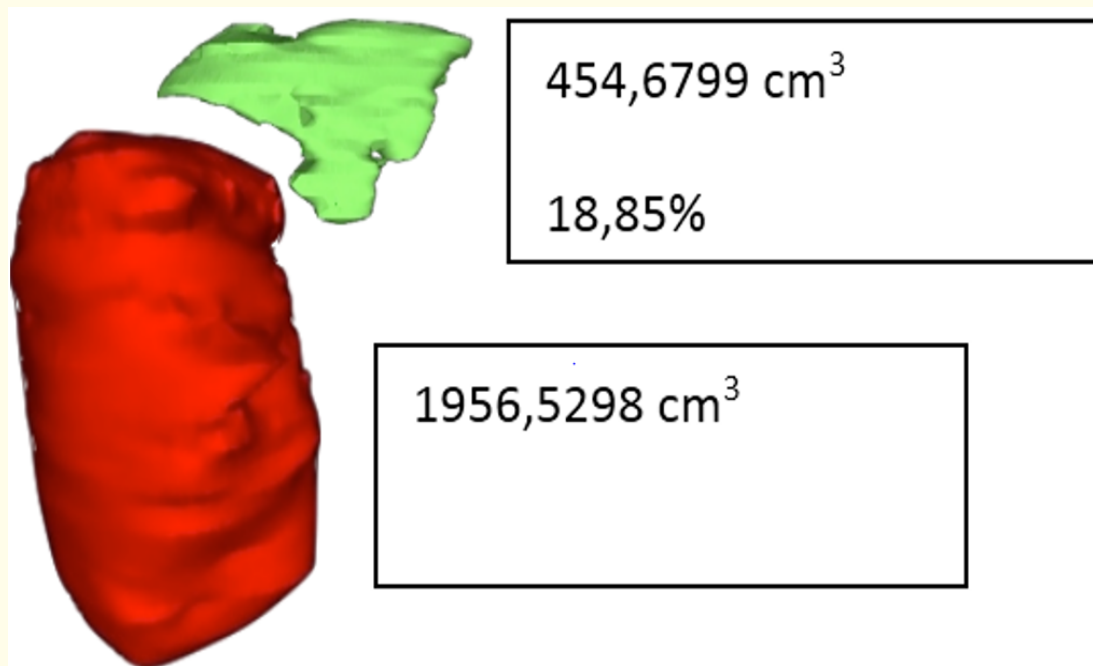


Figure 2: Liver volumetry and future liver remnant.

We record the succes of PVL with compensatory hypertrophy in the left liver, seen at seven weeks after PVL (Figure 3). The new recorded future liver remnant volume was 25,86% (Figure 4).

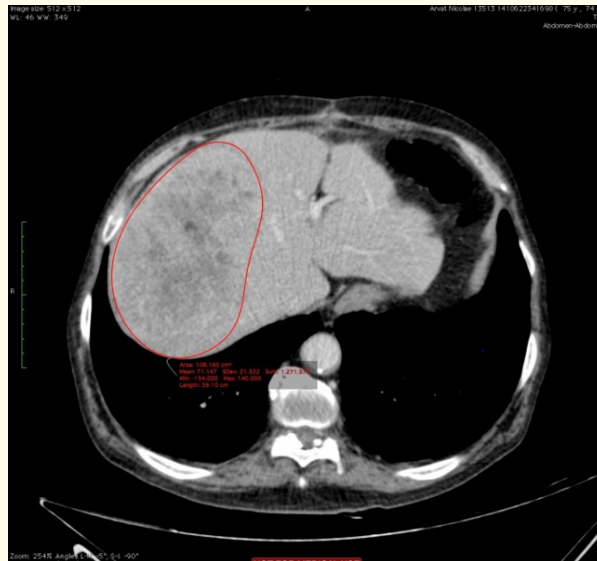


Figure 3: Aspect at seven weeks after PVL.

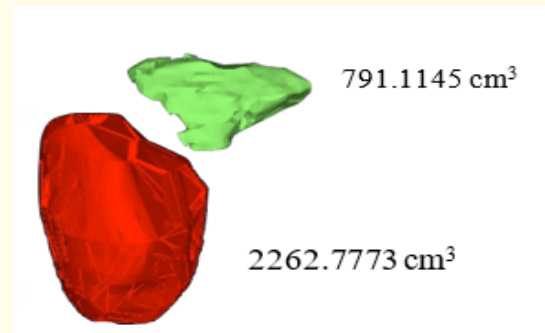
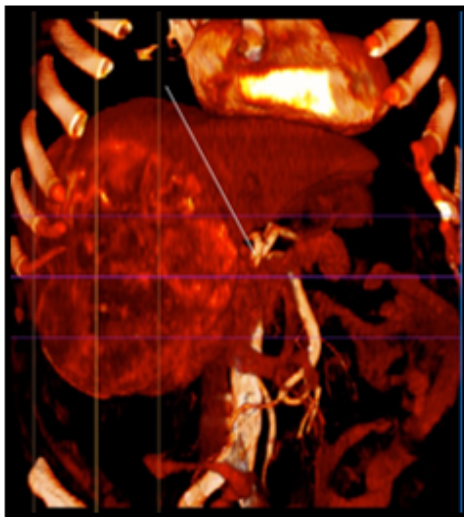
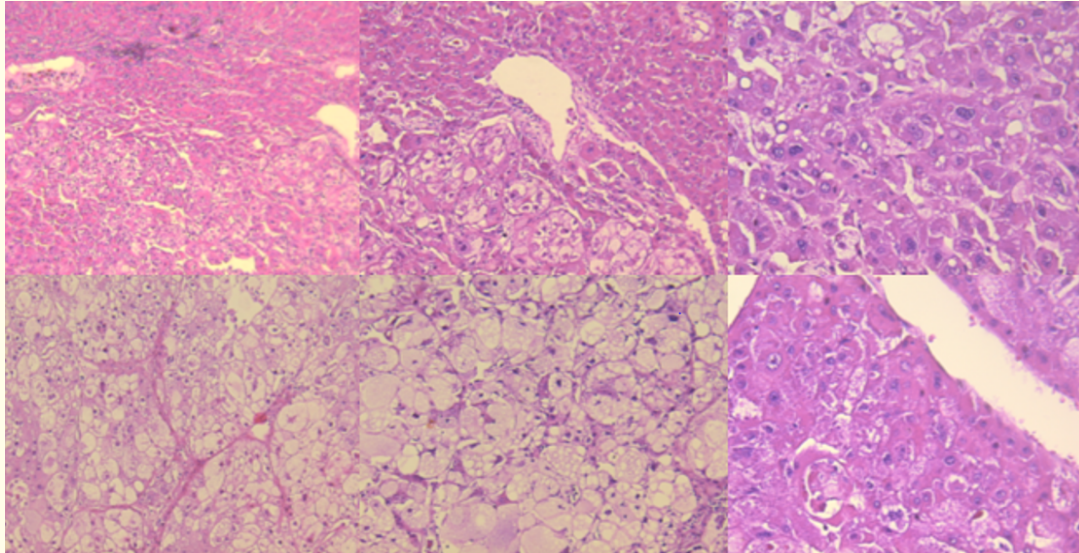


Figure 4: Reconstruction and volumetry after PVL.

The patient underwent planned laparotomy and right hepatectomy. Postoperative follow-up was uneventful and discharge in the ninth day.

Intraoperative time was 300 minutes with a difficult liver hilum dissection after PVL. The total pringle maneuver time was 40 minutes and the blood loss 600 ml. The resection specimen weighed 2900g and had 20 cm/18 cm/14 cm in dimensions. The pathology report was positive for hepatocellular carcinoma, the clear cell form (Figure 5).



**Figure 5:** Hepatocellular carcinoma; clear cell form.

## Discussion

Hepatocellular carcinoma within a normal liver, meaning a noncirrhotic, nonfibrotic, seronegative liver (without evidence of viral hepatitis B or C infection) is a rare pathological entity [3].

Usually HCC develops when there is an already existing liver disease and the existing treatment guidelines addresses to this situation. When talking about patients with pre-existent liver disease the treatment of choice for HCC's lesser than five centimeters in diameter is surgery or transplantation. Giant HCCs are those over ten centimeters in diameter. Treatment of those is controversial and the majority of clinical guidelines recommend palliative treatments such as transcatheter chemoembolization and systemic therapy [4]. This happens because of the risk of postoperative liver failure for those with unsatisfactory volume and quality of the future liver remnant and because of the risk of cancer recurrence after surgery [5].

For HCC patients only liver resection or transplantation can be considered curative. If for patients with chronic hepatopathies there are screening programs for detection of early HCC, for patients with HCC arising in a normal liver we lack this screening. Thus they tend to present at later stages and usually fall outside the transplantation criteria mentioned in guidelines because of the tumors size [6].

Even if the guidelines do not recommend resection for giant HCC, centers around the world use this procedure to treat HCC, especially in patients with a normal liver and a satisfactory future liver remnant, since this is the only curative option when they fall outside transplantation criteria. Resectability of the tumor needs enough future liver remnant regarding quantity and quality. If quality is not a problem

for HCC arising in normal livers, quantity can be and this can be increased through hypertrophy. Hypertrophy, in selected cases, can be achieved by several techniques, such as: ligation or embolization of the portal vein which supplies the liver lobe to be resected or ALPPS procedure. If resectability can be achieved even for giant HCC, the main concern is regarding its safety, outcomes and the predictive factors for disease free survival time and overall survival.

Tsoufas, *et al.* in their review of the literature „Surgical treatment for large hepatocellular carcinoma: does size matter?“ found 5223 patients with HCC tumors over 10 centimeters in 22 non-duplicated papers across 18 years and showed that for patients with single HCC lesion and no cirrhosis the 5-year disease free survival ranged between 41% and 56%, respectively. The main risk factors affecting the outcome of patients undergoing surgery for giant HCC were vascular invasion, cirrhosis, high levels of alpha-fetoprotein and the presence of multiple lesions. They concluded that resection for large HCC can have good outcomes in carefully selected patients [7]. In our case only the alpha-fetoprotein was elevated. We had no macrovascular invasion on CT scan and there was no venous thrombosis. Also there was a single large lesion.

In another review of the literature „Resection for Hepatocellular Carcinoma“ by Hariharan Ramesh, the results were similar when treating HCC patients with normal liver. The conclusion was that resection is the treatment of choice for patients with normal liver if an R0 resection can be reached and leaving a satisfactory liver remnant [8].

In a study analyzing 81 patients with large HCC resection and healthy future liver remnant, Alastair, *et al.* concluded that although challenging techniques were required, if an R0 resection can be carried out, excellent outcomes can be achieved [2].

When thinking at recurrence risk, A Laurenzi, *et al.* in a study where they had 81 patients undergoing liver resection for HCC within a normal liver and a follow up of more than 10 years they concluded that micro and macrovascular invasion were the only predictive factors for recurrence [9].

In „Results of hepatic resection for hepatocellular carcinoma invading major portal and/or hepatic veins“ published by Ikai I., *et al.* the reported 5-year overall survival 63% in those without vascular invasion, respectively 46% [10]. Portal vein invasion and intrahepatic dissemination is thought to be the mechanism of in-liver recurrence.

Another important concept is the one of macrovascular invasion or microvascular invasion. Roayaie S., *et al.* demonstrated in „A system of classifying microvascular invasion to predict outcome after resection in patients with hepatocellular carcinoma“ that overall survival differs when macrovascular invasion is present (20%) versus microvascular invasion (40%) [11].

The biggest HCC resection described in literature has been published by Ming-Chen Ba., *et al.* They report the successful resection of a hepatocellular carcinoma weighing 10,050g and 35 cm/30 cm/15 cm in size [12].

Achieving hypertrophy for further liver remnant prior curative liver resection can increase survival. Miyoshi A., *et al.* published a portal vein embolization study in which they compared the survival, in patients who had and who had not this procedure done before resection. The 5-year overall survival was 45% in the group who had not portal vein embolization prior to surgery, respectively 58% in the group who had portal vein embolization [13].

### Conclusion

Functional liver reserve, more than the size of the lesion, is an important factor in the selection of patients for surgical resection. Resection for giant hepatocellular carcinoma in normal liver is a safe procedure in selected cases and the only curative procedure for patients. This requires experienced teams of surgeons and anesthesiologists. The majority of studies shows that size does not influence surgi-

cal outcomes in resection of giant hepatocellular carcinoma. Excellent outcomes can be achieved in patients for which this tumors can be completely resected. A consensus meeting and elaborating guidelines for giant hepatocellular carcinoma should be taken into account by the specialized personnel.

### **Author Contributions**

All authors contributed equally to this work.

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