



# Treatment of Hepatocellular Cancer Due to Hepatitis Delta with Yttrium-90 Radioembolization in a Patient with Cirrhosis: A Case Report

Delta Hepatitine Bağlı Sirozlu Hastada Hepatosellüler Kanserin Yttrium-90 ile Radyoembolizasyon Tedavisi: Olgu Sunumu

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## ABSTRACT

Cirrhosis due to delta hepatitis is one of the most important etiologic factors in our country. Hepatocellular carcinoma (HCC) often develops on the base of cirrhosis. Recently, yttrium-90 radioembolization therapy has been increasingly used in the treatment of HCC. Transarterial infusion of yttrium-90 radioactive microspheres is a new promising method in treating unresectable liver tumors. Herein, we present a 55-year-old male HCC patient who developed HCC due cirrhosis associated with delta hepatitis and was successfully treated with yttrium-90 radioembolization therapy. (Viral Hepatitis Journal 2014; 20(3): 131-133)

**Key words:** Hepatocellular cancer, yttrium-90

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## ÖZET

Ülkemizde sirozun önemli etyolojik nedenlerinden biri delta hepatitidir. Hepatosellüler kanser (HSK) sıklıkla siroz zemininde gelişmektedir. HSK tedavisinde radyoembolizasyon olarak adlandırılan yttrium-90 tedavisi son yıllarda gittikçe daha yaygın kullanılmaktadır. Radyoaktif mikropartiküllerin transarteriyel olarak infüze edilmesinden oluşan ve daha yeni bir yöntem olan radyoembolizasyonun rezeke edilemeyen karaciğer tümörlerinde umut vaat ettiği bildirilmiştir. Delta hepatitine bağlı kompense karaciğer sirozu zemininde HSK gelişen ve yttrium-90 ile başarılı kemoembolizasyonu yapılan 55 yaşında erkek hasta sunulmuştur. (Viral Hepatit Dergisi 2014; 20(3): 131-133)

**Anahtar kelimeler:** Hepatosellüler kanser, yttrium-90

**Çıkar çatışması:** Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

## Introduction

Hepatocellular carcinoma (HCC) is one of the most widely seen malignities in the world; it constitutes 90% of liver cancers and its incidence is still increasing. Its curative treatments are surgical resection and liver transplantation, but many patients lose their chance of surgery for being at an advanced stage. Its palliative treatments include radiofrequency ablation therapy, transarterial chemoembolization, chemotherapy and radiotherapy (1).

Cirrhosis associated with hepatitis B virus (HBV) infection is still one of the major risk factors in developing HCC. In Turkey, HCC is

hardly diagnosed at an early stage (2,3). Hepatitis delta virus (HDV) infection increases the risk for HCC 3 times, and for mortality, 2 times (4). Our country is moderately endemic in terms of HBV and the prevalence of HDV is around 5%. Chronic delta hepatitis is difficult to treat and is one of the major etiologic reasons of cirrhosis and HCC in our country (5,6,7).

Besides transarterial chemoembolization (TACE), yttrium-90 therapy (Y90), which is defined as transarterial radioembolization (TARE), is being used increasingly in recent years to treat HCC. It has been also reported that radiation lobectomy using Y90 is an effective and safe technique for the hypertrophy of the remaining

part of the liver and this new technique can be used as a bridge to resection and transplantation (8,9).

This procedure is named as radioembolization and has two separate stages: the first one is the injection of embolic particles as a medium (embolization) and the administration of radiation from this medium (radio). The procedure involves transarterial administration of radioisotope loaded micron-sized particles. Emergence of complications is rare, but nausea, weakness, abdominal pain, hepatic failure, biliary damage, fibrosis, radiation pneumonia, gastrointestinal ulcers, and vascular damage may be seen. These side effects can be prevented by a meticulous evaluation before the treatment, careful selection of patients and adequate dosimetry (10).

A 55-year-old male patient who was diagnosed with HCC on the basis of compensated liver cirrhosis associated with delta hepatitis was administered radioembolization with Y90.

## Case

The patient had been known to have a positive HBsAg for a long time, but had not been monitored regularly. HCC indicating lesions of 2 cm in the cirrhotic segment 7 and 6 cm in segment 6 of the liver were detected by abdominal magnetic resonance imaging (MRI) during his examinations in November 2008. The patient had positive HBsAg and anti-delta and negative HBV-DNA and HDV-RNA. He was hospitalized to be assessed for transplantation.

On physical examination, there was no hepatomegalia, Traube's space was open and there was no acid. His tests revealed the following results: WBC:4000/mm<sup>3</sup>, hemoglobin:12.4 g/dL, hematocrit: 35.8%, thrombocyte: 105000/mm<sup>3</sup>, glucose: 111 mg/dL, BUN: 16 mg/dL, creatinine: 0.7 mg/dl, ALP: 290 U/L, GGT: 95 U/L, AST: 43 U/L, ALT: 48 U/L, LDH: 325 U/L, Tbil: 0.47 mg/dL, PT: 15.2 sec and AFP: 14 ng/mL.

100-300 micron drug eluting microspheres loaded with 50 mg doxorubicin was injected through his distal cystic artery into his right hepatic artery and polyvinyl alcohol (PVA) particles were given to the artery feeding the lump to complete the embolization procedure. Following the procedure, he had a fever of up to 39 °C during his monitoring, but his overall condition did not get worse. His hemodynamic parameters remained stable, his highest CRP value reached 114 mg/dL (normal less than 0.1 mg/dL) and, there was no growth in his hemocultures and urine cultures. No abdominal sensitivity or pain in his upper right quadrant was detected on his physical examination. His abdominal ultrasonography revealed changes in his liver due to radioembolization, but there were no signs suggesting any septic complication. When empirical ampicilline-sulbactam 4x1 g and paracetamol tablet 4x1 were started, his fever went down and CRP values declined. At post-embolization day 14, his unenhanced abdominal computed tomography was taken to assess the effectiveness of the procedure. Necrosis and air were seen in the lesion and the procedure was accepted to be successful. He was then discharged after deciding that his antibiotic treatment was to be completed orally through 3 weeks. It was planned to reassess the patient for transplantation based on his results by taking his MRI 3 months later.

## Discussion

Chronic infection associated with delta virus is a risk factor for cirrhosis and HCC. High HDV viremia increases the risk of developing cirrhosis and HCC. A HDV replication is a predictor for poor prognosis in a patient developing cirrhosis (11). A persistent HDV replication causes cirrhosis and HCC at annual rates of 4% and 2.4%, respectively; and it is the only predictor for liver mortality (12). In our patient, cirrhosis and HCC developed due to delta hepatitis. Although the patient had been known to be HBsAg-positive for a long time, anti-delta was detected just recently. His HBV-DNA and HDV-RNA was found to be negative.

HCC is a tumor exhibiting heterogeneity depending on morphologic, biological and hepatic functions. There is a risk of recurrence and deficient treatment after TACE depending mostly on the size and multitude of the tumors in a medium stage HCC. Suppression of angiogenic stimulation after TACE may be a rational approach and radioembolization with Y90 is promising for medium-stage HCC. Information on internal radiation therapy with Y90 for advance-stage HCC is still not satisfactory (13). Preoperative TARE may be an option for curative treatment for HCC patients with unresectable liver cancer and are candidates for palliative care (14). Our patient was a medium-stage patient and was administered TARE as he had no chance of having transplantation immediately.

A study made in Turkey reported that when compared to TACE, TARE caused less systemic toxicity and could be administered without hospitalization, to the advantage of both physicians and their patients. With the limited experience in the study, it was shown that TARE was a promising method in the initial-stage treatment of a liver cancer not allowing resection, however, it was also reported that there was a need for further randomized, controlled and multicenter studies (15). Another study reported low frequency of experiencing complications, including nausea, weakness, abdominal pain, hepatic failure, biliary damage, fibrosis, radiation pneumonia, gastrointestinal ulcers and vascular damage that can be prevented by meticulous evaluation before treatment, careful selection of patients and adequate dosimetry (10). Our patient, had fever, his condition did not get worse, his hemodynamic parameters remained stable and CRP levels were high. His abdominal ultrasonography revealed no signs suggesting any septic complication. When empirical ampicilline-sulbactam 4x1 g and paracetamol tablet 4x1 were started, his fever went down and CRP values declined.

A radical treatment following a tumor regression therapy with TARE in advanced HCC patients exceeding the UCSF/Milan criteria may be applicable in selected subgroups (UNOS T3 stage) by also considering the other restrictive factors. The overall survival without tumors after transplantation in patients who are administered a successful regression therapy is as excellent as in patients meeting the required criteria (16,17). Our patient had HCC indicating lesions of 2 cm in the cirrhotic segment 7 cm and 6 cm in segment 6 of the liver detected by MRI and he was at the limit with respect to the Milan criteria, but he had no donor for immediate transplantation. With a successful TARE, time was gained for transplantation and the procedure proved to be a bridge to a perfect transplantation.

Patients with portal vein thrombosis (PVT) have an extremely poor prognosis and have relatively minimal treatment options. Evidences have shown that TARE is a good option for such patients. The accumulated data on Y90 radioembolization have shown that it is a potent anticancer treatment method with acceptable side effects, provided that appropriate assessments including dosimetry are employed before treatment. The combination of TARE and the molecular agents directly aiming the target exhibit a synergic effect on survival. With the Y90 TARE method, the disease is controlled at a rate more than 80% and it is generally well tolerated. It's major complication is PVT, however, this is not due to its microembolic effect but its radiation effect on untargeted tissues including the liver (18,19,20,21). No PVT was detected in our patient. Despite some side effects, the procedure was successful.

In conclusion, Y90 radioembolization should be considered as a treatment option in patients with HCC with unresected liver cancer or in those with no chance of immediate transplantation.

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