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Hepatocellular Carcinoma with Increased AFP Levels and Extrahepatic Manifestation after Liver Transplantation: A Case of Late-Onset Recurrence

Karaciğer Nakli Sonrası AFP Yüksekliği ve Extrahepatik Tutulum Saptanan Hepatoselüler Karsinoma: Gecikmiş Rekürensli bir Olgu Sunumu

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ABSTRACT

Liver transplantation is the best treatment modality in patients with hepatocellular carcinoma. The major concern after liver transplantation for hepatocellular carcinoma treatment is recurrence, because it's the most important factor for the long term survival. There are two forms of recurrence; early-onset (within 2 years of liver transplantation) and late-onset (after 2 years of liver transplantation). A lot of factors have been reported in the literature to foresee recurrence after liver transplantation and one of them is alpha-fetoprotein. Many studies have shown that high levels of pre-transplant alpha-fetoprotein is related to early-onset recurrence and worse outcomes in the long term. In this case report, we report a case of late-onset recurrence, despite having high levels of pre-transplant alpha-fetoprotein in contrary to the literature, and still survive with a high quality of life 6 years after transplantation.
Keywords: Hepatocellular carcinoma; alpha-fetoprotein; recurrence.

ÖZ

Hepatoselüler karsinoma tedavisinde en iyi tedavi metodu karaciğer transplantasyonudur. Hepatoselüler karsinoma tedavisi için uygulanan karaciğer transplantasyonu sonrası en büyük endişe rekürenstir, çünkü uzun dönem sağkalım için en önemli faktördür. Rekürens erken (karaciğer transplantasyonu sonrası 2 yıl içinde) ve geç (karaciğer transplantasyonundan 2 yıl sonra) olmak üzere iki çeşittir. Literatürde karaciğer transplantasyonu sonrası rekürensi öngörmek için pek çok faktör öne sürülmüştür ve bunlardan biri de alfa-feto proteindir. Pek çok çalışma, transplantasyon öncesi yüksek alfa-feto protein düzeylerinin erken rekürens ve uzun dönemde kötü sonuçlar ile ilişkili olduğunu göstermiştir. Bu olgu sunumunda, literatürde bildirilenin aksine transplantasyon öncesi yüksek alfa-fetoprotein düzeylerine sahip olmasına rağmen geç rekürens gösteren ve transplantasyondan 6 yıl sonra hala yüksek bir yaşam kalitesi ile sağkalım gösteren bir vaka bildiriyoruz.
Anahtar kelimeler: Hepatoselüler karsinoma; alfa-fetoprotein; rekürens.

INTRODUCTION

Liver transplantation (LT) is the best treatment option for hepatocellular carcinoma (HCC) in select cases. LT is usually performed according to Milan Criteria, but the recurrence can be seen up to 15% of cases. Recurrence is the biggest concern after LT because it's the most important prognostic factor. There are two forms of recurrence; (1) early-onset (<2 years after LT) and late-onset (>2 years after LT). Serum markers are useful to determine and to foresee recurrence after LT (1).

Alfa-fetoprotein (AFP) is the most used serum marker for HCC and it can also be used to determine recurrence after LT. There is a correlation between pre-transplant high AFP levels and post-transplant recurrence (2).

CASE REPORT

A 64-year-old male patient with the diagnosis of chronic viral hepatitis-B in 2007 and on routine follow-up under entecavir treatment. During routine follow-up in 2011, abdominal ultrasound showed two focal lesions in the right lobe of the liver and

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dynamic liver magnetic resonance imaging (MRI) confirmed the diagnosis of HCC in segment-7 (2 cm) and segment-8 (1.5 cm). Radiofrequency ablation (RFA) has been performed separately. Three months after the procedure both lesions were progressed up to 5 cm and new lesions were found in the right lobe of the liver. Trans-arterial chemoembolization (TACE) was performed and the patient had LT in 2012 despite being out of the Milan Criteria and with an AFP level of 3295 IU/ml. Three months after LT, AFP levels were 5 IU/ml.

On routine follow-up in 2015, a sudden increase in AFP levels (145 IU/ml) was encountered but no lesions were detected on the MRI. AFP levels kept increasing and no lesions were detected on routine trimonthly MRI scans. AFP levels reached up to 2049 IU/ml in 2017, therefore the patient diagnosed as recurrence and started on Sorafenib treatment. 6 months after initiation of the therapy, AFP levels kept rising up to 7724 IU/ml and MRI showed pre-caval 20x13mm and pre-aortic 20x18mm HCC lesions (Figure 1). Positron emission tomography (PET-CT) showed a pre-caval lymph node (SUVmax:4) and a pre-aortic lymph node (SUVmax:6.7) consistent with HCC (Figure 2). The patient started on regorafenib treatment. A signed informed consent form was obtained from the patient for this case presentation.

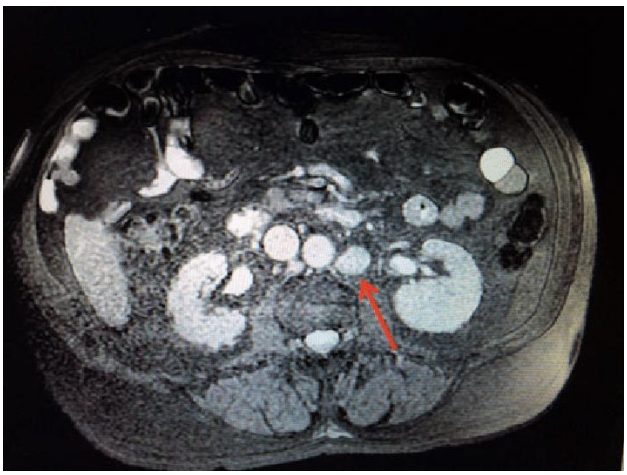

Figure 1. Para-aortic lymph node in magnetic resonance imaging

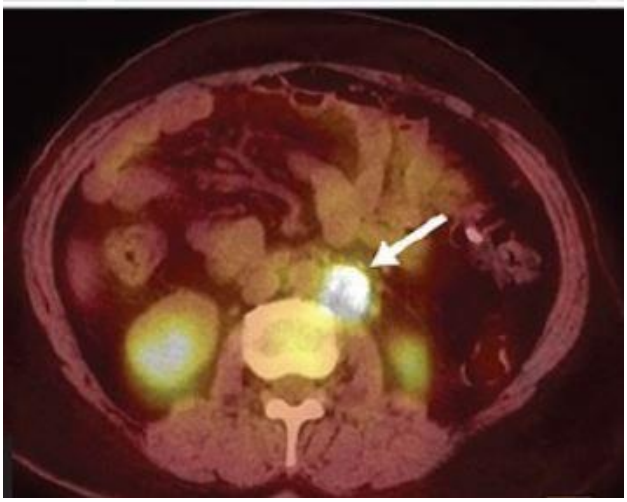

Figure 2. Para-aortic lymph node in positron emission tomography

DISCUSSION

We presented a case of late-onset recurrence after LT, despite having pre-transplant high levels of AFP and detected in a rare localization. Pre-transplant high levels of AFP (>400 IU/ml) were identified as a high-risk factor for recurrence after LT (3). In our case, pre-transplant AFP was 3295 IU/ml but we did not encounter early-onset recurrence. Microvascular invasion, large tumor diameter, high AFP levels, and poor histological differentiation are defined as high risk factors for recurrence after LT (4). Despite having a large tumor diameter and high AFP levels, the patient had a long-term survival with a late-onset recurrence. This can be explained with tumor biology and heterogenicity. The clinical course of HCC may vary significantly. Multifocal mutations can be seen even in a single tumor and tumor doubling time may vary between tumor nodules (5). It should also be noted that the tumor microenvironment has high inflammatory properties and may cause changes in tumor behavior (6).

The liver, lungs, and bones are the most common sites of recurrence after LT respectively (7). In our case, we found metastatic lymph nodes in a very rare localization. We suggest that in suspected cases of late-onset recurrence, rare localizations for the tumor should be suspected and PET-CT can be used to strengthen the diagnosis.

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