Journal of Liver
ISSN: 2167-0889

Alazzawi et al., J Liver 2017, 6:1
DOI: 10.4172/2167-0889.1000207

Case Report Open Access

A Confusing Complication of Liver Biopsy: First Case Report of Seeding/Implantation of Hepatocellular Carcinoma 9 Years from the Original Liver Biopsy

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Recieved date: December 10, 2016; **Accepted date:** January 02, 2017; **Published date:** January 09, 2017

Abstract

The incidence of seeding/implantation of hepatocellular carcinoma (HCC) after liver biopsy or radio frequency ablation (RFA) is not well reported but estimated to be low. With the introduction of immunosuppression the risk has been increased and most of the seeding sites are chest wall and abdominal muscles. We report the first case report of HCC seeding after 9 years from the original liver biopsy.

A 66 years old gentleman with cirrhosis secondary to hepatitis C virus infection and long history of alcohol abuse found to have a liver lesion during his screening by ultrasound and underwent percutaneous liver biopsy, which revealed hepatocellular carcinoma in 2006 and then the patient had a liver transplantation surgery in 2006 from cardiac death donor.

The post transplantation course was uneventful and started on dual immunosuppression including Tacrolimus and Mycophenolate mofetil with acceptable levels through the whole treatment duration. All the follow up routine check ups including CT scan, liver biopsy, liver function tests and cancer screening were unremarkable and alpha-fetoprotein (AFP) was within acceptable level except slight increase in the AFP early 2015.

His increase in AFP raised the concern for recurrence of HCC and his work up for possible recurrence or metastasis was negative including CT scan of the chest, abdomen and pelvis. Later in the 2015, the patient presented to his primary care physician complaining of right upper quadrant pain and swelling for which he underwent excisional biopsy of the skin. The skin nodule been fully resected and was 1.5 cm in diameter and its 10-15 cm from the original HCC. The pathology results of the specimen revealed that its metastatic hepatocellular carcinoma involving the subcutaneous tissue with negative margins, the immunostains were positive for Heppar1 immunestains and equivocal for glypican 3. This represents a local seeding of the original HCC 9 years after the liver biopsy location. This finding also was confirmed upon reviewing the images of the original HCC and the new metastatic HCC that showed it has same track of the liver biopsy in 2006.

This case report is to increase the awareness of hepatologist and primary care physicians of the risk of skin HCC implantation and consider a routine check during the clinic visits in addition to the dermatologist skin screening visits. More research needed to investigate the rule of immunosuppression on seeding and implantation of HCC.

Keywords: Hepatitis C virus; Hepatitis B virus reactivation; Human immunodeficiency virus; Direct acting antivirals

Introduction

The incidence of seeding/implantation of hepatocellular carcinoma (HCC) after liver biopsy or radio frequency ablation (RFA) is rare but expected to increase after the introduction of the immunosuppression in organ recipient transplanted patients and its widely use in the last ten years. Most of the seeding sites are chest wall and abdominal muscles. We report the first case report of seeding/implantation of HCC in transplanted liver 9 years after the original liver biopsy.

Case Report

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The post transplantation course was uneventful and started on dual immunosuppression including Tacrolimus and Mycophenolate mofetil with acceptable levels through the whole treatment duration. All the follow up routine check ups including CT, liver biopsy, liver function tests and cancer screening were unremarkable and alpha-fetoprotein (AFP) was within acceptable level except slight increase in the AFP early 2015 (Figure 1).

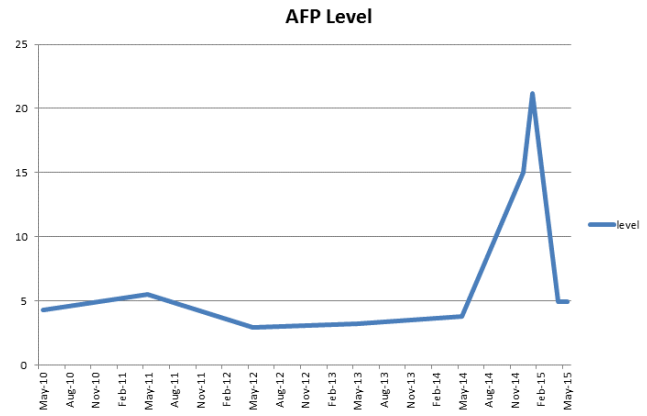

Figure 1: Acceptable level except slight increase in the AFP early 2015.

His increase in AFP raised the concern for recurrence of HCC and his work up for possible recurrence or metastasis was negative including CT scan of the chest, abdomen and pelvis. Later in the 2015, the patient presented to his primary care physician complaining of right upper quadrant pain and swelling for which he underwent excisional biopsy of the skin. The skin nodule been fully resected and was 1.5 cm in diameter and its 10-15 cm from the original HCC.

The pathology results of the specimen revealed that its metastatic hepatocellular carcinoma involving the subcutaneous tissue with negative margins, the immunostains were positive for Heppar1 immunestains and equivocal for glypican 3 (Figure 2A-2C). This represents a local seeding of the original HCC 9 years after the liver biopsy location. This finding also was confirmed upon reviewing the images of the original HCC and the new metastatic HCC that showed it has same track of the liver biopsy in 2006 (Figure 3A and 3B). Follow up in the clinic with CT scan did not show any signs of metastasis or recurrence of the HCC found and his AFP level returned back to normal.

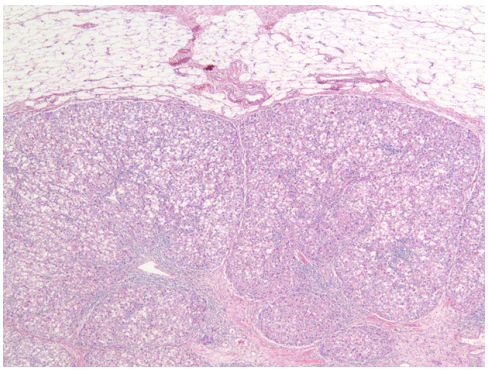

Figure 2A: Metastatic hepatocellular carcinoma involving the subcutaneous tissue with negative margins.

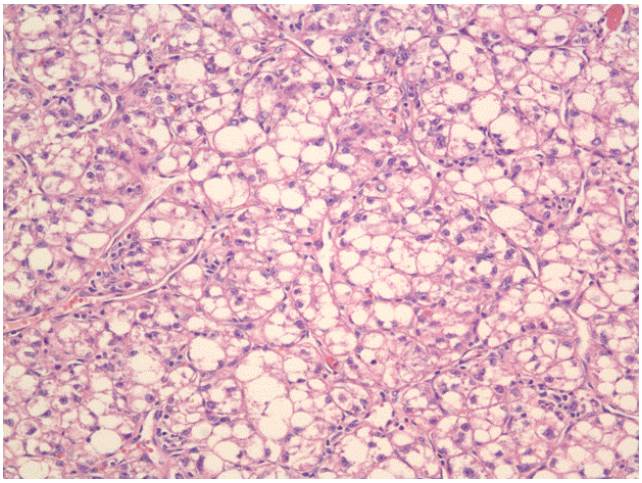

Figure 2B: Metastatic hepatocellular carcinoma involving the immunostains were positive for Heppar1 immunestains.

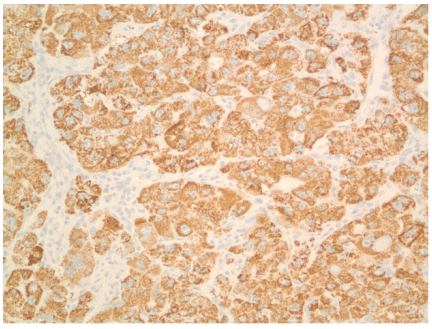

Figure 2C: Metastatic hepatocellular carcinoma involving the immunestains equivocal for glypican 3.

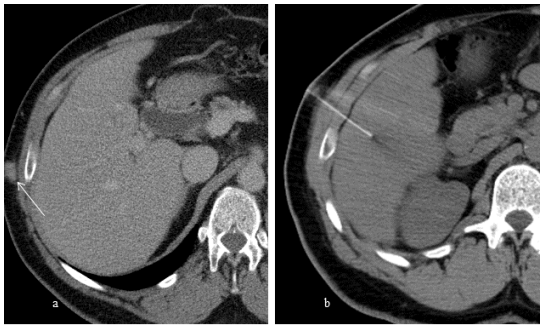

Figure 3: local seeding of AFP levels for different years a: original HCC in 2006; b: new metastatic HCC.

Discussion

HCC is the second leading cause of cancer related death in the world and the annual incidence of hepatocellular carcinoma was at least 6 per 100,000 in 2010 in the USA [1]. The development of a

screening program for early detection and diagnosis of primary hepatocellular carcinoma, such as a regular check-up for alpha-fetoprotein levels and an ultrasonogram in the high-risk group increased the survival rate by formulating a curative approach when the tumor is small rather than palliative approach when the tumor size is big and metastasized.

Liver Lesions that detected by ultrasound should be evaluated with dynamic MRI or helical multidetector CT scan using contrast that has the characteristic diagnostic features of the hyper-vascular lesion with delay washout. For the small lesions especially less than 1 cm in diameter and those without the classic characteristic features of HCC, liver biopsy should be considered. In our case report the liver lesion did not show the characteristic features of HCC and the patient underwent percutaneous liver biopsy for better evaluation [1-3].

Liver biopsy procedure is like any other procedure has some complications including but not limited to hemorrhage, perforation, infection, death and seeding of the tumors [4,5]. Very few cases reported the implantation/seeding of the original HCC following the liver biopsy or RFA and incidence is estimated to be 2.1-5% with a mean time for seeding is estimated between 8 and 48 months. The location of the implantation varies from the chest wall, abdominal wall, and abdominal muscles or can be presented as skin lesion like in our case [6,7].

Our patient developed a skin lesion that was investigated like any other skin lesions in the transplant patients especially those on immunosuppression medication with a high concern of a skin cancers, the skin lesion been evaluated extensively and biopsied. The skin biopsy surprisingly revealed a percutaneous HCC. Most of the studies showed that there is an increase in the risk of skin malignancies specifically squamous cell carcinoma and basal cell carcinoma which are the most common forms of malignancy in recipients of solid organ transplants especially in the smokers, elderly and inflammatory bowel disease and reported as 0.9-3.2% [8].

The incidence of seeding of malignancy following biopsy is low and estimated as (0.003-0.009) and it was first reported in a case series by Dr. Smith which his findings was based on questionnaires to many centers between 1986 and 1987 [8,9]. While the highest incidence case series of HCC seeding following liver biopsy was documented by Takamori et al. [7] with an estimate of 5% in a small study group of 59 patients. One of the biggest retrospective studies enrolled 1055 patients studying the seeding of malignancy following biopsy procedure, the study reviewed the CT scan from the day the patient underwent the liver biopsy to the date the patient diagnosed with HCC on the track of the biopsy. The study showed that a mean time interval between biopsy and the emergence of the implanted tumor on CT scan was 267 days (range, 116-619 days) with mean doubling time of 112 days. Only 8 patients from the total 1055 developed HCC on the site of the biopsy with an incidence of 0.76% [4].

Despite the fact that there is no data regards the immunosuppression's influence on seeding of HCC, our patient had a stable immunosuppression levels throughout the course of post transplant follow up and his seeding HCC developed after 108 months from the date of the biopsy which longer than any documented case.

Huang et al. [6] in his study of 420 patients that the implanted HCCs along the needle tract developed in 9 of 420 patients with incidence of 2.1% with 18-36 months range of the diagnosis from the biopsy date while Maturen et al. [10] indicates that Utilizing a 17-gauge introducer and an 18-gauge biopsy needle introduced along a coaxial plane decrease the risk of seeding as away to minimize the risk of seeding [6,10].

With the increase in the types of immunosuppression therapy in transplant recipients, we expect an aggressive pattern of seeding/implantation and a faster doubling time but in our case report, our patient developed percutaneous HCC after 108 months from the date of the biopsy. That's elucidate the fact that there is no actual data or studies examined the effect of immunosuppression on the incidence of seeding of HCC following liver biopsy but expected to be higher and has more aggressive pattern than patients without immunosuppression. Our case report enlightens that a future research is essential to investigate the effect of deferent kinds of immunosuppression medication and its correlation with the incidence of seeding HCC.

Conclusion

Liver biopsy is one of the diagnostic tolls to investigate liver lesion and to confirm hepatocellular carcinoma in patients with liver lesion in whom the radiologic characteristic features of HCC are equivocal and questionable. Liver biopsy is not without any complication, one of the complications is seeding of the original tumor that is underestimated and can be missed through the routine check up. This case report is to increase the awareness of hepatologist and primary care physicians of the risk of skin HCC implantation and consider a routine check during the clinic visits in addition to the dermatologist skin screening visits. More research needed to investigate the rule of immunosuppression on seeding and implantation of HCC.

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