中文題目：肝癌患者接受肝動脈化學藥物栓塞合併放射線治療後慢性 B 型肝炎復發

英文題目：Reactivation of hepatitis B virus after TACE combined radiotherapy: a case report

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Introduction and aim

Hepatocellular carcinoma (HCC) caused by chronic hepatitis B virus (HBV) infection is a major health problem in Asian people[1].In Taiwan , the annual incidence of HBV-related HCCs was 378 per 100,000 persons in 2002.[2]The posthepatectomy HBV reactivation is an independent factor of HBV related HCC that affects the overall survival and disease free survival.[3] Transarterial chemoembolization (TACE) is one of the treatment choice of intermediate stage HCC .The TACE does have a systemic effect through arterio-venous shunt or peritumoral microcirculation, by which host immune regulation is often compromised. Several evidences show that TACE or radiotherapy(RT) alone is directly associated with an increased rate of HBV reactivation.[4] In Korea, HBV reactivation with TACE than with other local therapies is 21.7% vs 1.6%,respectively[5] and it occurs after a median of 3.5 cycles following initiation of TACE.[6]The rate of HBV reactivation after TACE is not a rare clinical condition. However, the prevalence of HBV reactivation after TACE in Taiwan is still not reported until now.

This case is aimed to share a case about reactivation of hepatitis B virus after TACE combined radiotherapy treatment and remind the importance of HCC patient with chronic HBV infection who should be closely monitored HBV status during treatment.

Case presentation

A 76-year-old male with past history of chronic hepatitis B infection, and liver cell carcinoma, cT3N0M0, stage 3 ,s/p Transcatheter Arterial Chemo-Embolization on 2019-09- 06, 2019-10-11, 2019-11-13 and 2019-12-31 ,s/p radiotherapy on 2019-12-26 to 2020-02-11 presented with general malaise for one week. (figure 1)

He had mild dyspnea after completing radiotherapy one week ago, accompanied with decreased appetite since then. He denied fever, dysuria, abdomen pain, nor diarrhea. His performance status was ECOG 1. He then visited radiation therapy(RT) out-patient clinic(OPD) where the lab data showed AST/ALT level

increased(2276/1987 (U/L)) (one week ago 448/443 (U/L)) and total bilirubin level increased (1.57 (mmol/L))(one week ago 1.30 (mmol/L))(Figure 2).He was then transferred back to Gastroenterology (GI) OPD at the same day.

At GI OPD, the mild epigastric pain was told by patient. The followed lab data showed HBsAg(concentration): Reactive (3716 IU/ml). The abdominal echo showed 1.a tumor over S4(9 x 8cm) with central necrosis over S4/8, c/w HCC 2. No CBD dilatation and gallbladder sludge. He was admitted due to highly suspected HBV flare up. The anti-viral drug of Tenofovir alafenamide 25mg#once daily was given. The SNMC(Glycyrrhizin)100ml daily was also given after admission for totally 6 days. HBV viral load showed 492520 (IU/mL) during hospitalization.

After treatment, there was no abdominal pain, no poor appetite, nor other specific discomfort. The AST/ALT level decreased to 117/305 (U/L) and total bilirubin level decreased to 1.2 (mmol/L) in 8 days. He then discharged and kept OPD followed up. (Figure 3).

Discussion

The HBV reactivation after TACE or RT had been reported since 2004.[4]But, this risk is sometimes neglected during the busy clinical scenario.

In this patient, the HCC was under controlled after the TACE plus RT. However, the HBV reactivation happened after the 4th TACE course and completing RT. It was compatible with the previous study that the HBV reactivation showed at a median of 3.5 cycles following initiation of TACE.[6]Besides,study by Jeong et al,2015 showed that the HBV reactivation rate was higher in combination-drug TACE plus RT than mono- or combi- TACE therapy.[7]As a result, the HBV reactivation might cause by the synergic of TACE and RT.

Another issue was how to follow the HBV status in these HCC patients. This patient was under the regular liver function survey every month, but neither the HBV status. The study by Yeo W et al,2006 had suggested “serial HBV DNA monitoring” done intensively at less than monthly intervals improved the accuracy of diagnosing HBV reactivation due to serum HBV DNA levels increase several weeks prior to increases in ALT levels.[8] In recent guidelines by American Gastroenterological Association and American Association for the Study of Liver. Diseases, the HBV DNA was also advised to monitor at least every 3 months.[9,10]

In this case, the patient was HBs Ag positive with normal ALT level. He didn’t take any anti-virus therapy after starting HCC therapy. The prophylactic anti-virus therapy is not indicated before or during TACE treatment by the criteria of Taiwan’s national health insurance. However, the most update studies suggested preemptive or

prophylactic anti-virus therapy could prevent the HBV reactivation and improved long-term survival in patient receiving TACE treatment. [4,7,11,12]In the future, if possible, the prophylactic anti-virus therapy might be indicated in these HBV-related HCC patients before TACE or RT therapy.

Conclusion

HBV reactivation is a common and a life-threatening complication in patients with HBV-related HCC. TACE alone or combined RT can compromise the host immunity and then cause the reactivation of HBV. Regular followed the HBV serology (ex. HBsAg, ALT, and HBV DNA) is important in HBV-related HCC patient during TACE or RT.[9,10] The preemptive anti-viral therapy in these group patients significantly reduces the risk of acute hepatic deterioration and risk of HBV reactivation. Finally, we strongly suggested that preemptive anti-viral therapy should be used for all HCC patient with HBV infection who will receive TACE therapy alone or combined RT.[7,11,12]

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Figures

Figure 1. Graph of Computed Tomography of HCC location and size post complete TACE plus RT treatment on 2020/03

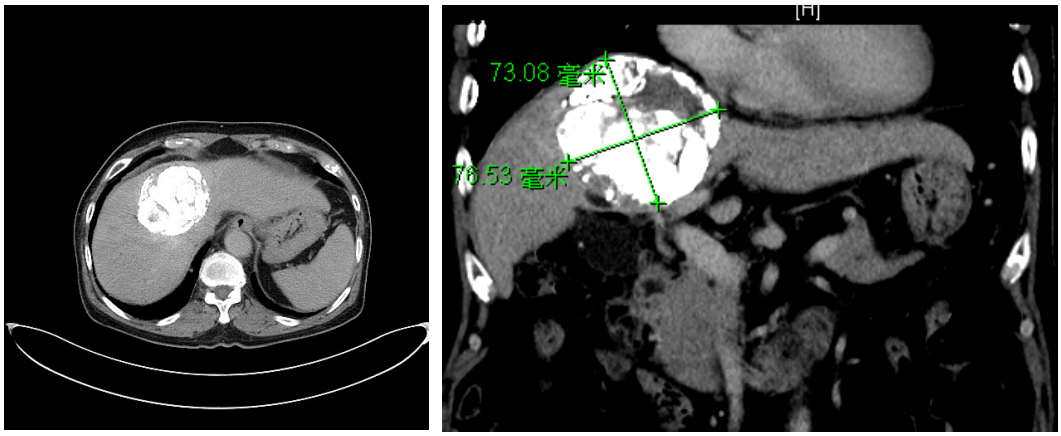
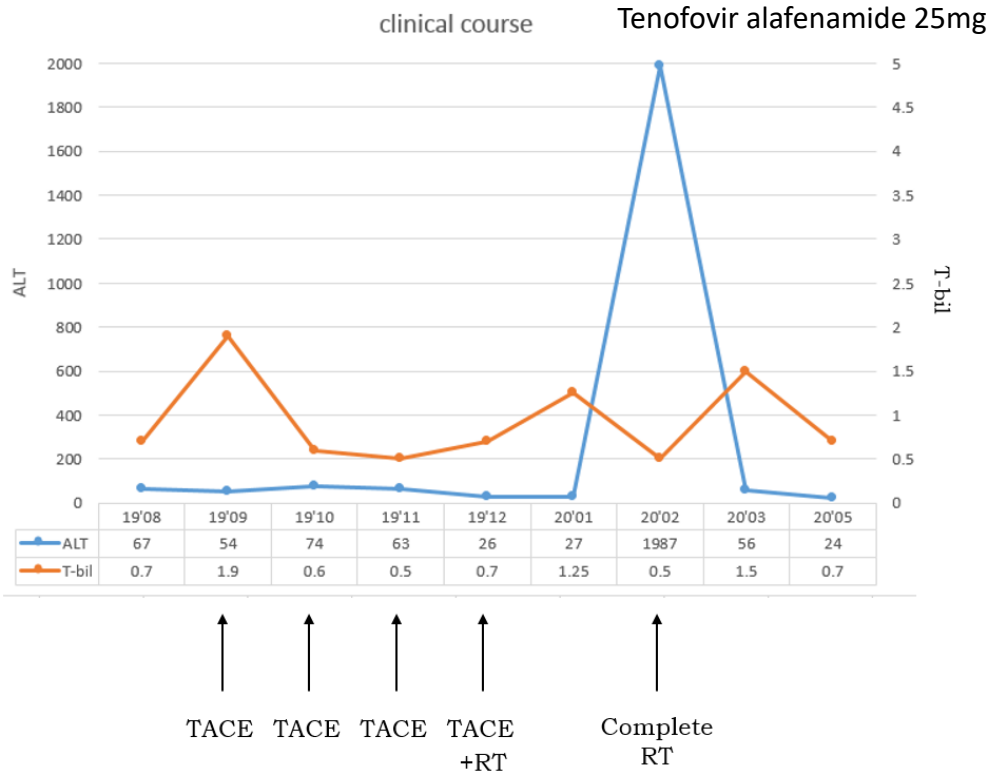


Figure 2. Graph showes the clinical course of the relationship of HCC treatment,liver function and HBV serology



HBsAg	576	3716	IU/mL
Anti-HBs			
HBeAg		-	
Anti-Hbe		+	
Anti-HBc			
HBV DNA		492520	IU/ml

Figure 3 Graph shows the whole clinical course of HCC treatment and HBV reactivation