HBV ECHO Case Recommendations

Session 9: October 24, 2022

Case Recommendations and Considerations: 56 y/o Vietnamese female with chronic HBV treated with entecavir, but with persisting measurable HBV DNA

CATEGORY	RECOMMENDATIONS	Relevant Presentation Question or Concern	REFERENCES RESOURCE LIN
History			
Physical Exam			
Diagnostic evaluation	1. Consider discussion of repeat liver biopsy for comparison to the 2016 biopsy based on most recent fibroscan data. If there is evidence of advanced fibrosis this may change management 2. It may be reasonable to repeat a Fibroscan every 2-3 years if you suspect progression of liver disease. However, Fibroscan doesn't always change management. It may take up to 5 years to see a significant difference in liver fibrosis. Based on a phase III clinical trial results of paired biopsies over 5 years. persistent suppression of HBV DNA showed fibrosis reversal even from cirrhosis. Therefore, fibrosis staging is not as critical as in NASH or as previously in chronic hepatitis C when fibrosis staging was a requirement before HCV treatment was permitted. 3. Baseline liver enzymes are dependent on muscle mass and body surface area. A larger muscular male may have baseline enzymes in the 30s while a smaller, thin, older woman may have baseline liver enzymes in the teens. Based on a study from the EU, blood donors who had a "normal" ALT and screened positive for HCV infection underwent liver biopsy and showed that some of the persons with "normal" ALT actually have hepatic	1. Based on the patient's most recent Fibroscan, the liver stiffness is 8 kPA which is between the stages F2-F3 fibrosis. In 2016, the biopsy showed stage F1-F2 fibrosis, so this may indicate progression of fibrosis. 2. When should you repeat a fibroscan? 3. What are the upper limits of normal for men and women and how are they established?	

	inflammation. By further analysis of those who had normal histology, a range of normal upper normal ALT was established: 30 for men and 20 for women. AASLD has revised this to 35 for men and 25 for women. While commercial labs may use a normal distribution curve to establish the normal range of lab values, the AASLD used population data of individuals affected with Hepatitis C and no histologic evidence of disease on biopsy to determine normal liver enzyme levels. 4. Elevated ALT indicates inflammation which suggests progression of liver disease. Isolated ALT elevation over time may be related to higher all-cause mortality based on a Korean population study. 5. Question was not directly answered due to limited time, but non-obese NAFLD remains a consideration and checking a lipid profile and HgBA1C is reasonable for this patient. The presenter, who has reviewed the liver biopsy slides done in 2016, indicated that there was no steatosis.	4. Are people at an increased risk of liver disease-related mortality if ALT remains elevated over time? 5. Should we evaluate this patient for NAFLD/metabolic syndrome in the setting of fibrosis progression while being treated?	
Medication Therapy & Adjustments	1. 2. Consider changing this patient's antiviral therapy. The presence of persistent low-level viremia indicates there may be a drug-resistant population of virus. Although mutation testing was performed, commercial labs typically use tests that are only able to detect drug resistance if the viral population is at a level of greater than 15%. If there is a degree of smoldering low level drug resistance in the viral population, the test will fail to detect this. Further continuation of the current antiviral may cultivate further resistance. A biopsy may not be useful clinically, as the current information already tells us Entecavir is not working well, although LFTs are within the normal range. As noted elsewhere, LFTs less than the lab-established normal range are not applicable to all patients, depending on muscle mass and body surface area. The recommended course of action would be to change antiviral agents to suppress the virus and	1. How should we treat this patient with persistent low-level viremia for several years? 2. The persistent viremia is concerning as it poses a risk for development of future viral resistance (due to continued mutation of the virus in the setting of antiviral therapy)	

	repeat testing. Regarding the Fibroscan, the patient's liver stiffness of 8kPa is close to 9-10kPa (a level at which patient is likely to have advanced fibrosis) based on established reference charts for liver stiffness in chronic HBV. This may indicate fibrosis is ongoing and thus the liver enzymes we see are not the true normal for the patient. Additionally, continued uncontrolled viral replication in this setting may produce falsely normal LFTs because in patients with advanced fibrosis we may observe liver enzymes to be lower (10-19 range for this particular patient). Obtain surveillance labs every 3-6 months to trend the fluctuation in LFTs. BMI is low so maybe this patient's ALT normal is near 12. This patient's LFTs were reportedly in 20-29 range over time, but even at an ALT of 26, her LFTs are 2x upper limit of normal, indicating that the disease has been progressing. This may explain the subsequent Fibroscan changes over time. 3. A second antiviral agent is rarely needed except on the rare occasion when a second drug is added if initial antiviral therapy produces an inadequate response in the inpatient setting in cases of acute liver failure due to reactivation of hepatitis B. It is unusual for 2 drugs to be used in chronic hepatitis B. In the outpatient setting it is more common for the medication to be switched if there is suspected antiviral resistance.	3. In what scenario would a second antiviral agent be added to achieve adequate viral suppression?	
Vaccination			
Social Determinants of Health (SDOH)			
Behavioral Health			
Screening			
Risk Reduction			
Other			

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