Persistent suppression of viral load in chronic hepatitis B

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Case

Ruby, 41 years of age, is from the Karen state of Myanmar. She migrated to Australia as a humanitarian entrant in 2008. Shortly after her arrival, she underwent refugee health screening and was diagnosed with chronic hepatitis B. Since that time, Ruby has been under primary care surveillance. She is not on treatment for hepatitis B and has a suppressed viral load. Abdominal ultrasonography and liver elastography at diagnosis showed no liver fibrosis. Ruby does not drink alcohol. She has no other chronic diseases and does not take any regular medication. Her serology at diagnosis is shown in Box 1 and her latest results are shown in Boxes 2 and 3.

Question 1

Looking at Ruby's results in January 2016 (Box 2), what phase of chronic hepatitis B infection is she in?

Question 2

On reviewing Ruby's past results, it appears that for the past four years, her hepatitis B DNA levels have been <20 IU/mL and her liver function tests (LFTs) have been normal. What additional tests would you request at her next monitoring visit?

Box 1. Ruby's serology results at diagnosis

- Hepatitis B surface antigen: Positive
- Hepatitis B surface antibody: Negative
- Hepatitis B e antigen: Negative
- Hepatitis B e antibody: Positive
- Hepatitis B core antibody: Positive

Question 3

Looking at Ruby's results six months later (Box 3), what does this mean for her? Does she require ongoing 6–12-monthly surveillance? Does she require monitoring for hepatocellular carcinoma (HCC) when she is older?

Answer 1

Immune control phase

Following initial infection with hepatitis B, if acute infection does not result in spontaneous resolution, infected individuals may seroconvert to hepatitis B e antibody (HBeAb)-positive, suppress their viral load and enter the immune control phase. Treatment is generally not required in the immune control phase, and 6–12-monthly monitoring of LFTs and viral load is sufficient.[1]

Box 2 . Ruby's results at January 2016

- Hepatitis B e antibody: Positive
- Hepatitis B DNA: <20 IU/mL
- Alanine aminotransferase: 14 IU/L

Box 3 Ruby's results at August 2016

- Hepatitis B surface antigen: Negative
- Hepatitis B surface antibody: >1000 IU/mL
- Hepatitis B e antigen: Negative
- Hepatitis B core antibody: Positive
- Alanine aminotransferase: 14 IU/L

Answer 2

Hepatitis B surface antigen and hepatitis B surface antibody

Generally, chronic hepatitis B infection persists for life; however, there is a small proportion of infected individuals (<2%) who will clear the infection without treatment.[2] A persistently suppressed viral load could indicate that spontaneous clearance of hepatitis B surface antigen (HBsAg) has occurred, and should prompt HBsAg and hepatitis B surface antibody (HBsAb) testing.[3]

Answer 3

Clearance of HBsAg and mounting an HBsAb titre of >10 indicates resolution of infection. Ruby is functionally cured. Monitoring and HCC surveillance is not generally required; however, there may be some situations where ongoing monitoring and HCC surveillance are required.

Ruby's risk of future liver disease in the absence of pre-existing cirrhosis is lower than in individuals who are HBsAg-positive; monitoring is generally not required in these patients.[4] However, hepatitis B is a complex virus that expresses reverse transcriptase. Viral DNA and covalently closed circular DNA (cccDNA) may persist in host cells even after HBsAg clearance.[5] There is a potential for future reactivation

in the setting of immunosuppression (eg immunosuppressive therapy for malignancy).[6] There is no best practice advice on future monitoring of these patients. Fortunately, reactivations are rare.[4] Consider specialist referral prior to planned future immunosuppression.

HCC surveillance in patients with resolved infection needs to be considered on a case-by-case basis. Once again, there is no clear consensus of opinion. In Ruby's case, as she has not reached the age at which screening would usually commence (50 years of age in women of Asian descent) and she does not have cirrhosis, it could be argued that she does not require further HCC screening. However, in patients who have other risk factors for HCC (eg cirrhosis or aged >45 years when HBsAg was cleared) a case could be made for ongoing HCC surveillance with six-monthly liver ultrasound.[7]

Key points

- A small proportion of individuals with chronic hepatitis B infection will clear the virus spontaneously.
- A persistently low viral load (below the level detectable by the laboratory, [usually <20 IU/mL]) should prompt testing for HBsAg.
- In patients who do not have cirrhosis, clearance of HBsAg indicates functional cure, and further monitoring and HCC surveillance are generally no longer required. However, consider ongoing HCC surveillance in individuals who have other risk factors such as cirrhosis or HBsAg clearance after the age of 45 years.
- For individuals who have cleared HBsAg, consider specialist assessment prior to planned future immunosuppression as viral DNA may persist in host cells with a potential for future reactivation.

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