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Letter to the Editor

What are the causes and outcomes of the coexistence of HBsAg and anti-HBs?



Dear Editor,

We read with great interest the article by Ding et al.,¹ “Mutations in the S gene and in the overlapping reverse transcriptase region in chronic hepatitis B Chinese patients with coexistence of HBsAg and anti-HBs”. We would like to specify some additional issues related to the coexistence of HBsAg and anti-HBs in a summary.

The rate of simultaneous HBsAg and anti-HBs serological profile ranged from 2.93% to 36% in different patient groups.^{1–4} Also, it has been recently reported that the prevalence progressively increased with age from 40 to 70 years old.³

As mentioned in the article, the mechanism underlying the concurrent detection of HBsAg and anti-HBs remains unclear.^{1,2} It is a fact that there is a relation between this special serological profile and mutations in S gene region, particularly in the ‘a’ determinant. However, as a result of some studies including this article, while no mutation has been described in some patients with coexistence of HBsAg and anti-HBs, some mutations which may be associated with this serological pattern have been detected in patients with only HBsAg positivity in the absence of anti-HBs.^{1,3,4} Hereby, coexistence of HBsAg and anti-HBs may result from not only mutations but also from some other causes.

Aside from mutations in S gene region, the presence of heterologous subtype-specific antibodies, superinfection with a new (second) hepatitis B virus (HBV) strain, occult HBV reactivation and false positivity for anti-HBs are the other factors considered to be associated with this serological pattern.² Diversity in the ‘a’ determinant between strains of the first and second infections in patients with superinfection and natural HBV sequence variations in patients with heterologous subtype coinfection may be the mechanisms underlying the profile.^{2,5} False positivity for anti-HBs may be caused by glycoproteins such as pili fractions isolated from *Neisseria gonorrhoeae* and *Escherichia coli*.²

Clinical outcomes of this serological profile are also controversial. Although it has been reported that there was no significant difference with HBeAg positivity rate and HBV deoxyribonucleic acid (DNA) concentration between the two

groups (anti-HBs negative or positive) in the article, both of them have been reported to be significantly higher in patients with coexistence of HBsAg and anti-HBs in another recent study.^{1,3} Hence, the authors stated that the concurrent detection of HBsAg and anti-HBs may be associated with an increased risk of adverse clinical outcome.³ Additionally, while some studies suggested that coexistence of HBsAg and anti-HBs can be associated with poor prognosis, advanced fibrosis, cirrhosis, or hepatocellular carcinoma, there are also studies showing no relation between this profile and severity of liver disease.^{1–4} However, transmission via HBV mutants not affected by vaccine induced anti-HBs and misdiagnosis in screening depending on the use of only anti-HBs can be other clinical problems due to the coexistence of HBsAg and anti-HBs.⁴

Conflicts of interest

The author declares no conflicts of interest.

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Murat Afyon

Gülhane Military Medical Academy Haydarpaşa Teaching Hospital, Primary Care Inspection, Clinic of Family Health Center and the Naval Academy, Tuzla/Istanbul, Turkey

E-mail addresses: muratafyon2002@yahoo.com,
muratafyon79@gmail.com

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