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Letter to the editor

Spontaneous HBsAg clearance in a patient with acute hepatitis B and pleural exudates

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TO THE EDITOR: Sir, spontaneous HBsAg+ clearance in patients with acute and chronic hepatitis B virus (HBV) infection has been reported worldwide.[1] Spontaneous loss of HBsAg is infrequent in adult HBV carriers. In children with chronic hepatitis B loss of HBsAg is rare (average incidence 0.6%/year), especially if they have been infected during the perinatal period and have mild histological changes. However, among HBV cases with spontaneous HBsAg clearance we can hardly find reports with co-existing pleural effusions in the absence of ascites. We report herein the therapeutic management of a patient with acute HBV infection and symptomatic pleural exudate who succeeded in HBsAg+ seroconversion.

A 51-year-old male patient was admitted to our Department because of fever and jaundice during the last five days. Patient medical history was unremarkable except of appendectomy. Clinical examination revealed hepatomegaly and laboratory investigation showed evidence of acute hepatitis B infection (HBsAg+, anti-HBcore IgM+, HBeAg-) with transaminasemia [alanine aminotransferase 3720 UI/ml] and HBV-DNA at $3.14x10^4$ UI/ml. Anti-HDV was negative as well as antibodies for other liver-related viruses. No clinical or laboratory sign for any other concomitant disease was evident. During the second day of hospitalization the patient started to cough and had mild dyspnea. Chest x-ray showed remarkable pleural effusion on the right side and subsequent paracentesis demonstrated that this was an exudate with cells of lymphocytic origin without neoplastic cells and no evidence of Dane particles.

During the next days of hospitalization respiratory discomfort persisted as pleural exudate further increased. Further investigation with additional fluid paracentesis, computed tomography, bronchoscopy and pleural biopsy did not reveal any signs of malignancy or other than acute hepatits B infection. There was no clinical, endoscopical or radiological sign of portal hypertension.

The patient was started on spironolactone 100mg every second day as signs of perihepatic fluid were demonstrated with an ultrasound at the beginning of the second week of hospitalization. After three weeks of hospitalization pleural exudates improved significantly and the patient was discharged with spironolactone 100mg every second day. At the one -month follow up the patient succeeded in hepatitis B virus serocoversion with HBsAg, anti-HBs+, anti-Hbe+, and not detectable HBV-NDA. HBcore IgM remained positive but with declining titers. Alanine aminotransferase was 257UI/ml and there were no signs of pleural or abdominal collections. Spironolactone was discontinued. Patient clinical and laboratory status on the three- and six-month follow up remained unchanged and he is currently followed up in our Hepatology outpatient clinic.

We described herein a patient with presumed acute hepatitis B infection who was hospitalized due to pleural exudates and who succeeded in spontaneous HBsAg+ seroconversion. This is a rare case as we are aware of only two additional cases which have been so far reported.[2-3]

There are also reports on chronic HBV patients with

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concomitant pleural exudates during HBsAg seroconversion and also during acute exacerbations of their chronic hepatitis B.[4] In these cases, without specific treatment, effusions resolved completely as hepatitis subsided.

We believe like others[2] that pleural effusion in this patient represented a hitherto manifestation of the hepatitis itself. However, we were not able to demonstrate any evidence of Dane particles in the pleural fluid as it occurred in one single case where Dane particles were demonstrated in a pleural effusion obtained from an individual with a protracted course of acute HBV infection.[4]

Our patient had no evidence of concomitant HCV or HDV infection. Thus, HBsAg clearance was not influenced by such co-existing factors. Nevertheless, the real role of HCV and HDV co-infection in HBsAg clearance remains contradictory.[5] According to a study[6], patients older than 35 years with concomitant HCV infection succeeded in higher HBsAg clearance rates. However, in other studies[2,8] no factor predicting HBsAg clearance was demonstrated, including HCV and HDV co-infection.

It seems that our report strengthens the findings of other studies[8-9] on chronic HBV carriers which demonstrated achieving that male sex is a positive predicting factor in HBsAg seroconversion. Males clear HBsAg easier but no evidence exists that HCV suppresses HBV replication. Interestingly, a molecular clearance mechanism associated with emergence of a novel pre-S2 mutation has been recently reported.[10]

We implemented a six-month follow up in this patient, as the occurrence of future adverse manifestations of this so called "cleared" HBV infection may be not minimized even in the absence of HBsAg (E.V.T., National Institutes of Health, project proposal). In fact, it has been suggested that patients with HBsAg seroconversion may nonetheless harbor HBV-DNA in their peripheral blood mononuclear cells and hepatocytes for prolonged periods.[11]

Thus, after HBsAg clearance, hepatitis B viremia may persist, and adverse complications are not infrequent in patients who "cleared" HBsAg.[12-15] All these patients should be closely monitored for an earlier detection of a probable hepatocellular carcinoma occurrence.

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