International Journal of Women's Dermatology 7 (2021) 826–827

Contents lists available at ScienceDirect

International Journal of Women's Dermatology

Case Letter

# Positive hepatitis B serology following IVIg treatment in a patient with mucous membrane pemphigoid

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ARTICLE INFO

*Article history:*
Received 8 December 2020
Revised 25 February 2021
Accepted 2 March 2021

*Keywords:*
Hepatitis B
IVIg
Mucous membrane pemphigoid

*Dear Editors,*

Intravenous immunoglobulin (IVIg) is a treatment option for autoimmune diseases such as mucous membrane pemphigoid (MMP; Ahmed and Dahl, 2003). Adverse effects are generally self-limited, but cases of biopsy-confirmed hepatitis B virus (HBV) infection, aseptic meningitis, and anaphylaxis have occurred (Ahmed and Dahl, 2003; Hellstern, 1994). To limit the spread of infectious agents through IVIg infusions, donations are screened and undergo viral inactivation procedures (Ahmed and Dahl, 2003; Hellstern, 1994). Prior to receiving IVIg, patients are screened for HBV through the triple serology of hepatitis B surface antibody (sAb), surface antigen (sAg), and core antibody (cAb; Lu et al., 2018; Ramsay et al., 2016). In general, the presence of sAg indicates current HBV infection, sAb indicates immunity from prior HBV infection or immunization, and cAb indicates past or present HBV infection. Passive transfer of HBV antibodies without true infection has been reported after IVIg (Lu et al., 2018; Ramsay et al., 2016) but has been scarcely discussed in the dermatology literature (Benton et al., 2012). Herein, we report a patient with MMP who developed positive HBV serology after receiving IVIg in the absence of a true infection.

A 64-year-old man with a history of refractory ocular MMP confirmed by histopathology and direct immunofluorescence presented in November 2019. He had most recently received two cycles of IVIg in September and early October 2019 without improvement in his disease. Incidentally, hepatitis serologies were collected in late October 2019, which showed the presence of sAb and cAb without sAg. Prior HBV serologies had been negative. There was concern for HBV infection through IVIg infusions.

The patient was subsequently evaluated by the gastroenterology department. Given the negative HBV polymerase chain reaction results, the patient was thought to have passively acquired antibodies through IVIg. Repeat antibody testing showed an expected decrease in titers. He received his scheduled rituximab without HBV prophylaxis and ultimately cleared all HBV serologies by August 2020 (Table 1).

Passive transfer of antibodies through IVIg confounds serologic testing, with reported rates for HBV varying from 15% to 46 (Benton et al., 2012; Lu et al., 2018; Ramsay et al., 2016). Additional antibodies have also been reported to be passively transferred through IVIg, such as antitreponemal and anti-*Toxoplasma gondii* antibodies (Benton et al., 2012). This phenomenon has been well-established in the hematology and infectious diseases literature, but we were only able to find one case report in the dermatology literature (Benton et al., 2012). This underreporting may be multifactorial. First, IVIg may be used less extensively in the management of dermatological conditions (Ahmed and Dahl, 2003). More importantly, HBV screening is not routine after IVIg infusion and typically occurs incidentally (Benton et al. 2012; Lu et al., 2018). Furthermore, the chance of detecting HBV serologies after IVIg has been found to decrease exponentially over time, with the probability of cAb detection at 34% at 7 days and 12% at 1 month (Lu et al., 2018), likely due to the clearance of antibodies. Our patient tested positive for cAb and sAb approximately 2 weeks after IVIg, with clearance of cAb and sAb after approximately 4 months and 10 months, respectively.

We present this case to raise awareness of the possible passive transfer of antibodies in dermatology patients receiving IVIg. For

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https://doi.org/10.1016/j.ijwd.2021.03.001

**Table 1**
Timeline of hepatitis B serology results

| | April 2018 | October 2019 | November 2019 | February 2020 | August 2020 |
|---|---|---|---|---|---|
| HBV surface antigen | Nonreactive | Nonreactive | N/A | N/A | N/A |
| HBV surface antibody | Nonreactive | **>1,000 IU/L** | N/A | **70 IU/L** | Nonreactive |
| HBV core antibody | Nonreactive | **Reactive** | N/A | Nonreactive | N/A |
| HBV PCR | N/A | N/A | Not detectable | N/A | N/A |

The bolded text was meant to indicate abnormal lab results.
HBV, hepatitis B virus; N/A, not applicable; PCR, polymerase chain reaction.

those who develop HBV antibodies, we recommend evaluation by the gastroenterology department, which will likely include HBV polymerase chain reaction and repeat antibody testing. Patients without true HBV infection do not require prophylaxis against HBV reactivation with immunomodulatory therapies such as rituximab.

## Conflicts of interest

None.

## Funding

None.

## Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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