Vaccine 37 (2019) 2527–2528

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Letter to the Editor

Poor vaccine-related immunity against HBV in children with autoimmune diseases: Early or late sign of immunological disorder?

Roberto Antonucci

Pediatric Clinic, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Roberta Frassetto

Pediatric Clinic, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Nadia Vacca

Pediatric Clinic, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Daniela Mura

Pediatric Clinic, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Rosanna Lampis

Pediatric Hospital A. Cao, A.O. Brotzu, Cagliari, Italy

Paolo Castiglia

Hygiene and Preventive Medicine, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Giovanni Sotgiu

Clinical Epidemiology and Medical Statistics Unit, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Andrea Piana

Hygiene and Preventive Medicine, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Maria Grazia Clemente *

Pediatric Clinic, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Dear editor,

A decline in the hepatitis B surface antibody (anti-HBs) titer lead us to question the effectiveness of hepatitis B virus (HBV) universal vaccine in a number of children [1]. Undetectable levels of anti-HBs after HBV vaccination do not necessarily mean lack of protection against HBV. Regardless of the anti-HBs titer, activity of T helper CD4+ and memory B cells has been shown to assure a prompt immune response in vaccinated subjects [2]. However, this biological assumption could not be confirmed in immunocompromised children, in whom vaccine preventable infections could be life-threatening. Given the high risk for severe HBV infection in immunocompromised children, screening for HBV immunity and one or more booster doses have been proposed for children who need to undergo immunosuppression who lack anti-HBs [3].

Herein, we would like to report two first cousins affected by autoimmune hepatitis (AIH), who were anti-HBs negative despite HBV immunization during their infancy. Their family history was positive for other autoimmune diseases, namely Type 1 diabetes mellitus in one first cousin and Hashimoto's thyroiditis in a grandmother and an uncle.

* Corresponding author.
E-mail address: mgclemente@uniss.it

https://doi.org/10.1016/j.vaccine.2019.02.043

The first case is a 5-year-old boy who received an unsuccessful HBV vaccine booster during maintenance therapy with 1 mg/kg/day azathioprine (AZA) and 5 mg/day prednisone (PDN).

The second case is a 7-year-old girl who received a successful HBV vaccine booster (anti-HBs titer: 200 UI/mL 2 months after the booster) during maintenance therapy with 10 mg PDN every other day.

It is unclear whether anti-HBs negativity was due to a "physiologic" decline of antibody level after primary immunization or to autoimmunity-associated impaired immunity.

The degree of liver impairment was different in the two cases: advanced with moderate inflammation and fibrosis in the first, while mild with minimal fibrosis in the second. The first was treated with the combined protocol of PDN (2 mg/kg/day) and AZA (1 mg/kg/day), while the second responded well to the initial daily PDN dose (1.5 mg/kg), which was subsequently tapered to a lower and every other day dosage (0.25 mg/kg) in the maintenance regimen. Therefore, it is difficult to interpret the efficacy of the HBV vaccine booster observed in the second case: was the detectable immunological response the result of a lesser degree of immunosuppression compared to the first case or rather of a different genetic HLA profile, or of both conditions?

Both children were heterozygote for the HLA DRB1*03 allele; furthermore, the one with advanced disease also carried the HLA DRB1*04 allele associated with AIH risk [4]. Previous studies have reported on autoimmunity and its effect on HBV vaccine response in celiac disease [5], with the suggestion of revising current immunization strategies. However, the possible role of the HLA DRB1*03 – DQB1*02 haplotype has not been clarified [5].

Several pressing clinical questions can be raised: do children with a positive family history for autoimmune diseases show an early impaired response to vaccines and should they undergo an early screening to assess their response to HBV vaccine? Is early detection of immunological impairment predictive of autoimmune disease occurrence? Which immunological responses can be involved before an autoimmune disease manifests? Which vaccine and how many doses should be used?

HBV vaccine is an important aspect of managing children who need to undergo immunosuppression. Considering that having a family member affected by an autoimmune disease is a well-known risk factor for developing an autoimmune disease during childhood, we believe there is a need to perform observational studies aimed to assess the efficacy of primary immunizations in children with a positive family history of autoimmune diseases. This is especially true for populations such as Sardinians, characterized by a high prevalence of autoimmunity-associated HLA haplotypes [4]. The timing of the immune dysfunction responsible for poor vaccine response needs to be clarified: does it occur early in life, or rather, when the autoimmune disease develops? Moreover, further studies will be needed to understand the role of early anti-HBs screening in real-life practice, as well as its cost-effectiveness in national or regional healthcare systems.

Acknowledgements

We are grateful to Professor Kathleen Schwarz, M.D. for advice and helpful discussion and for assistance with editing English language. The study was supported by Fondazione di Sardegna, Sassari, Italy, as part of the 'Bisogni di Salute' project (Prot n. 2015.1639) and by AISERNUI (Associazione Italiana di Studio e Ricerca per le NefroUropatie Infantili) Rome, Italy.

References

[1] Li X, Xu Y, Dong Y, Yang X, Ye B, Wang Y, et al. Monitoring the efficacy of infant hepatitis B vaccination and revaccination in 0-to 8-year-old children: protective anti-HBs levels and cellular immune responses. Vaccine 2018;36(18):2442–9. https://doi.org/10.1016/j.vaccine.2018.03.044.

[2] Bauer T, Jilg W. Hepatitis B surface antigen-specific T and B cell memory in individuals who had lost protective antibodies after hepatitis B vaccination. Vaccine 2006;24(5):572–7.

[3] Moses J, Alkhouri N, Shannon A, Raig K, Lopez R, Danziger-Isakov L, et al. Hepatitis B immunity and response to booster vaccination in children with inflammatory bowel disease treated with infliximab. Am J Gastroenterol 2012;107(1):133–8. https://doi.org/10.1038/ajg.2011.295.

[4] Clemente MG, Frau F, Bernasconi M, Macis MD, Cicotto L, Pilleri G, et al. Distinctive HLA-II association with primary biliary cholangitis on the Island of Sardinia. United European Gastroenterol J 2017;5(4):527–31. https://doi.org/10.1177/2050640616665030.

[5] Filippelli M, Garozzo MT, Capizzi A, Spina M, Manti S, Tardino L, et al. Immune response to hepatitis B virus vaccine in celiac subjects at diagnosis. World J Hepatol 2016;8(26):1105–9. https://doi.org/10.4254/wjh.v8.i26.1105.