Correspondence

No Benefit to Delaying Pneumococcal Polysaccharide Vaccination in HIV-Positive Adults

TO THE EDITOR—The Advisory Committee on Immunization Practices (ACIP) recommends pneumococcal vaccination immediately after a diagnosis of human immunodeficiency virus (HIV) infection [1]. However, for patients with a CD4⁺ T-cell count of ≤ 200 cells/ μ L, the timing of pneumococcal vaccination, either immediately or 6–12 months after initiation of antiretroviral therapy (ART), is left to the discretion of the practitioner, owing to the lack of supporting evidence [2]. HIV-positive individuals not receiving ART commonly have high uncontrolled

viral titers, abnormal distribution of B-cell populations, and poor responses to the pneumococcal polysaccharide (PPS) vaccine (PPV) [3]. Current pneumococcal vaccine recommendations by the ACIP for HIV-positive individuals are based on limited available data and would greatly benefit from additional clinical studies.

Rodriguez-Barradas et al recently reported a double-blinded, randomized, placebo-controlled PPV study in HIV-positive individuals with a CD4⁺ T-cell count of ≥ 200 cells/ μ L. In this study, PPS-specific total and functional antibody responses were assessed as surrogates of protection against vaccine serotypes 1, 3, 4, 6B, and 23F [4]. On the basis of their results, the authors concluded there was

no benefit in delaying receipt of PPV in HIV-positive individuals with a CD4⁺ T-cell count of ≥ 200 cells/ μ L [4].

We recently evaluated the response to immediate versus delayed receipt of PPV in newly individuals with recently diagnosed HIV infection and a CD4⁺ T-cell count of ≤ 200 cells/ μ L [5]. PPS-specific total antibody titers, functional antibody titers, and B-cell response were assessed against vaccine serotypes 14 and 23F. After vaccination, increases in total and functional antibody titers were noted. Overall, these findings suggest that PPV receipt is beneficial for HIV-positive individuals. However, no differences in the functional antibody titers or PPS-specific B-cell responses were noted between

Figure 1. Human immunodeficiency virus (HIV)–negative ($n = 29$) and HIV-positive ($n = 20$) donor samples from adults 18–30 years old were compared on day 7 after receipt of 23-valent pneumococcal polysaccharide vaccine. Lymphocyte-enriched peripheral blood samples stained with fluorescently labeled pneumococcal polysaccharide serotype 14 (PPS14; A) or PPS23F (B) were evaluated by flow cytometry for distribution of CD27 and immunoglobulin M (IgM) among PPS-selected CD19⁺ B cells. B cells were expressed as a percentage of total PPS-selected CD19⁺ B cells. In each sample, 100 000 events were recorded. Data are mean $\pm$ standard error of the mean.

individuals who received PPV immediately versus those for whom PPV receipt was delayed [5].

Taken together, these findings are in agreement with the recent report by Rodriguez-Barradas et al, who showed that delaying PPV receipt for 6–12 months after ART initiation did not improve the immune response [4]. HIV infection results in high, uncontrolled viral titers and chronic inflammation, which disrupt the immune system and cause early damage to critical B-cell subsets [3, 6]. Moreover, once these B-cell populations are damaged, virological control by using ART, even for prolonged periods, is insufficient to allow restoration of these essential B-cell populations [6, 7].

HIV infection and aging share several similarities [8]. Similar to the HIV-positive population, elderly people (age, >65 years) are at an increased risk of acquiring pneumococcal disease and exhibit diminished antibody and PPS-specific B-cell responses to pneumococcal vaccines [3, 9]. Since HIV-positive patients in the studies by Rodriguez Barradas et al and Leggat et al were middle aged [4, 5], we assessed whether the diminished PPS-specific B-cell response in HIV-positive adults was primarily a consequence of age or HIV infection. We evaluated PPS-specific B-cell responses in young (age, <30 years) HIV-positive individuals and compared them to those for age-matched HIV-negative adults (Figure 1). After vaccination, PPS-specific immunoglobulin M (IgM) memory B-cell responses were significantly diminished in young HIV-positive adults, compared with those in young HIV-negative adults. Reductions in postvaccination PPS-specific IgM memory B cells were, however, accompanied by significant increases in switched memory

B cells. These PPS-specific B-cell deficiencies were similar to those seen in the antigen-specific B-cell populations of middle-aged HIV-positive adults. In contrast, the response to PPV in HIV-negative elderly individuals consists primarily of switched memory B cells [10]. These findings demonstrate unique B-cell responses in HIV-positive and elderly individuals despite a significant overlap in B-cell dysfunction and immunosenescence.

It remains to be seen whether the distinct age-related and HIV-related deficiencies may combine in the ever-growing aging HIV-positive population. Overall, diminished total antibody and functional antibody titers in HIV-positive individuals, compared with those in HIV-negative individuals, suggest a need for alternative robust therapeutic approaches, which may need to be tailored depending on an individual's age and disease state.

Notes

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