Emerging viruses in organ transplant recipients - immune responses to H1N1/09 influenza vaccine and hepatitis E virus infection

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III. Marie Felldin, Sanja Johansson, Jan Holgersson, Vanda Friman. HLA antibody responses in adult solid organ transplant recipients after AS03-adjuvanted influenza A (H1N1) vaccination. In manuscript.

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Abstract
Solid organ transplant (SOT) recipients run the risk of serious infections. The pandemic influenza A H1N1/09 had unknown severity, so large-scale vaccination was needed. The AS03-adjuvanted vaccine (Pandemrix®) had unknown effects among SOT recipients. We aimed to explore the influenza-antibody (ab) response, ab persistence one year later and subsequent response to the seasonal influenza vaccine (TIV/10) among adult SOT recipients. Reports of narcolepsy and possible allo-sensitisation following the H1N1/09 vaccination necessitated an analysis of HLA abs and further follow-up. 80% of SOT recipients and 100% of controls had seroprotective H1N1/09 titre levels after 2 vaccine doses ($p=0.003$). A significant loss of protection after 1 year was seen in all subjects. TIV/10 boosted a rise in seroprotection from 47% to 71% in the SOT group and 63% to 100% in controls. Non-responders were more often on triple immunosuppression and had lower renal function. No SOT recipient developed de novo HLA abs, but HLA abs with new specificities were detected in 7 patients. No acute rejection was seen within 2 years after vaccination. Two had chronic rejection within one year but a lower and mixed DSA response to the vaccine. The 4th study aimed to investigate the prevalence of hepatitis E (HEV) IgG, IgM and HEV infection, as chronic infection has been reported among SOT recipients. At transplantation, the anti-HEV IgG prevalence was significantly higher in SOT patients compared with blood donors, 30.6% and 16.8% respectively ($p<0.0001$). The patients appeared to have been infected at an earlier age. Two cases of de novo and 2 chronic HEV infection were suspected but could not be verified by HEV-RNA.

To summarise, the AS03-adjuvanted H1N1/09 influenza vaccine was effective among SOT recipients but significantly less compared with controls. One third of all subjects lost their seroprotection after one year, but TIV/10 reproduced some of the former protection. No patient developed de novo HLA abs. The unexpected high prevalence of anti-HEV IgG among the Swedish SOT recipients highlights the possibility of hepatitis E as a new opportunistic infection in the immune compromised host.

Keywords: Solid organ transplant, SOT, Hepatitis E, Influenza, H1N1, AS03 adjuvant, HLA antibodies, DSA, rejection.