ABSTRACT

Human cytomegalovirus (HCMV) infects approximately 60% of the world's population. Although largely asymptomatic, it causes substantial morbidity and mortality in infants infected via congenital exposure and is the leading infectious cause of birth defects. Congenital infection occurs in the context of both primary and non-primary infection. The transmission risk is higher in primary infection, suggesting that underlying immunity may offer partial protection. The HCMV viral envelope is studded with numerous glycoproteins, including glycoprotein B and pentamer, both targets of neutralizing antibody responses. A previous study of primary maternal HCMV infection showed that antibodies specific for particular epitopes on pentamer were higher in non-transmitters, suggesting that such antibodies could be protective. However, maternal correlates of protection have not been clearly defined, especially in non-primary infection.

We compared key anti-HCMV antibody responses in mothers who transmitted HCMV to their children with those of non-transmitting controls in maternal non-primary infections. These responses included total antigen-specific antibody targeting pentamer and glycoprotein B, as well as antibodies targeting particular pre-defined epitopes of each of these antigens.

Unlike a previous study, we found that pentamer-directed antibody levels were significantly higher in transmitting mothers at birth compared to control non-transmitting mothers. The total epitope-specific antibodies targeting gB and pentamer were also higher in transmitters. There was no evidence that higher levels of any HCMV-specific antibodies correlated with reduced risk of congenital HCMV infection in non-primary maternal infection. Also, total gB antibody levels were higher in HIV-1 infected mothers however, this was only apparent in non-transmitters.

These data indicate boosting of antibody levels by maternal HCMV reactivation/re-infection, ultimately resulting in fetal infection, and not protection.

267 words