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50 Years Ago in *The Journal of Pediatrics*

Congenital Cytomegalovirus Infection: Can It Recur in a Sibling?

Embil JA, Ozere RJ, Haldane EV. Congenital cytomegalovirus infection in two siblings from consecutive pregnancies. J Pediatr 1970;77:417-21.

Embil et al reported congenital cytomegalovirus (CCMV) infection in subsequent infants of a young mother. They challenged the widely accepted notion at that time that CCMV resulted from viral transmission when mothers had primary infection during pregnancy.

Fifty years later, the factors affecting in utero transmission of CMV are still not well-elucidated. CCMV can occur even if the mother has CMV antibodies during pregnancy owing to past infection (nonprimary or recurrent infection). However, the rate of transmission in utero is much higher for primary infections.[1] Nonprimary maternal infections can occur either owing to reinfection by immunologically variant (envelope glycoprotein epitopes) strain or reactivation of latent infection. There is uncertainty as to what triggers the reactivation and transfer of virus in a previously immune mother, so most such CCMV infections are considered to be due to reinfection. Primary and recurrent maternal infections are differentiated based on a lack of CMV IgM antibody and presence of high-avidity IgG antibody (indicating maturity), but the reliability of this is questionable.[2] In CCMV owing to recurrent infection, the placenta is thought to induce local immunosuppression in the uterus, triggering reactivation of latent virus in macrophages ($CD14^+$ monocytes), which then transmits to the fetus despite persistent maternal immunity.[3]

The complex nature of protective response to CMV (involving both innate and humoral immunity), capability of CMV to evade host immune responses, widely prevalent immunologically variant strains, and a high possibility of reactivation of latent infection pose crucial challenges in the development of an effective CMV vaccine. Prenatal screening using maternal serology for CMV is not routinely recommended owing to the lack of approved therapeutic prenatal interventions for prevention or treatment of CCMV after primary maternal infection. Nonprimary maternal CMV infections still pose a diagnostic challenge owing to the lack of specific virologic or immunologic markers, and preventive modalities targeting the same are still a work in progress.[1]

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