Association between congenital cytomegalovirus infection and autism spectrum disorder

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The association between congenital CMV (cCMV) and autism spectrum disorder (ASD) has been previously proposed in different studies, but there were some limitations due to sample size or lack of control groups. We aimed to describe the prevalence of ASD in patients with cCMV compared to non-cCMV patients in two large cohorts.

A retrospective cohort study was conducted. One cohort consisted of children with cCMV, selected from the European registry cCMVnet. The second consisted of patients in whom cCMV was ruled out at birth through a neonatal screening program (saliva PCR) conducted at Hospital 12 de Octubre (non-cCMV-cohort). Children older than four years were included in both cohorts. Demographic information, blood tests, and imaging findings at birth and development of neurological abnormalities, SNHL, and ASD were collected.

Among the 1477 children in the cCMVnet registry, 377 met inclusion criteria, and 250 non-cCMV children were randomly selected from the neonatal screening program database. Median follow-up duration was 67.8 [IQR:46.4,91.7] months in the cCMV cohort versus 83.4 [83.0,83.9] months. The prevalence of ASD in the cCMV-cohort was 7.7%, compared to 2.8% in the non-cCMV-cohort (p=0.018). cCMV children showed more motor impairment (12,3% vs 0%;p<0,001) and intellectual disabilities (18,1% vs. 1,2%;p<0,001) than children in the non-cCMV-cohort.

Among children with cCMV, those who developed ASD were more frequently male (73.1% vs. 48.9%, p=0.03), had more diffuse white matter abnormalities in cranial MRI (27.8% vs. 8.2%;p=0.024), more epilepsy (16% vs 5.8%;p<0.001), more motor impairment (28% vs 11%;p=0,03), and more intellectual disabilities (52.4% vs 15.2%;p<0,001) than non-ASD cCMV children. There were no differences in cCMV children with and without ASD regarding physical examination, blood tests, and blood and urine viral loads at birth, or in other findings in imaging.

We found a higher prevalence of ASD in children with cCMV than in children without cCMV. ASD in cCMV children is associated with other neurological impairments and with male sex. Diffuse white matter involvement at birth in children with cCMV was associated with a higher risk of ASD, but no other biological or imaging findings at birth were found to be linked to the development of ASD.