Temporal trends in the clinical presentation, management and outcomes of children with congenital cytomegalovirus infection in Europe

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Background
The cCMVnet database is an European multicentre prospective cohort study, including 1475 children with cCMV since 2011. We aimed to study temporal changes in characteristics of cCMV children during periods P1(2011-2016) and P2(2017-2024).

Methods
We compared standard characteristics between pregnancies/children born before 31.12.2016(P1) and those born from 1.1.2017 onwards (P2).

Results
There were 1475 patients in the registry, 562 in P1 and 903 in P2.

Prenatal period
Amniocentesis was performed more often after 2017 (28.1% vs.19,1%, p<0.001), and earlier (24weeks vs.22weeks, p=0.002) in P2. Congenital CMV diagnosis was made during the fetal period significantly more often during P2 (12.8% in P1 vs.21.1%, p<0.001).

Newborn period
Physical examination at birth was more often found abnormal in P1(29.7% vs.19.5%, p=0.002).

On ultrasonography, white matter abnormalities were less frequent after 2017 (3.1% vs.7.0%; p=0.002), with less periventricular cysts (5.7% vs.11.0%; p=0.001) and less intracranial calcifications (1.5% vs.7.9%;p<0.001). Hearing loss at birth was more frequent in P1 (37.2% vs.26.1%, p<0.001).

Treatment

Maternal treatment with immunoglobulins was more frequent in P1 (11.4% vs.7.6%;p=0.020), while valaciclovir treatment was more frequent in P2 (0.4% vs.10.7%;p<0.001). Proportion of children receiving antiviral treatment was higher in P1 (62.5%, vs.45.9% p<0.001). Isolated ganciclovir and valganciclovir treatment were more frequent in P1 (7.3% vs.2.7%;p<0.001), and P2 (43.9% vs.78.3%;p<0.001), respectively, while combined treatment was more common in P1 (48.8% vs.19.0%;p<0.001). The length of treatment with ganciclovir was shorter in P2 [14.0d (6.0-22.0) vs.18.0d (11.0-31.0);p=0.001], with longer use of valganciclovir [179.0d (122.0-183.0) vs. 161.0d (56.0-182.0);p<0.001].

Follow up

Sequelae at 24 months of age were evaluated in 631 children, being more frequent in P1 (37.0% vs.25.0%) (SNHL; 31.2% vs.23.6% p=0.034, motor impairment; 15.8% vs.5.9% p< 0.001, and epilepsy; 5.3% vs.1.3%, p=0.009).

Conclusions

We describe the changes observed in children born with cCMV in Europe over the past 14years. It is clear that in most recent years children are more oftenly diagnosed during the fetal period, are less likely to be born symptomatic, more likely to be treated with oral valganciclovir and have a better outcome. In children born post 2017, SNHL, motor impairment and epilepsy are less prevalent at the age of 24months.