New ideas are needed to understand neonatal arterial ischaemic stroke pathophysiology

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EDITOR–We appreciate the commentary from Professor Steven J Korzeniewski,[1] in response to our article exploring the association between perinatal inflammation exposure and development after neonatal arterial ischaemic stroke (NAIS).[2] In this research work, we found that perinatal inflammation exposure was independently associated with an increase of

the Full-Scale IQ score 7 years after NAIS, and that children exposed to perinatal inflammation had less extensive lesion distributions and a lower median lesion volume compared to non-exposed children.[2]

Our research now points to the existence of two NAIS categories regarding the perinatal inflammation exposure status. Perinatal inflammation is the only independent risk factor of NAIS consistently reported across case–control studies, with adjusted odds ratios of the order of 10 across studies.[3,4] We previously reported that perinatal inflammation contributed to the NAIS pathophysiology given (1) the links existing between systemic inflammation, thrombosis, and vasoconstriction; and (2) the results from a rat model in which an end-gestational inflammation by lipopolysaccharide led to focal arteritis of NAIS-susceptible cerebral arteries, and a NAIS when combined with a prothrombotic stress.[3] The marked differences in developmental outcome and lesion characteristics observed between children exposed and unexposed to perinatal inflammation were the last piece of the jigsaw puzzle supporting two NAIS categories with distinct mechanistic pathways: arteritis-associated NAIS and embolism-associated NAIS.[2]

The definition of perinatal inflammation is another challenge to gaining further insights into the pathophysiology of NAIS. Criteria purely based on postnatal ex vivo pathological examination of the placenta provide delayed results, while potential perinatal and specific inflammatory blood markers are yet to be identified. In addition, the low prevalence of NAIS, which usually occurs in newborn infants born at term after uneventful pregnancies and its delayed diagnosis several days after birth, remains a limitation in the feasibility of research protocols.[5] To circumvent these challenges, we used a validated composite criterion of perinatal inflammation in our study, defined as maternal fever in the delivery room, histological chorioamnionitis, or early-onset neonatal infection.[2]

Further understanding NAIS pathophysiology is mandatory before considering any therapeutic strategies in clinical practice. Identifying distinct NAIS categories opens the possibility for specific curative strategies. To that end, anti-inflammatory and recanalization strategies targeting arteritis-associated NAIS versus embolism-associated NAIS should be considered in future research. Because the hypothetico-deductive model is the grammar of scientific research, new ideas are needed to understand NAIS pathophysiology.

References

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