Proteomic analysis of cerebrospinal fluid and plasma during neonatal late-onset sepsis investigations: a way to define neuro-flogosis and maturation of blood-brain barrier in newborn infants

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Objective. Animal studies have shown that the integrity and function of the blood-brain barrier (BBB) in foetuses and preterm mammals are still developing, making neurological damage easier during sepsis. This study aimed to investigate the variation in protein content in cerebrospinal fluid (CSF) and plasma during neonatal late-onset sepsis (LOS) to define the concept of neuro-flogosis and BBB maturation.

Materials and Methods. Simultaneous CSF and blood samples were obtained from all hospitalized newborns with a clinical suspicion of LOS. Proteomic analyses of both the samples were performed using liquid chromatography and high-resolution mass spectrometry. Three incremental levels of flogosis and four GA groups were created based on plasma CRP and GA-at-birth, respectively. ANOVA and Tukey's post-hoc tests were used to identify the proteins that were significantly modulated.

Results. 47 patients were included in this study. Among the three CRP-based groups, notable variations were observed in the expression of 57 and 20 proteins in CSF and plasma, respectively. Regarding the four GA-based groups, notable variations were identified in the expression of 259 and 53 proteins in CSF and plasma, respectively.

Conclusions. There was considerable up- and down-regulation in the expression of proteins in the plasma, CSF, or both. Thus, the variation in CSF protein content could reflect flogistic involvement of the CNS, which occurs by alteration of the permeability of the BBB (*i.e.*, CRP, C9) or as a local reaction (*i.e.*, LRG1). Additionally, CSF proteins exhibit substantial variation in expression at different GAs, reinforcing the idea of preterm BBB maturation rather than dysfunction.