Introduction: Neuroinflammation often develops in sepsis along with increasing permeability of the blood-brain barrier (BBB), which leads to septic encephalopathy. The barrier is formed by tight junction structures between the cerebral endothelial cells. We investigated the expression of tight junction proteins related to endothelial permeability in brain autopsy specimens in critically ill patients deceased with sepsis, and analyzed the relationship of BBB damage and measures systemic inflammation and systemic organ dysfunction.

Methods: Case series included all adult patients deceased with sepsis in the years 2007-2015 with brain specimens taken at autopsy available. Specimens were categorized according to anatomical location (cerebrum, hippocampus, cerebellum). The immunohistochemical stainings were performed for occludin, ZO-1 and claudin. Patients were categorized as having BBB damage if there was no expression of occludin in the endothelium of cerebral microvessels.

Results: 38% (18/47) developed multiple organ failure before death. 74.5% (35/47) had septic shock. The deceased with BBB damage had higher SOFA maximum scores (16 vs. 14, p=0.04), and had more often procalcitonin levels above 10 (56% vs. 28%, p=0.045). BBB damage in cerebellum was more common in cases with C-reactive protein above 100 mg/L as compared with CRP less than 100 (69% vs. 31%, p=0.025). Absence of ZO-1 expression in cerebral meningeal samples associated with BBB damage (17% vs. 0%, p=0.046). Positive blood cultures (n = 22) were associated to absence of ZO-1 expression in cerebellar glial cells (92% vs. 44%, p=0.018).

Conclusion: In fatal sepsis, damaged BBB defined as loss of cerebral endothelial expression of occludin is related with severe organ dysfunction and systemic inflammation. Loss of ZO-1 in endothelial cells associates with BBB damage, and sepsis contributes to ZO-1 loss in cerebellar glial cells.

References:
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No expression of occludin