ABSTRACT

Ventriculomegaly induced by the abnormal accumulation of cerebrospinal fluid (CSF) leads to hydrocephalus, which is accompanied by neuroinflammation and mitochondrial oxidative stress. The mitochondrial stress activates mitochondrial unfolded protein response (UPRmt), which is essential for mitochondrial protein homeostasis. However, the association of inflammatory response and UPRmt in the pathogenesis of hydrocephalus is still unclear. To assess their relevance in the pathogenesis of hydrocephalus, we established a kaolin-induced hydrocephalus model in 8-week-old male C57BL/6J mice and evaluated it over time. We found that kaolin-injected mice showed prominent ventricular dilation, motor behavior defects at the 3-day, followed by the activation of microglia and UPRmt in the motor cortex at the 5-day. In addition, PARP-1/NF-κB signaling and apoptotic cell death appeared at the 5-day. Taken together, our findings demonstrate that activation of microglia and UPRmt occurs after hydrocephalic ventricular expansion and behavioral abnormalities which could be lead to apoptotic neuronal cell death, providing a new perspective on the pathogenic mechanism of hydrocephalus.

RESULTS

- Ventricular enlargement at 5 days after kaolin injection
- Neurobehavioral defects in KIH model mice
- Microgliosis in KIH model mice
- Neuronal damage in KIH model mice
- UPRmt activated in KIH model mice

CONCLUSION

1. Kaolin-injected mice showed prominent ventricular dilation, motor behavior defects at the 3-day, followed by the activation of microglia and UPRmt in the motor cortex at the 5-day. In addition, PARP-1/NF-κB signaling and apoptotic cell death appeared at the 5-day.

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