G6 Responses of Mast Cells in the *Dura* to Traumatic Brain Injury in an Animal Model

Kazuhiko Kibayashi, MD, Tokyo Women's Medical University, Department of Legal Medicine, School of Medicne, 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, JAPAN; and Ryo Shimada, PhD, and Rui Furutani, PhD, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjyuku-ku, Tokyo, 162-8666, JAPAN*

After this presentation, attendees will understand the responses of mast cells in the *dura* to traumatic brain injury (TBI), the histamine- mediated brain damage after TBI, and the significance of histological examinations of the dura in cases of head trauma.

This presentation will impact the forensic science community by providing evidence for changes in the dural mast cells after TBI and the role of dural mast cells in the development of brain injuries. This presentation will also emphasize the need for histological examinations of the dura in autopsies of head trauma cases.

Mast cells secrete stored histamine in response to extrinsic stimuli. Histamine plays a role in the formation of brain edema and induces histamine receptor expression in the brain. Histamine receptors exert a protective effect against histamine neurotoxicity. Because the *dura* contains mast cells, it is hypothesized that blunt force to the head activates dural mast cells, leading to the release of their histamine and exacerbation of brain injury. Therefore, the time-dependent changes in dural mast cells and histamine receptor expression in the brain after TBI in a rat controlled cortical impact model was investigated.

Male adult rats (7-10-weeks-old) weighing 200−310 g were used in this study. Under general anesthesia, a craniotomy of 6.0 mm in diameter was performed over the left parietal bone taking care not to penetrate the dura. A blunt force impact was applied to the craniotomy site using a pneumatic impact device and generated a cortical contusion on the left cerebral hemisphere. In sham-operated rats, the same surgical procedures were performed, but no impact was applied. Rats were perfused transcardially with phosphate-buffered saline under general anesthesia at 1, 4, 7, or 14 days after the surgery. Toluidine blue staining for mast cells and immunohistochemistry for histamine receptor H3 were performed on paraffin sections of the dura and cerebrum. Real-time PCR analysis of histamine receptor H3 mRNA expression was performed on total RNA extracts from the cerebrum.

The number of toluidine blue-stained dural mast cells at the site of impact was significantly decreased at one and four days after the trauma. The immunoreactivity and mRNA expression of histamine receptor H3 at the cortical contusion of the cerebrum were significantly increased at one and four days after the trauma. A previous report showed that activated mast cells release histamine-containing vesicles and appear unstained with toluidine blue. Therefore, the present results indicate that blunt force to the head causes dural mast cell degranulation and induces histamine receptor H3 expression in the cerebrum. The findings further indicate that a decreased number of toluidine blue-stained mast cells in the dura provide evidence of head trauma, suggesting that histological examinations of the dura may help to diagnose blunt force impacts to the head.

Forensic Neuropathology, Head Injury, *Dura*

 ** Presenting Author*