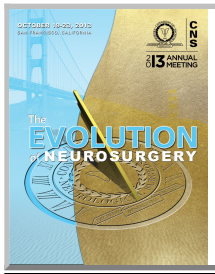

Meningeal Mast Cell-dependent Exacerbation of Brain Injury After Stroke in Mice

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Introduction

Mast cells (MCs), perivascular cells best known as effector cells involved in the development of inflammatory processes, do not circulate but are resident in virtually all anatomical sitesincluding brain parenchyma and meninges. Brain parenchymal MCs have been reported to exacerbate stroke pathology,however the role of meningeal MCs, if any, in stroke pathology is not known. To address this, we used ‘mast cell knock-in’ mouse models whereby genetically MC-deficient mice were selectively repaired of their MC deficiency by engraftment of in vitro grown mast cells, either systemically or locally in the meninges.

Methods

The WBB6F1-KitW/W-v MC-deficient mouse model was used. 3 groups were tested: wild-type, MC-deficient, and MC-engrafted (after systemic or meningeal engraftment). Mice were subjected to 30 min occlusion of the middle cerebral artery. Brain swelling and infarct size were assessed by T2-weighted MRI and histology. The immune response was quantified by flow cytometry.

Results

MC-deficient mice had less brain swelling at 3d post-stroke, smaller lesions at 3d and 2wk post-stroke, and fewer brain granulocytes at 3d post-stroke than their corresponding wild-type or systemically MC-engrafted groups, implying that MCs exacerbate ischemic injury. Analysis of the central nervous system MC distribution in wild-type and MC-engrafted mice revealed equivalent numbers of MCs in meninges in both groups but almost no MCs in brain parenchyma of MC-engrafted groups. This suggests that meningeal MCs, rather than parenchymal MCs, are key effectors of stroke pathology. To test this, MCs were engrafted locally into the meninges. These meningeal MC-engrafted mice had significantly more brain swelling, larger infarcts, and more brain granulocytes after stroke than MC-deficient mice.

Learning Objectives

By the conclusion of this session, participants should be able to understand the importance of meningeal mast cells for stroke.

Conclusions

Our results support the conclusion that meningeal MCs can exacerbate stroke pathology. Hence, targeting these cells may be a novel therapeutic strategy for stroke.

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