IJAE
Vol. 120, n. 1 (Supplement): 194, 2015
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Immunolocalization of CCL2-expressing cells in EAE and EAE-MSC cerebral cortex

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The chemokine CCL2 has been considered as a mediator of inflammation in different diseases of the central nervous system, including experimental autoimmune encephalomyelitis (EAE), where the chemokine mediates extravasation of mononuclear leukocytes and loss of microvessel barrier function [1]. Previous studies have demonstrated that cellular sources of CCL2 during both EAE and multiple sclerosis (MS) are astrocytes and microvessel endothelial cells (ECs). Initially, we have demonstrated that in a MOG-induced model of EAE in C57BL/6 mice, 6 hrs after the intravenous treatment with bone marrow derived mesenchymal stem cells (MSCs) [2], the junctional staining patter of blood-brain barrier (BBB) microvessels and their functional effectiveness to permeability tracers seem to be restored. We have subsequently analysed, in the same experimental models, EAE and EAE-MSC mice, expression and immunolocalization of chemokine CCL2 by double immmunolabelling with cell-specific markers: endothelial PECAM-1 (CD31), OPCs (oligodendrocyte precursor cells) proteoglycan NG2, astrocytic GFAP, and Iba1 for microglia cells. Surprisingly, in the adopted model of cerebral cortex EAE, astrocytes and ECs do not show any detectable CCL2 expression, instead a strong staining is observed on activated parenchymal and perivascular microglia. Astrogliosis, microglia activation, and CCL2 overexpression appearing strongly reduced in EAE mice after MSC treatment. These observations identify microglia cells as the major source of CCL2 in EAE mice, whose barrier is damaged, and suggest the downregulation of the chemokine in perivascular microglia as a possible mechanism involved in BBB protection after MSC administration.

References

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Keywords
Experimental autoimmune encephalomyelitis; Mesenchymal stem cells; Blood-brain barrier; Microglia; Chemokine CCL2.