Deciphering the Immunological Signature During the Early Brain Injury in Subarachnoid Hemorrhage Patients.

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CNS 2016 ANNUAL MEETING San Diego CALIFORNIA SEPTEMBER 24-28, 2016

Introduction

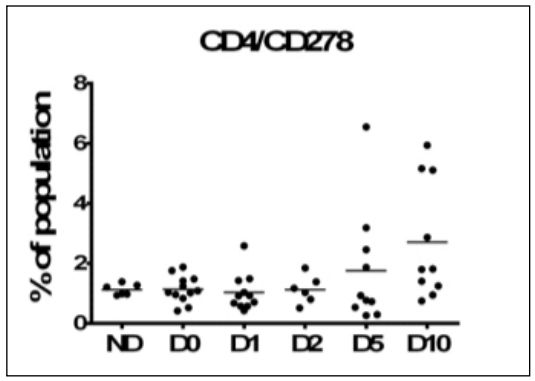
Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating disease with an incidence rate of approximately 10 per 100,000 patient years in the general population. Sadly despite the recent medical advances, the long-term prognosis has not improved significantly. Historically, the vasospasm was the culprit to explain these deficits. However, despite reduction of the incidence of vasospasm, the outcome was not changed. Thus, it is becoming clear that early inflammatory events after the SAH are crucial in the death of neurons that will lead to the altered functional status of these patients. However, the exact nature of this early injury and the nature of the immune activation are ill defined.

Methods

In order to decipher the immune phenotype of sub-arachnoid haemorrhage patients, we collected blood and CSF (when available) at admission, and days 1, 2, 5, and 10. After leukocyte isolation, using multicolor flow cytometry, the leukocyte phenotype was determined. 40 soluble molecules were measured in sera and CSF with a multiplex platform.

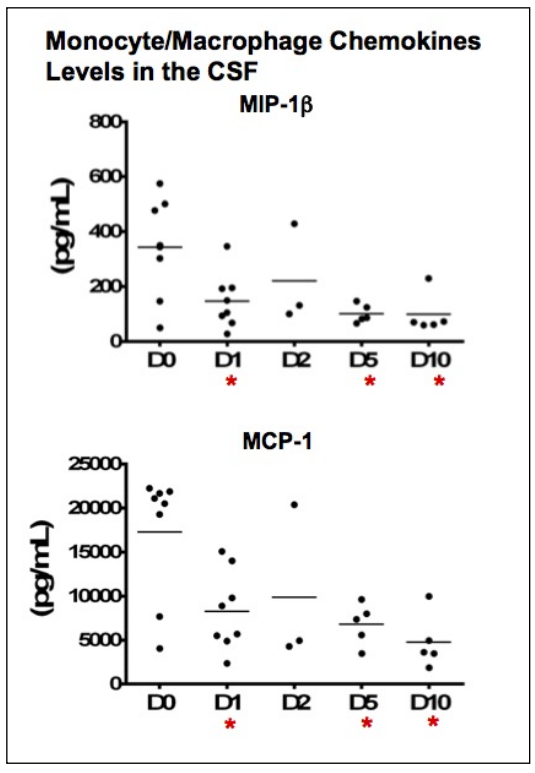
Results

Monocyte phenotypes: Increased Numbers of Inflammatory Monocytes at Early Time-Points

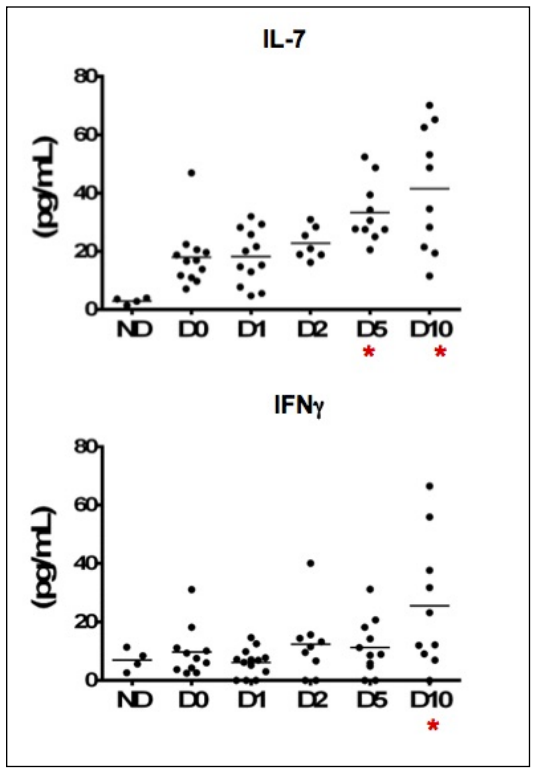


Lymphocyte Phenotype: Increased Expression of ICOS on Activated Lymphocytes at Late Time-Points

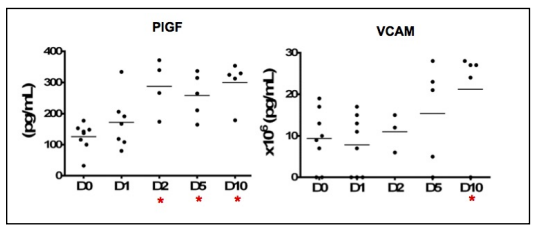
Monocyte/Macrophage Chemokines Are Increased in the CSF Early After SAH



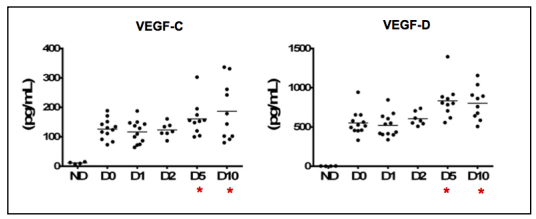
Increased Lymphocyte Activating Factor Levels in the Blood at Late Time-Points After SAH



Increased Angiogenic Factor and Vascular Inflammation Levels (PIGF and VCAM) in the CSF Late After SAH



Increased Angiogenic Factor Levels in the Blood at Late Time-Points after SAH



Conclusions

Our platform helped us to decipher the sequencial activation of immune cells. Monocytes adopted a pro-inflammatory phenotype early after the ictus, whereas lymphocyte activation was seen at later time-points. Furthermore, simultaneously to the peripheral monocyte activation, increased cerebrospinal fluid levels of monocyte chemoattractants were increased early after the ictus. Moreover, blood lymphocyte activation product and activating cytokine were higher at later time-points after the SAH. This project highlighted novel immunological targets that could be manipulated to improve the clinical outcomes of this patient population.

Learning Objectives

By the conclusion of this session, participants should be able to:
1) Describe the importance of early brain injury in the outcome of SAH patients
2) Discuss the immune activation following SAH.
3) Identify potential immunological targets.

Acknowledgments:
The Chair Claude-Bertrand in Neurosurgery from the Université de Montréal. Patients and their Families that Helped Us to Perform this Research.