Thromboinflammation before and after stroke: the bloody interactions of the lectin complement pathway

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Abstract
Stroke is associated with vascular events that involve the activation of several pathophysiological cascades including coagulation, contact/kinin and complement cascade, interacting at multiple levels. Key to these interactions is the complement system, a physiological component of innate immunity which is rapidly activated after stroke. Among the four different complement activation pathways, the lectin pathway (LP) has a critical pathological role both in humans and in animal models. LP controls and coordinates multiple pathogenic cascades being a hub in vascular injury. Its initiator molecules, by recognition of membrane-anchored proteins, deposit on damaged endothelium which is a site where the complement, the kinin and the coagulation systems, all active on endothelial cell surface, can interact. Their interplay is generally referred to as 'thromboinflammation'.
I will discuss the central role of the LP in:
1) coordinating the post-ischemic thromboinflammation. To this purpose, I will present data obtained in mice lacking mannose-binding lectin (MBL), a starter of the LP, subjected to focal brain ischemia. Briefly, MBL deficient mice had better flow recovery and less extravasation than wild type mice, along with decreased endothelial and platelet activation, overall yielding protection from ischemic injury.
2) Preceding an acute cardiovascular event. I will present data obtained in a human study on atherosclerosis, a thromboinflammatory mechanism representing a risk factor for acute cardiovascular events. Plasma and intraplaque levels of the LP initiator proteins MBL and ficolin-2 are associated with vulnerable plaques, a condition increasing the risk of stroke.
As such the LP may offer a promising therapeutic opportunity in stroke therapy and prevention. This observation is further supported by clinical data documenting the association of the LP activation/consumption with poor outcome in stroke patients, making this pathway attractive for development of novel pharmacological tools.