

Popular Science Summary: Understanding inflammation in Cerebral Cavernous Malformation

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Cerebral Cavernous Malformation (CCM) is a disease caused by enlarged blood vessels of the brain and spinal cord. The engorged vessels mature into mulberry-like structures that are prone to rupture and lead to symptoms such as intracranial bleeding and epileptic seizures (uncontrolled body movements and a momentary loss of awareness). CCM can be inherited and affect 1 in 10,000 individuals or it can occur spontaneously in 1 out of every 200 people. In the familial version, multiple mulberry-like lesions develop in the brain vasculature; while the spontaneous form is characterized by a single isolated abnormal blood vessel. No pharmacological treatment exists for CCM, and the only available therapy is surgical removal of the irregular blood vessels and this is considered a very high-risk procedure depending on the location of the lesion.

Inflammation plays a large role in infection and diseases such as CCM. Inflammation is a protective biological response to harmful stimuli such as pathogens or irritants. It is well established that during an inflammation defense cells in the blood communicate with the cells lining the inside of blood vessels via chemical signals. During this cellular communication, cells aim to reconstruct the damage caused to the tissue from pathogens or diseases. In CCM, the blood vessels in the brain become extremely inflamed, therefore this project used mouse models of familial CCM to define the cells and mediators causing inflammation in CCM. This study detected a significant increase in two chemical signals called ICAM-1 and VWF. These chemical signals are used between blood vessel cells during an inflammation. The chemical signals appeared to be inside of the damaged blood vessels and in their periphery. In addition, this study spotted an increase in fibrin, a substance present in the blood that is necessary for the formation of blood clots. Lastly, this study also identified T-lymphocytes and Natural Killer (NK) cells in brain lesions of CCM mice. T-lymphocytes and NK cells are key regulators in inflammation as they recruit other inflammatory proteins and cells. It is of utmost importance to define and understand inflammation as it can be used as a tool in parallel with pharmaceuticals. Today, there is no pharmacological therapy for human CCM, however the investigation of inflammation in mouse models of CCM have helped identify (and continue to identify) numerous potential therapeutic agents that can potentially give rise to a therapeutic for human CCM.