Secondary vasospasm and disturbances in cerebral autoregulation are associated with the development of delayed cerebral ischemia (DCI) following aneurysmal subarachnoid hemorrhage (SAH).

Aneurysmal subarachnoid hemorrhage (SAH) remains a serious cerebrovascular disease. Even if SAH patients survive the initial insults, delayed cerebral ischemia (DCI) may occur at 4 days or later post-SAH. DCI is characteristics of SAH, and is considered to develop by blood breakdown products and inflammatory reactions, or secondary to early brain injury, acute pathophysiological events that occur in the brain within the first 72 hours of aneurysmal SAH. The pathology underlying DCI may involve large artery vasospasm and/or microcirculatory disturbances by microvasospasm, microthrombosis, dysfunction of venous outflow and compression of microvasculature by vasogenic or cytotoxic tissue edema. Recent clinical evidence has shown that large artery vasospasm is not the only cause of DCI, and that both large artery vasospasm-dependent and -independent cerebral infarction causes poor outcome. Animal studies suggest that mechanisms of vasospasm may differ between large artery and arterioles or capillaries, and that many kinds of cells in the vascular wall and brain parenchyma may be involved in the pathogenesis of microcirculatory disturbances. The impairment of the paravascular and glymphatic systems also may play important roles in the development of DCI. As pathological mediators for DCI, glutamate and several matricellular proteins have been investigated in addition to inflammatory molecules. Glutamate is involved in excitotoxicity contributing to cortical spreading ischemia and epileptic activity-related events. Microvascular dysfunction is an attractive mechanism to explain the cause of poor outcomes independently of large cerebral artery vasospasm, but needs more studies to clarify the pathophysiologies or mechanisms and to develop a novel therapeutic strategy [1)]

Though traditionally attributed to vasospasm of large capacitance arteries and the resulting down-stream disruption of cerebral blood flow, the pathogenesis of DCI has proven to be more complex with early brain injury, blood-brain barrier disruption, microthrombosis, cortical spreading depolarizations, and the failure of cerebral autoregulation as newly elucidated factors [2)].

To facilitate translation, clinically relevant animal models that reproduce the pathophysiology and cardinal features of DCI after SAH are urgently needed [3)].

1)
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