Cerebral Venous Sinus Thrombosis Pathophysiology

The pathophysiology of CVST depends on two interconnected events, local signs due to venous infarct, e.g., hemiparesis and global signs due to raised ICP from an obstructed venous system–papilloedema and isolated intracranial hypertension being one of them. Pathophysiology of CVST is diverse and makes it easier to understand the diversity of clinical presentations [1].

Dural venous sinuses are connected by channels to large cortical veins and together make up the venous system that allows blood to drain from the cranium. Thrombus formation within a venous sinus can create a partial or complete blockage and localized congestion within the venous system and the brain; both are secondary to decreased venous outflow

Exacerbation of venous congestion causes increased intracranial pressure, massive ischemia, and infarction of cerebral tissue. Hemorrhagic conversion can occur in larger infarctions.

Rashad et al., from Sendai, Japan showed the intense activation of immune cells, particularly the microglia, along with the increase in macrophage activity and NLRP3 inflammasome activation that is indicated by NLRP3, Interleukin 1 beta (IL-1β), and Interleukin 18 gene and caspase 1 upregulation and cleavage as well as pyroptosis.

Leukocytes were observed in the brain parenchyma, indicating a role in cerebral venous thrombosis (CVT)-induced inflammation. In addition, astrocytes were activated, and they induced glial scar leading to parenchymal contraction during the subacute stage and tissue loss. MMP9 was responsible primarily for the BBB breakdown after CVT and it is mainly produced by pericytes. MMP9 activation was observed before inflammatory changes, indicating that BBB breakdown is the initial driver of the pathology of CVT. These results show an inflammation driven pathophysiology of CVT that follows MMP9-mediated BBB breakdown, and identified several targets that can be targeted by pharmaceutical agents to improve the neuroinflammation that follows CVT, such as MMP9, NLRP3, and IL-1β. Some of these pharmaceutical agents are already in clinical practice or under clinical trials indicating a good potential for translating this work into patient care [2].

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Itrat A, Shoukat S, Kamal AK. Pathophysiology of cerebral venous thrombosis–an overview. J Pak Med Assoc. 2006 Nov;56(11):506-8. Review. PubMed PMID: 17183977.
2)
Rashad S, Niizuma K, Sato-Maeda M, Fujimura M, Mansour A, Endo H, Ikawa S, Tominaga T. Early BBB breakdown and subacute inflammasome activation and pyroptosis as a result of cerebral venous thrombosis. Brain Res. 2018 Jul 4. pii: S0006-8993(18)30362-7. doi: 10.1016/j.brainres.2018.06.029. [Epub ahead of print] PubMed PMID: 29981290.