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# Pathophysiological Mechanism of Seizure in Cerebral Venous Sinus Thrombosis

Dear Editor,

We read the article titled "Outcomes of Cerebral Venous Thrombosis in Al-Yarmook Teaching Hospital" on the esteemed "Medical Journal of Babylon" with great interest. Mizeel *et al.* studied the incidence of seizures and their associated risk factors for patients with cerebral venous sinus thrombosis (CVST). They found that the most common type of seizure was generalized, which was correlated with superior sagittal sinus occlusion. Also, oral contraceptives were significantly associated with early seizure onset.[1]

CVST can present with variable clinical manifestations such as headaches, unexplained altered sensorium, focal neurological deficit, and subarachnoid hemorrhage. In this context, the occurrence of seizures in CVST may adversely affect the prognosis because they are correlated with high morbidity and mortality.[2] In addition, the mechanism of seizure in individuals with CVST is not clear, so the majority of studies aimed at determining the potential risk factors for epileptogenesis.

Herein, we would like to discuss the pathophysiological mechanism of seizure in CVST [Figure 1]. A literature search was performed in Medline/Pubmed, on a set of terms that included cerebral venous sinus thrombosis, seizure, and mechanism [Table 1]. The seizures presented in CVST appear to have a different mechanism from those in epilepsy-related stroke. This can be supported by the fact that some studies showed a higher percentage of Todd's paralysis and abnormal dynamic control of intracranial pressure in CVST.[3]

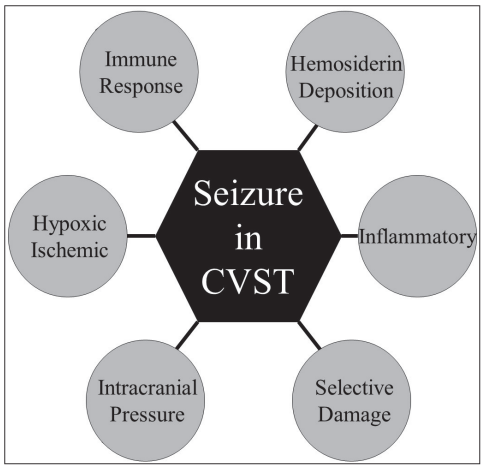


**Figure 1:** Pathophysiological mechanism of seizure in cerebral venous sinus thrombosis (CVST)

Amornpojnimman *et al.* retrospectively studied 180 individuals with CVST in Thailand. They showed that intracerebral hemorrhage and dependency status at admission predict seizures in CVST. Also, focal to bilateral tonic-clonic seizure was the most frequent seizure type. These findings are interesting since they could support the hypothesis of hemosiderin deposition and selective neuronal damage leading to abnormal electrical discharge.[2]

Another cohort from Serbia revealed that CVST individuals without headache at presentation have the worst outcome when compared with those with headache. Petrović *et al.* observed that the seizure group had more neurological deficits or altered mental status.[4] This can support the hypothesis of diffuse cerebral damage due to thrombosis. Increased intracranial pressure, inflammatory reactions, and hypoxic–ischemic injury pathways could explain these neurological manifestations.

A recent study from China assessed the outcomes of individuals with CVST during pregnancy and postpartum managed with anticoagulation therapy. Meng *et al.* revealed that pregnancy-related CVST subjects are three times more likely to have seizures when compared with non-pregnancy-related individuals. Other parameters that were more prevalent in the pregnancy group included hyperlipidemia, headache, nausea, fever, neurological deficits, and prothrombotic state.[5] Thus, we can assume that, apparently, there is some role in immunological reactions contributing to worse outcomes.

In sum, there are six main mechanisms proposed, which are abnormal immunological response, deposition of extracellular substances, hypoxic–ischemic injury, abnormal inflammatory reaction, increased intracranial pressure, and selective neuronal loss. Moreover, we believe that seizures in CVST are related to a combined group of mechanisms rather than only a simple pathway.

## Ethical consideration

Not applicable

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**Table 1: Pathophysiological mechanisms of seizure in CVST**

| Mechanism | Pathophysiology | Reference |
|---|---|---|
| Autoimmune | During pregnancy, a state of immune tolerance is noted toward the half-allogeneic fetus. So, it is believed that during the gestational period immunological mechanisms may induce epilepsy. | Farzi F, Abdollahzadeh M, Faraji R, Chavoushi T. Seizure in Pregnancy Following Cerebral Venous Sinus Thrombosis. Anesth Pain Med 2015;5:26866. |
| Hemosiderin | In rat models with cerebral hemorrhage, it was observed that the extravasation of serum-derived components can induce seizures. Thus, it is believed that hemorrhagic lesions could impair the blood–brain barrier stimulating the cerebral cortex by the exudation of hemosiderin and its metabolites. | Seiffert E, Dreier JP, Ivens S, Bechmann I, Tomkins O, Heinemann U, *et al*. Lasting blood-brain barrier disruption induces epileptic focus in the rat somatosensory cortex. J Neurosci 2004;24:7829-36. |
| Hypoxia | After a hypoxic–ischemic injury, the extracellular concentrations of glutamate increase and GABA decrease, which could lead to secondary neuronal injury. Also, there is the possible contribution of abnormalities in ion channels to the development of epileptiform discharges. It is worthy of mentioning the occurrence of increased levels of intracellular sodium/calcium with concurrently increased levels of extracellular potassium. | Monteiro AM, Lima CM, Ribeiro ÉB, Lins MC, Miranda S, Miranda LE. Imaging diagnosis and clinical findings of cerebral venous thrombosis in full-term neonates without brain damage: a ten-year review. Rad Bras 2010;43:149-53. |
| Inflammatory | In predisposed patients, altered gene expression could cause an upregulation of inflammation leading to cell death. Also, abnormalities in neuronal plasticity were observed in studies with functional neuroimaging. | Wang L, Duan J, Bian T, Meng R, Wu L, Zhang Z, *et al*. Inflammation is correlated with severity and outcome of cerebral venous thrombosis. J Neuroinflammation 2018;15:329. |
| Intracranial pressure | The dural venous sinuses, especially the superior sagittal sinus, play an important role in cerebrospinal fluid absorption; so, the thrombus may seriously affect the intracranial pressure dynamics. | Habibabadi JM, Saadatnia M, Tabrizi N. Seizure in cerebral venous and sinus thrombosis. Epilepsia Open 2018;3:316-322. |
| Selective neuronal loss | It is presupposed that there are some mechanisms specific to CVST seizures. Therefore, the occurrence of selective damage to determined neurons can lead to altered synaptic plasticity, collateral sprouting, and deafferentation causing neuronal synchrony and hyperexcitability. | Singh RK, Bhoi SK, Kalita J, Misra UK, Gupta D. A comparative study of seizures in arterial and venous stroke. Int J Epi 2017;4:6-11. |

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## Conflicts of interest
There are no conflicts of interest.

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