



Type of Paper: Case Report

Cerebral Venous Sinus Thrombosis Secondary to Pediatric Meningoencephalitis with Temporal Association to Japanese Encephalitis Vaccination: A Case Report

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Article history:

Received: March 25, 2026

Revised: April 20, 2026

Accepted: April 30, 2026

How to Cite: Hutagaol, FI.; Megaputri, FA.; Kristiani, D. (2026). Cerebral Venous Sinus Thrombosis Secondary to Pediatric Meningoencephalitis with Temporal Association to Japanese Encephalitis Vaccination: A Case Report. JoMaSSH, 2(2), 126-137. doi: 10.21831/jomassh.v2i2.2828



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Abstrak:

Pendahuluan: Meningoensefalitis pada anak merupakan salah satu penyebab penting gangguan neurologis akut dan dapat disertai komplikasi serius seperti trombosis sinus vena serebral (CVST). Munculnya gejala neurologis setelah vaksinasi seringkali menimbulkan dilema diagnostik, terutama dalam membedakan apakah hubungan tersebut bersifat kausal atau hanya kebetulan temporal.

Laporan kasus: Seorang anak laki-laki usia 6 tahun datang dengan demam, kejang berulang, dan penurunan kesadaran. Pemeriksaan cairan serebrospinal menunjukkan gambaran yang lebih mengarah pada infeksi viral. Pemeriksaan magnetic resonance venography mengonfirmasi adanya trombosis pada sinus transversus dan sigmoid kiri. Riwayat vaksinasi Japanese encephalitis 13 hari sebelum onset serta keluhan gigi sebelumnya sempat menjadi pertimbangan dalam penelusuran etiologi. Pasien ditatalaksana dengan antiepileptik, terapi penurunan tekanan intrakranial, antibiotik empiris, serta antikoagulan. Selama perawatan, kondisi klinis pasien menunjukkan perbaikan bertahap hingga akhirnya pulang tanpa defisit neurologis.

Kesimpulan: Kasus ini menekankan pentingnya kewaspadaan terhadap kemungkinan CVST pada meningoensefalitis anak, serta perlunya interpretasi yang hati-hati terhadap hubungan temporal dengan vaksinasi. Penegakan diagnosis yang tepat dan tata laksana yang komprehensif berperan penting dalam mencapai luaran klinis yang baik.

Kata kunci: Infeksi; Meningoensefalitis; Pediatrik; Trombosis Sinus Vena Serebral; Vaksin Japanese Encephalitis

Introduction: Pediatric meningoencephalitis is a significant cause of acute neurological morbidity and may be complicated by secondary cerebrovascular events such as cerebral venous sinus thrombosis (CVST). The occurrence of neurological symptoms following recent vaccination presents a diagnostic challenge, particularly in distinguishing causal relationships from coincidental associations. **Case presentation:** A 6-year-old boy presented with fever, recurrent seizures, and altered consciousness. Cerebrospinal fluid analysis demonstrated lymphocytic pleocytosis suggestive of a viral etiology. Magnetic resonance venography confirmed thrombosis of the left transverse and sigmoid sinuses. A history of Japanese encephalitis vaccination 13 days prior to symptom onset was noted, along with preceding dental symptoms initially raising suspicion of a possible odontogenic source. The patient was managed with antiepileptic therapy, intracranial pressure control, empirical antibiotics, and anticoagulation. Clinical improvement was observed, with full neurological recovery at discharge. **Conclusion:** This case highlights the importance of considering CVST as a potential complication of pediatric meningoencephalitis and underscores the need for cautious interpretation of temporal associations with vaccination. Early recognition and appropriate multidisciplinary management, including anticoagulation when indicated, are essential to optimize clinical outcomes

Keywords: CVST; Infection; Japanese Encephalitis Vaccine; Meningoencephalitis; Pediatric

1. Introduction

Meningoencephalitis is still the most common infectious disease of the central nervous system in children (1,2). Diagnosis is determined based on neurological manifestations and supporting examinations. Clinical manifestations that often appear such as fever, seizures, headache, vomiting spurring, decreased consciousness, and neck stiffness. Supporting examinations such as cerebrospinal fluid analysis (CSF) followed by CSF culture and Polymerase Chain Reaction (PCR) are still the gold standard in establishing diagnosis. The limitations of facilities due to the absence of culture and PCR examinations are diagnostic challenges in determining the etiology of infection (1,2).

Cerebral Venous Sinus Thrombosis (CVST) is a rare complication that arises due to secondary causes such as meningoencephalitis with morbidity and mortality reaching 10% (3,4). Pathophysiological, CVST occurs through the Virchow's Triad mechanism, including endothelial dysfunction triggered by inflammatory reactions, hypercoagulability triggered by prothrombotic mechanisms, and cerebral venous stasis that interferes with the venous flow of the brain (3,4). The presence of thrombus in the venous flow is an important sign to establish the diagnosis of CVST, where the Magnetic Resonance Venography (MRV) examination is the gold standard of diagnosis due to its sensitivity and high specificity (3).

The vaccination program is the main strategy to reduce the number of illnesses and deaths currently implemented in Indonesia, especially in the prevention of cases of Japanese encephalitis (JE) (5,6). Until now, JE is still an endemic disease of viral infection of the central nervous system that is commonly experienced by children in the Southeast Asian region. Although this vaccine has been declared safe by WHO and the occurrence of serious side effects is also reported to be rare (7–9), the emergence of neurological manifestations after immunization gives rise to the suspicion of a temporary causal relationship. This actually poses dilemmas and challenges in determining the direction of diagnosis and patient handling.

Limited research reporting the incidence of CVST due to secondary causes of meningoencephalitis in children, especially in the context of post-immunization events. This overlapping event poses challenges in the diagnosis and management of patients, especially in determining the cause of CVST complications as a result of secondary infection, as a cause of post-immunization events, or other causes. (10,11). We report a case of CVST secondary meningoencephalitis in children and temporal association with recent immunization, highlighting the importance of careful etiological evaluation and cautious interpretation of temporal relationships.

2. Case Presentation

A 6-year-old boy patient came to the tertiary hospital emergency room with complaints of fever and decreased consciousness. Three days before entering the hospital, the patient experienced three episodes of tonic-clonic seizures that lasted less than one minute. Two days before entering the hospital, the patient also experienced symptoms of fever, severe headache, and vomiting that lasted five times. During the trip to the hospital, the patient had one episode of seizures and decreased consciousness.

Based on the national vaccination protocol, the patient has an incomplete history of basic immunization. According to alloanamnesis, the history of diphtheria-pertussis-tetanus vaccination has only been carried out one time. Eight days before the onset of symptoms, the patient was only given the JE vaccine once. There is no history of other post-immunization events. The patient also has a history of dental caries that has lasted about two weeks. Even though he has been treated, the patient still does not feel an improvement in symptoms. There is no recent history of febrile seizure, otitis, sinusitis, or mastoiditis. History of tuberculosis infection is denied.

Based on the nutritional status of the patient, the patient was shown in the underweight category, with a height of 130 cm and a body weight of 23 kg. Based on the physical examination, the patient had a fever (38.1°C), pulse rate of 129 x/minute and a respiratory rate of 48 x/minute. Consciousness level was E3V2M4, the patient showed a decrease in consciousness. Neurological examination showed signs of stiffness of the knee, positive Kernig Sign, and positive Brudzinski Sign. These results showed signs of meningeal stimulation. The pathological reflex examination was positive bilaterally positive on the examination of Babinski, Chaddock, and Oppenheim,

accompanied by hyperreflexia and increased clonus. These results showed lesions of the upper motor neurons. Further detailed neurological assessment was limited due to decreased consciousness. There were not Cardiovascular, respiratory, and abdominal examinations were normal. Examination of both eyes showed direct and indirect light reflexes of positive value. Positive pupil reflex with a bilateral pupil size of 4 mm. Funduscopy examination by ophthalmologists found a cup and disk ratio of < 0.3 with an arterial-venous ratio of 2/3 and a clear border, no signs of papilledema were found.

Supporting examinations were carried out in series when the patient was treated at the PICU (Table 1). The initial complete blood test showed that leukocytosis ($15.8 \times 10^3/\text{mm}$) corroborated the suspected infection. CSF examination was carried out on the second day of treatment and mononuclear pleocytosis with low levels of C-reactive protein (CRP) was found to corroborate the direction of the suspected etiology towards viral infection. To rule out extracranial causes such as tuberculosis bacterial infection, GeneXpert examination was carried out on CSF samples and negative results were obtained. In the microbiology sputum examination, only gram-negative bacteria (*Cedecea sp*) were found, which were not strong enough to be an extracranial causal indication. Although bacterial and viral culture examinations were not available due to limited facilities, this laboratory results were very consistent with viral infections. Based on anamnesis, physical examination, and laboratory, the differential diagnosis is consistent toward viral meningoencephalitis.

A CT scan of the head was also performed on the second day of treatment (Figure 1). The results of the discovery of signs of cerebri edema with an increase in the density of the falx cerebri were consistent with meningoencephalitis accompanied by an increase in the density of bilateral transversus sinuses and sagittal sinuses. The results were confirmed by MRV examination on the third day of treatment with the result of a filling defect in the left transversus sinus that extends to the left sigmoid sinuses, a strong sign of thrombus (Figure 2). No venous infarction or signs of bleeding transformation were found. The D-dimer examination was performed to determine the potential for sepsis or coagulopathy dan as an initial screening detects the presence of thrombus so MRV is needed. The results showed an increase from normal limits at the beginning of the examination followed by a decrease back to normal. Normal or increased D-dimer results did not rule out a strong suspicion of CVST. These results only showed a mechanism of thrombosis that was more likely to be local in the venous brain than systemic, which was associated with better clinical improvement. Through these results, the patient's final diagnosis is CVST of the left transversus sinus and left sigmoid sinus with the secondary cause of viral meningoencephalitis.

Patient assessment was carried out comprehensively and multidisciplinary. Oxygenation was administered with a nasal cannula of 3 liters per minute. Seizure management was administered intravenous diazepam 0.5 mg/kg while in the emergency room, replaced with intravenous phenytoin 15-20 mg/kg twice daily for 5 days, then tapering off. Empirical antibiotics were administered intravenous ceftriaxone 1 g twice daily for 5 days. Intracranial pressure was lowered with intravenous mannitol 0.25 – 1 g/kg every 6 hours for 4 days and tapering off. Antipyretic treatment was administered intravenous paracetamol 10–15 mg/kg/dose every 6 hours. The main treatment in the form of anticoagulation in the acute phase was initiated with subcutaneous enoxaparin 1 mg every 12 hours for two days, followed by once-daily dosing for five days. To reduce inflammation, patients were given intravenous dexamethasone 2 mg four times daily was administered and gradually tapered following clinical improvement. Supportive care included intravenous fluids with Ringer Lactate at 55 - 65 mL/hour.

During the treatment there was clinical improvement of the patient. On the fourth day of PICU treatment, the patient's body temperature was relatively absence of fever, even neurological manifestations were still visible. The patient's consciousness level was E3V4M5, signs of meningeal stimulation were negative, the pathological reflex was still positive but one side. The clonus was no longer visible and the physiological reflex was 2/2. The value of leukocytes had returned to normal, indicating that the infection had resolved. The level of D-dimer showed normal resolution and the value of the neutrophil-lymphocyte ratio (NLR) decreased from the first day.

On the fifth day of treatment, the patient was still absence of fever, the patient's consciousness level increased to E4V5M5, the neurological manifestations of significant improvement. Meningeal stimuli are still

negative, bilateral negative pathological reflexes, physiological reflexes 2/2, clones negative, motor strength can be evaluated 4/4. The patient was transferred to a regular inpatient room and observed for the next 3 days. Other therapies were continued and by lowering the dose slowly. Antibiotics were continued and replaced with oral cefixime 100 mg twice a day.

During treatment in the ward for three days, the patient did not have seizures, did not have a fever, and was fully conscious. The patient's consciousness was E4V5M6, the meningeal sign was still negative, the pathological reflex was negative bilateral, the physiological reflex was 2/2 with motor strength of 5/5. Cranial nerve examination also found no abnormalities. On the eighth day, the patient was discharged with stable neurological clinical considerations even though a repeat MRV examination was not performed. The patient was given the main therapy of the anticoagulant rivaroxaban 5 mg orally once a day and given for 3 months. For the prevention of seizures, the patient was given valproate acid syrup 250 mg/5 ml twice a day and phenytoin 15 mg/kg twice a day.

At the three-month follow-up, the patient remained asymptomatic with normal neurological examination findings. Although outpatient follow-up MRV was not performed, significant clinical recovery was observed. Anticoagulant and anticonvulsant therapies were continued until six months. At five-month follow-up, the patient was asymptomatic, no bleeding complication, with a normal neurological exam. Anticoagulation was stopped, and anticonvulsants continued as needed.

Table 1. Patient timeline during hospitalization

Time Point	Event	Key Findings
Day - 14	Toothache onset	Onset of dental caries; dental treatment without improvement
Day - 8	JE Vaccination	Japanese encephalitis vaccination (first dose)
Day - 3	Neurological symptom onset	Fever, headache, vomiting, three generalized tonic-clonic seizures
Day 1 (Admission)	Referral and PICU admission	Admission; fourth seizure; GCS E3V2M4; PICU admission; treatment initiated
Day 2	Lumbar Puncture, Laboratory Workup, Neuroimaging	CSF showed lymphocytic pleocytosis suggestive of viral infection; D-dimer elevated, CRP normal. Cranial CT scan revealed cerebral edema with hyperdensity of bilateral transverse sinuses and superior sagittal sinus
Day 3	Advanced neuroimaging	MRV confirmed cerebral venous sinus thrombosis involving the left transverse and sigmoid sinuses; no evidence of tuberculosis from CSF evaluation
Day 4	Clinical Recovery and Management	GCS improved to E3V4M5; pathological reflexes still present; dexamethasone and mannitol were gradually tapered; anticoagulant and anticonvulsant therapy continued; D-dimer normalized
Day 5	Further clinical improvement	GCS E4V5M5; motor strength 4/4; transferred to general ward; other therapies continued
Day 6	Continued recovery	Fully conscious (GCS E4V5M6); normal motor strength; no meningeal signs; pathological reflexes absent; ongoing therapy
Day 7	Continued recovery	Stable neurological status; no meningeal signs; therapy continued
Day 8	Discharge	Fully conscious with no neurological deficits; discharged with oral medications
3-month follow-up	Outpatient evaluation	No recurrence of symptoms; neurological examination normal; follow-up MRV not performed
5-month follow-up	Outpatient evaluation	No recurrence of symptoms; neurological examination normal, anticoagulant stopped

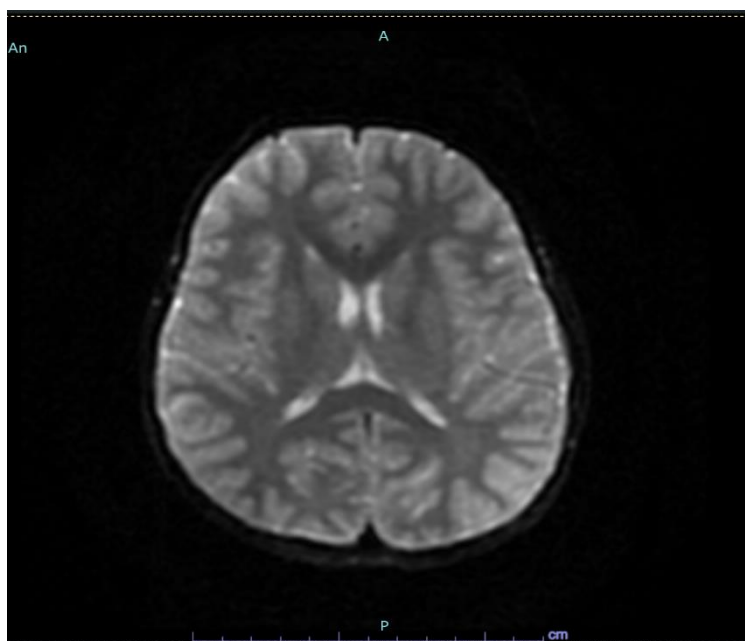


Figure 1. A cranial CT scan performed on the second day demonstrated cerebral edema with increased density of the falx cerebri, along with hyperdensity of the bilateral transverse sinuses and superior sagittal sinus.

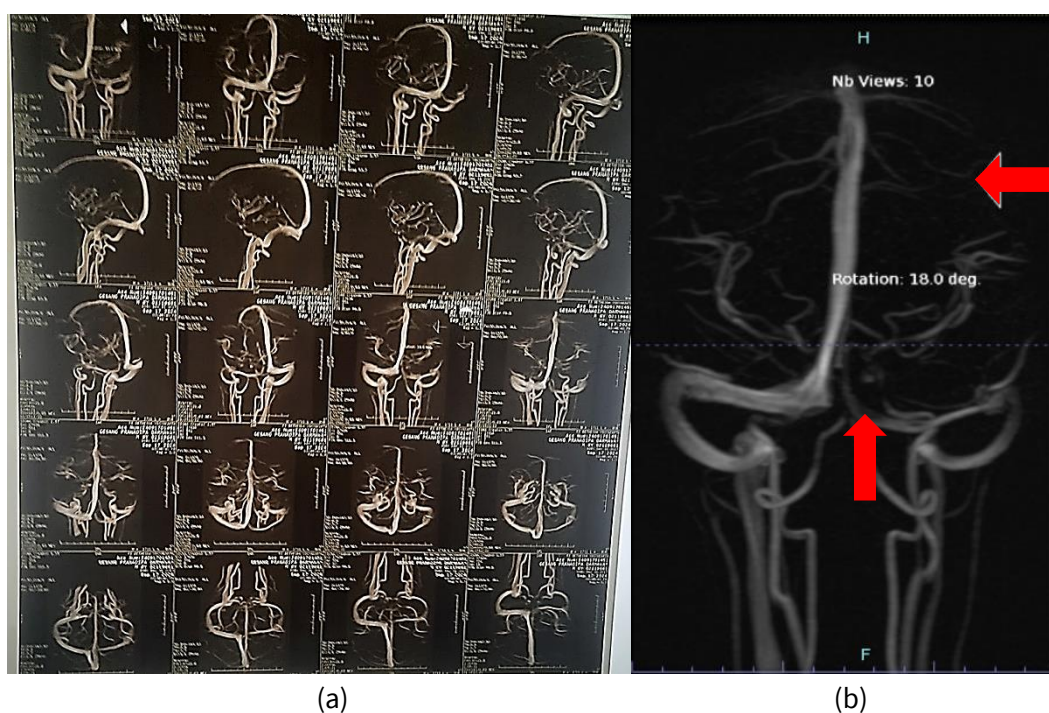


Figure 2. Magnetic resonance venography (MRV) demonstrating findings consistent with cerebral venous sinus thrombosis. (a) Multiple MRV projections showing reduced visualization of the left transverse sinus. (b) Maximum intensity projection image demonstrating absence of flow-related signal in the left transverse sinus with extension into the left sigmoid sinus (arrow), consistent with venous thrombosis.

Table 2. Results of Laboratory Examination conducted during 4 days of treatment at PICU

Type of examination	Test	Unit	Results				Reference Value
			Day 1	Day 2	Day 3	Day 4	
Complete Blood Count	Leukocytes	thousand/mm ³	15.80	-	-	6.13	5 - 12
	Erythrocytes	million/mm ³	4.72	-	-	4.27	4-5.2
	Hemoglobin (Hb)	g/dL	12.4	-	-	11.0	12 - 16
	Hematocrit	%	38.3	-	-	33.5	35 - 49
	Platelets	thousand /mm ³	366	-	-	252	150 - 400
	Lymphocytes	%	37.6	-	-	44.9	20 - 40
	MCV	fL	81.2	-	-	78.5	80 - 99
	MCH	pg	26.3	-	-	25.8	27 - 32
	MCHC	g/dL	32.4	-	-	32.8	32 - 36
	Neutrophils	%	54.8	-	-	44.8	40 - 75
	Monocytes	%	5.5	-	-	9.5	2 - 8
	Eosinophils	%	2.1	-	-	0.5	1 - 3
	Basophils	%	0	-	-	0.3	0 - 1
	NLR		3.0	-	-	1.0	< 3.13
	Sodium	mmol/L	140.58	-	-	-	135 - 145
	Potassium	mmol/L	3.35	-	-	-	3.50 - 5.50
	Chloride	mmol/L	97.87	-	-	-	96 - 106
	Random Blood Glucose (GDS)	mg/dL	143	89	-	-	60 - 199
Complete CSF Analysis	Color	-	-	Clear	-	-	-
	Clarity	-	-	Clear	-	-	Clear
	Pandy Reaction	-	-	Negative	-	-	Negative
	Nonne Apelt	-	-	Negative	-	-	Negative
	Leukocyte Count	thousand/mm ³	-	5.0	-	-	0 - 5
	PMN	%	-	0	-	-	30 - 40
	MN	%	-	100	-	-	60 - 70
	CSF Glucose	mg/dL	-	65.8	-	-	60 - 80
CSF Swab	CSF CRP	mg/dL	-	< 0.2	-	-	< 0.5
	Protein	mg/L	-	308	-	-	150 - 450
	BTA	+/-	-	-	Negative	-	Negative
	MTB	+/-	-	-	Negative	-	Negative
Coagulation Test	Rifampicin Resistant	+/-	-	-	Negative	-	Negative
	D-dimer	g/mL	-	1.2	-	0.22	≤1.0
Sputum Microbial Examination	Gram Strain	-	-	Gram Negative Bacteria Detected (Cedecea sp)	-	-	Negative

3. Discussion and Conclusions

Meningoencephalitis is an infectious disease of the central nervous system that triggers inflammation in the meningeal membrane and parenchyma of the brain. It is reported that enteroviruses, adenoviruses, herpesviruses, and Japanese encephalitis are the most common viral causes of meningoencephalitis (12). The prevalence of this case is mostly experienced by children with a morbidity rate of up to 50% and mortality reaching 30% (12,13). The clinical manifestations that arise involve pathological abnormalities in these areas as experienced by these patients, including fever, decreased consciousness, seizures, severe headache, projectile vomiting, and meningeal stimulation. Inflammation of the meningeal membrane and parenchyma of the brain causes symptoms of increased intracranial pressure accompanied by signs of meningeal membrane irritation (positive Kernig sign and positive Brudzinski sign) (14–16).

The diagnosis of meningoencephalitis was established by CSF analysis examination which was confirmed by PCR examination or bacterial culture (17). The results of CSF examination in this patient were showed as mononuclear pleocytosis with low levels of C-reactive protein (CRP), where this result was more likely to be caused

by viral infection than bacterial infections dominated by polymorphonuclear with high CRP as in sepsis (17). To confirm the causative agent of infection, PCR examination was not carried out due to limited facilities. However, these results have strengthened the temporary suspicion of the presence of viral meningoencephalitis.

Hematogenic and focal infections are the main mechanisms of infection in meningoencephalitis, so it is important to trace the history of infection that is suspected as the source of the spread of the infection (18,19). This importance in order be able to distinguish the source of this infection from intracranial or extracranial infection. Extracranial causes such as sepsis, pneumonia, tuberculosis infection, otitis, mastoiditis, sinusitis, or caries/tooth abscesses are the most common causes caused by bacterial infections than viral infections (20,21). In this patient, the presence of a history of dental caries 2 weeks before the onset of initial symptoms raises new suspicions whether there is a causal relationship between the two. The suspicion of tuberculosis infection can also be excluded on the GeneXpert examination with negative results. Although the sputum examination found gram-negative bacteria *Cedecea sp*, these results are not strong enough to prove the existence of a suspected systemic infection and are rarely reported as the cause of meningoencephalitis. However, CSF test results that are more likely to be consistent with viral infection remain the main anchor in directing the diagnosis for these patients.

CVST is a reaction to the formation of thrombus in the venous sinuses of the brain which is closely related to increased fatality of the patient's prognosis. The incidence of CVST is reported to be rare, especially in the child population with an estimated incidence of 0.67 per 100,000 children under the age of 18 years (22,23). The most triggers of CVST include: infection, trauma, coagulation factor deficiency (C/S factor deficiency). In this case, viral meningoencephalitis is strongly suspected to trigger the formation of thrombus in the cerebral sinuses through the release of inflammatory mediators such as cytokines, IL-1, IL-6, and TNF- α . This will trigger hemostasis instability resulting in endothelial dysfunction, hypercoagulability, and cerebral venous stasis. The formation of thrombus in the cerebral venous sinuses will trigger cerebral venous sinus occlusion, inhibit CSF circulation, and CSF reabsorption disorder (Figure 3) (22–24). In accordance with the Monro-Kellie doctrine, if compensation for this mechanism fails, there will be an intracranial increase, a weakening of the blood-brain barrier, and a vasogenic edema (22,24). Increased intracranial pressure appears as a manifestation of decreased consciousness, projectile vomiting, or brain herniation. Over time, if this compensation fails, subsequent hemorrhagic and cerebral venous infarction will occur, which will be very dangerous. Unlike arterial infarction, venous infarction typically preserves some degree of arterial perfusion, which may account for the greater reversibility observed in many pediatric cases (22,23).

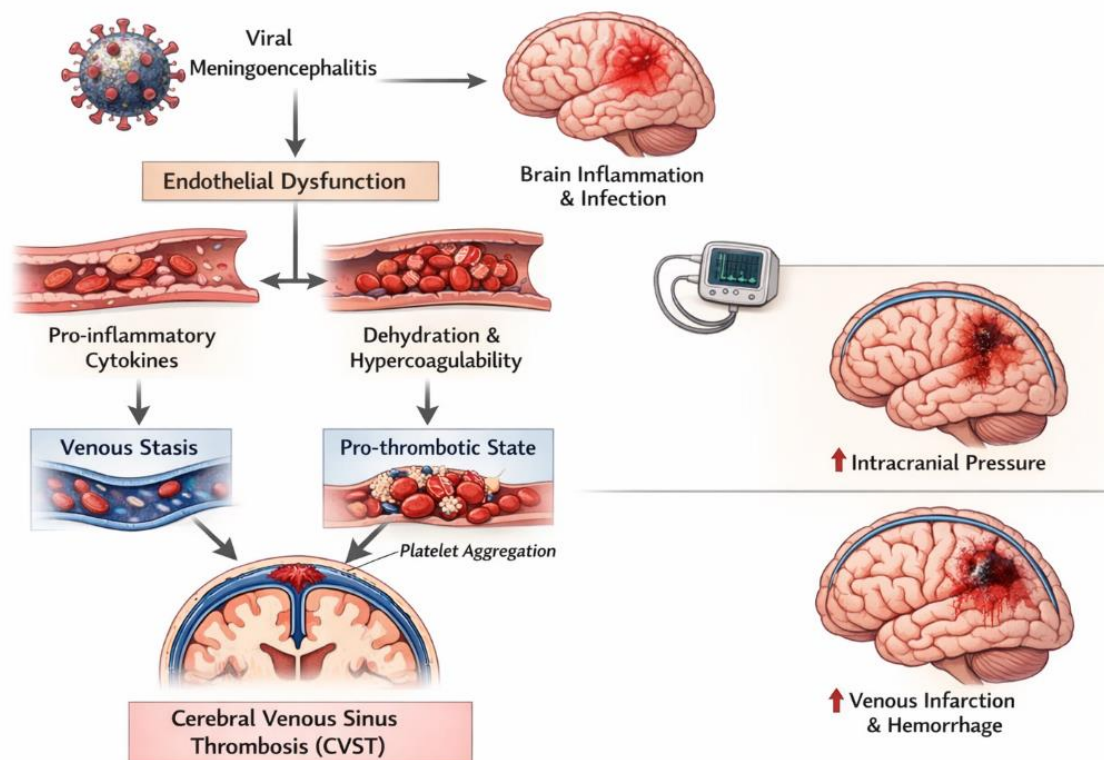


Figure 3. The illustration pathogenesis of CVST in the setting of meningoencephalitis shows that spreading infection to the venous sinus walls may result in increasing pro inflammatory cytokines, endothelial injury, hypercoagulability leading to increasing intracranial pressure

The main diagnosis of CVST is determined through neuroimaging examination, including in the case of children. Magnetic Resonance Imaging (MRI) and MRV examinations are the gold standard due to their high sensitivity and specificity in detecting thrombus and abnormal venous flow or feeling defect (25). In this patient, thrombus was found to be the result of a feeling defect in the left transversus sinus that extends to the left sigmoid sinuses, a strong sign of CVST. Notably, the thrombosis in this patient involved the transverse and sigmoid sinuses rather than the superior sagittal sinuses, suggesting that impaired CSF reabsorption through the arachnoid granulations a commonly cited mechanism of intracranial hypertension in CVST may have played a lesser role. CT Scan examination is also the main alternative in the acute phase but must be accompanied by CT Venography examination to still determine the location of the thrombus (22,23). In this case, the results of the head CT-Scan precede the MRV examination and confirm the signs of cerebral edema with an increase in the density of the falx cerebri were consistent with meningoencephalitis accompanied by an increase in the density of bilateral transversus sinuses and sagittal sinuses (25). The absence of haemorrhagic infarction on MRV indicates that venous congestion did not progress to irreversible tissue injury, consistent with the favourable clinical trajectory.

D-dimer examination is used as a marker of thrombus formation and degradation activity which usually increases in CVST. However, an increase in D-dimer or normal levels does not rule out the diagnosis of CVST (25). In CVST assessing the area and location of the thrombus is more important than the numerical value of the coagulation process that occurs, so MRV remains the gold standard. In this case, the D-dimer level was examined twice and the results significantly decreased within two days. This shows that there is a resolution of the inflammatory induced thrombosis mechanism compared to the process of forming the thrombus itself. In addition. In this case, the D-dimer examination is also carried out at the beginning to precede and detect the thrombus before MRV is performed and detect if there is a potential for sepsis or coagulopathy. Thrombophilia tests such as C/S protein or Leiden factor V are important to detect other causes of CVST (22,24), but in these patients it is not performed due to limited facilities. The presence of indications of viral meningoencephalitis and CVST makes the final diagnosis of the left transversus sinus and left sigmoid sinus CVST with the secondary cause of viral meningoencephalitis.

In this case, the history of JE vaccination eight days before the appearance of the initial neurological manifestations also raises a new line of thinking whether there is a temporary causal relationship between the two, so it needs to be a concern. According to research, the JE vaccine has a good level of efficacy and safety, although there are reported serious post-immunization events (26,27). According to studies on live-attenuated SA14-14-2 vaccines, severe neurological side effects are very rare (28). There are also few studies that report serious post-immunization events in the JE vaccine. Serious post-immunization events are reported to be less than 5% and there are only acute disseminated encephalomyelitis manifestations where it is still difficult to find a causal relationship between the two (29). Reports and studies of CVST events related to the JE vaccine are also very limited, so in this case strong evidence of a diagnosis leading to viral meningoencephalitis is clearer in triggering the formation of cerebral venous thrombus. In this case based on the WHO AEFI framework, the temporal association observed in this case is more consistent with a coincidental event rather than a causal relationship (30).

Management consisted of the administration of anticonvulsants, antibiotics, antiinflammation, intracranial pressure management, and anticoagulants. In this case, the administration of benzodiazepines, mannitol, and dexamethasone was in accordance with the protocol by adjusting daily clinical considerations (30). Dexamethasone was given to reduce cerebral inflammation, despite its role in viral meningoencephalitis being unclear and its use not being standard practice (22,24). The administration of antibiotics in this case was intended as an empirical therapy, but also as a strategy that the management of bacterial infections remained at levels that were not systemically detected and opportunistic infectious conditions (24).

Anticoagulation is generally recommended in pediatric CVST to prevent thrombus propagation and promote recanalization. The EPNS/SFNP guideline recommends initiating anticoagulation during the acute phase of CSVT in children (Class IIa, level of evidence B), and the ASH 2018 guidelines similarly support anticoagulation, although recommendations are largely extrapolated from adult data in the absence of pediatric randomized controlled trials (24,31,32). A recent ASH/ISTH 2024 meta-analysis pooling seven studies of 732 pediatric CSVT patients reported that anticoagulation was associated with reduced mortality and increased thrombus resolution, though the certainty of evidence was very low (26,33). However, the role of anticoagulation in infection-associated CVST remains specifically controversial. Typically, low-molecular-weight heparin (LMWH) is initially recommended over unfractionated heparin, followed by a transition to oral vitamin K antagonists for a duration of 3 to 12 months in cases of transient risk factors, or for a longer period if chronic major risk factors for thrombosis are present (23,32). Some guidelines recommend managing septic CVT with infection treatment alone without anticoagulation due to haemorrhagic risk concerns, while recent observational studies suggest anticoagulation can be safely administered in this context, with some patients also achieving favourable outcomes without it (33).

In this patient, LMWH is given in acute and long-term treatment. According to the protocol, LMWH enoxaparin is given 1 mg/kg every 12 hours and must be balanced with monitoring anti-Xa levels. In this case, enoxaparin is given about 1 mg twice a day. The dosage and administration are in accordance with the protocol, especially in pediatric cases, even though the anti-Xa level is not carried out due to limited facilities. During treatment, no evidence of intracranial hemorrhage was found. For the long term, the patient was given rivaroxaban 5 mg for 5 months. The dosage and administration were in accordance with the protocol and at the patient's third and fifth month polyclinic visits, the patient showed good outcomes (23,33,34). No history of seizures, decreased consciousness accompanied by stable consciousness, negative pathological reflexes, motor strength (5/5), and normal cranial nerves although MRV realignment was not performed due to favorable clinical considerations. At the 5th month anticoagulant was discontinued according to protocol. Through this case, it was proven that rivaroxaban has a good impact as a long-term anticoagulant therapy.

The family's initial concern was understandable, given the patient's seizures and altered consciousness. However, the clinical course was reassuring. The patient gradually regained consciousness, had no further seizures during hospitalization, returned to normal daily activities after discharge, and remained symptom-free at the five-month follow-up.

This case has limitations, among others: serological examination or viral PCR is not available in meningoencephalitis, so the standard gold standard of screening is not facilitated, even though CSF examination is consistent with viral infection. MRV follow up examination is not carried out to confirm whether the thrombus is really no longer present because of its position as the standard gold standard. However, in practical daily practice, consideration of neurological clinical improvement is considered sufficient to assess the prognosis. Bacterial culture examination of dental caries bacteria is also not carried out to rule out the source of infection originating from the teeth. Although anti-Xa tests for monitoring the administration of LMWH are not carried out due to limited facilities, patient outcomes are still good. Finally, the temporal association with JE vaccination should not be interpreted as evidence of causation. As a single case report, these findings should be considered as hypotheses rather than definitive.

The main clinical implication is that CVST should be considered in children with meningoencephalitis who show worsening neurological symptoms, clinical deterioration, or delayed recovery. Neurological symptoms occurring after vaccination should not be judged only by their timing, but should be assessed in the overall clinical context. This case also highlights the challenge of managing patients based on guidelines despite limited diagnostic certainty and resource facility.

Acknowledgments: We would like to acknowledge the administrative and technical support provided by the staff of Duta Wacana University Medical Faculty and Bethesda Hospital, particularly in the management and processing of patient data.

Author Contributions: Frans Iqlessias Hutagaol: Conceived and designed the case study, wrote the manuscript, and assisted in patient management. Fannia Aviandani Megaputri: reviewed and edited the manuscript. Devie Kristiani: attending physician responsible for examining and providing treatment in patient's management. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

List of Abbreviations

CVST	Cerebral Venous Sinus Thrombosis
CSF	Cerebrospinal Fluid
PICU	Pediatric Intensive Care Unit
MRV	Magnetic Resonance Venography
GCS	Glasgow Coma Scale
Hb	Hemoglobin
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
NLR	Neutrophil-to-Lymphocyte Ratio
PMN	Polymorphonuclear
MN	Mononuclear
BTA/AFB	Acid-Fast Bacilli
MTB	Mycobacterium Tuberculosis
CRP	C-Reactive Protein
JE	Japanese Encephalitis
EPNS	European Paediatric Neurology Society
SFNP	Société Française de Neurologie Pédiatrique
ASH	American Society of Hematology
ISTH	International Society on Thrombosis and Haemostasis
PCR	Polymerase Chain Reaction
WHO	World Health Organization
AEFI	Adverse Events Following Immunization
LMWH	Low Molecular Weight Heparin

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