Annals of Case Reports
Khallikane S, et al. Ann Case Rep: 9: 102074
www.doi.org/10.29011/2574-7754.102074
www.gavinpublishers.com

OPEN ACCESS

Case Report

GAVIN PUBLISHERS

Repeated Cerebral Thrombophlebitis and Pregnancy: A Case Report with Literature Review

Said Khallikane[1*], ELabdi Monsef[2], Amine Bentaher[3], Salek Monsif[3], Kbiri Hicham[4]

[1]Former anesthesiologist-intensivist, Hassan II Military Hospital, Laayoune, Mohammed VI Hospital, Dakhla,

Anesthesiology service, Avicenna Military Hospital, Faculty of Medicine and Pharmacy, Cadi Ayyad University,

Marrakech, Morocco

[2]Orthopedic traumatology department of HASSAN II Military Hospital, Laayoune, Faculty of Medicine, Pharmacy and Dentistry, Sidi Mohamed Ben Abdellah University, Fes, Morocco

[3]Diagnostic and interventional radiology department of the Moulay Ismail Military Hospital, Meknes, Faculty of Medicine, Pharmacy and Dentistry, Sidi Mohamed Ben Abdellah University, Fes, Morocco

[4]Anesthesiology, Intensive Care Unit, Avicenna Military Hospital, Marrakech, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco

***Corresponding author**: Said Khallikane Sr, Anesthesiology and Critical Care, Hôpital militaire avicenne, Marrakech, Royaume du Maroc, Marrakech, MAR, Morocco

Citation: Khallikane S, Elabdi M, Bentaher A, Salek M, Kabiri H (2024) Repeated Cerebral Thrombophlebitis and Pregnancy: A Case Report with Literature Review. Ann Case Report. 9: 2074. DOI:10.29011/2574-7754.102074

Received: 12 November 2024, **Accepted:** 18 November 2024, **Published:** 19 November 2024

Abstract

Cerebral thrombophlebitis (CVT) that occurs during pregnancy is rarer than postpartum thrombophlebitis. The main risk factors are pregnancy and thrombophilia. Symptoms vary and may be misleading. It is necessary to discuss its diagnosis to start an early anticoagulation. We report the case of a 33-year-old pregnant woman, who had a history of postpartum cerebral thrombophlebitis in her second pregnancy, and presented at 15 weeks of amenorrhea in a disorder of consciousness associated with partial seizures becoming generalized, due to vein thrombosis of the right lateral sinus diagnosed with MRI, with a normal thrombophilia balance, through this observation, we analyse the clinical, paraclinical characteristics and the evolution of CVT during pregnancy. The current gold standard is based on a combination of MRI and magnetic resonance venography. Treatment involves curative anticoagulation, continued for at least 6 months postpartum. The prognosis is generally favourable, ensured by early diagnosis and anticoagulant treatment. CVT, including that related to pregnancy or postpartum, does not contraindicate future pregnancies. For pregnant patients with a history of CVT in previous pregnancies, prophylaxis with low molecular weight heparin (LMWH) is recommended and should be continued for at least six weeks after delivery.

Keywords: Cerebral Thrombophlebitis; Pregnancy; Curative Anticoagulation; Prevention.

Introduction

Cerebral venous thrombosis (CVT) occurring during pregnancy is rarer than those that occur in the postpartum period [1]. The main contributing factors are the hypercoagulable state of pregnancy and the presence of thrombophilia. Its clinical symptoms are highly variable, and it is crucial to consider the diagnosis early to initiate prompt anticoagulation [1]. CVT should be suspected when a patient presents with a combination of intracranial hypertension and/or focal neurological deficits and/or seizures to varying degrees. The clinical symptoms also vary depending on the location of the venous thrombosis, and in some cases, CVT may have an unusual presentation [2]. Brain MRI combined with magnetic resonance venography is the reference method for diagnosis, while cerebral angiography is only performed if there is still uncertainty [3]. Through this case, we analyse the clinical, paraclinical, and evolutionary characteristics of recurrent CVT during pregnancy.

Case Report

33-year-old woman, in her third pregnancy, second parity, with her first pregnancy carried to term with an uncomplicated vaginal delivery, has a history of cerebral venous thrombosis occurring on day 10 of the postpartum period following her second pregnancy. The delivery was performed via cesarean section due to failure to progress at full dilation, associated with dynamic dystocia at the end of labor, with no complications. She was treated with long-term vitamin K antagonists [acenocoumarol] for 6 months. At 15 weeks of amenorrhea during her current pregnancy, she experienced partial motor seizures affecting the left hemi body, with secondary generalization. Examination revealed a Glasgow Coma Scale score of 8/15, leftward deviation of the head and eyes, right hemiparesis with facial involvement, and hypoesthesia on the same side. Detrostix was 1.55. The hemogram was normal (hemoglobin at 12 g/L, white blood cells: 8,000/mm³, platelets at 347,000/mm³, hematocrit at 45%), erythrocyte sedimentation rate was 12/23, CRP was 4 mg/L, and blood electrolyte levels were normal. Fundoscopy showed bilateral papilledema. A brain CT scan revealed diffuse cerebral edema, and brain MRI confirmed cerebral venous thrombosis. Magnetic resonance venography demonstrated thrombosis in 2D venous angiographic sequences of the transverse segment of the right lateral sinus in sagittal view (Figure 1) and (Figures 2,3) in coronal view. Testing for antinuclear antibodies and antiphospholipid antibodies was negative. Hemostasis and thrombophilia workups were normal, with normal levels of protein S and antithrombin III. The patient was placed on hypo coagulant dose heparin and was subsequently intubated and ventilated due to neurological deterioration and the persistence of status epilepticus, treated with continuous Hypnovel, fentanyl, and the introduction of diprivan on the second day, in addition to Levetiracetam, clobazam, and mannitol. She was extubated 5 days after intubation. A medical termination of the pregnancy was performed after stabilizing her neurological condition due to the fetal risk following multiple episodes of convulsions and maternal coma. The outcome was favourable. The follow-up MRI after 6 months showed regression of the infarction with recanalization of the venous sinus.

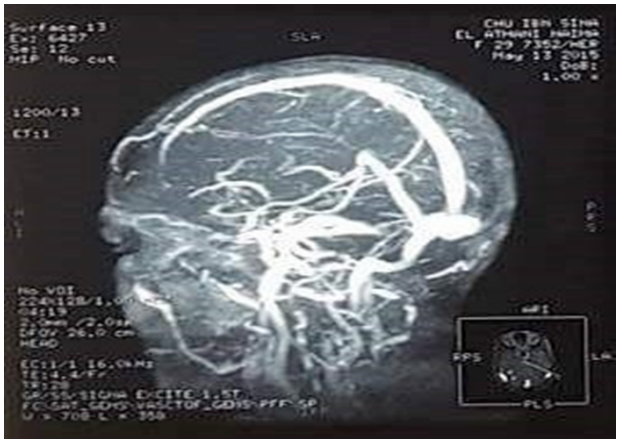
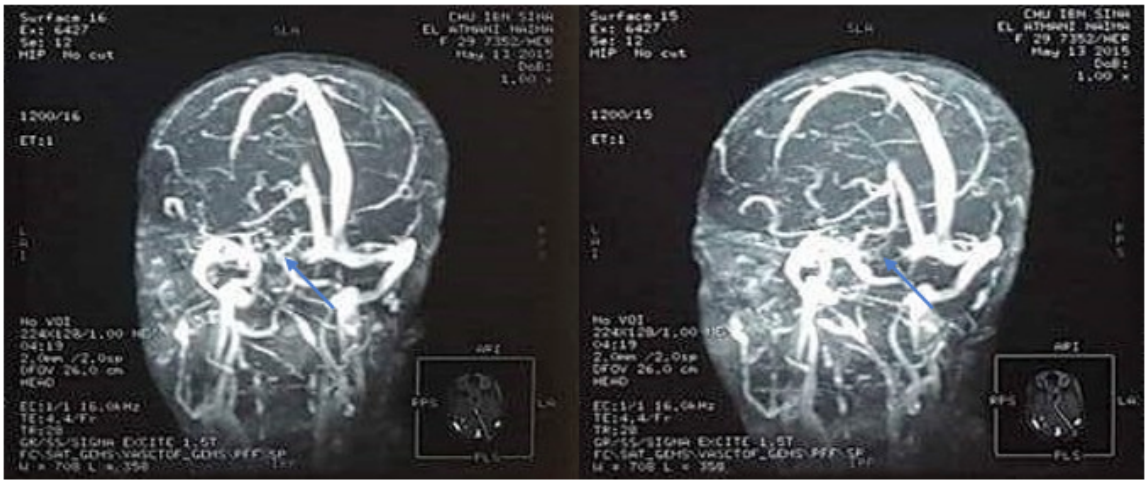


Figure 1: 2D venous angiographic sequences (sagittal view) showing an amputation of the transverse segment of the right lateral sinus (blue arrow).



Figures 2,3: 2D venous angiographic sequences (coronal view) showing an amputation of the transverse segment of the right lateral sinus (blue arrows).

Discussion

CVT refers to the formation of thrombi in the cerebral veins or venous sinuses. It is a rare cause of stroke in the general population (0.5 to 1% of all strokes) but has a higher incidence during pregnancy (2% of pregnancy-related strokes), with a prevalence of approximately 12 cases per 100,000 pregnancies [4]. It occurs particularly in the third trimester and postpartum (80% of cases within the first three weeks postpartum), and especially in women with multiple pregnancies [1]. In contrast to our case, where CVT recurred during pregnancy, assessing the risk and advising women with a history of CVT regarding future pregnancies is challenging due to the lack of data on the associated thrombotic risk. Since pregnancy and the puerperium are prothrombotic risk factors, gynecologists and general practitioners are often reluctant to encourage women with a previous CVT to become pregnant [5]. This increased frequency is due to the fact that pregnancy constitutes a state of relative hypercoagulability caused by venous stasis, changes in the arterial wall, and an increase in procoagulant factors (fibrinogen, factors VII, VIII, X, XI, prothrombin), as well as a decrease in coagulation inhibitors (antithrombin III, protein C, and protein S) [1]. Other factors include dehydration, trauma, infections, and acquired thrombophilia, as reported in Julie Roth's study. There is evidence of a very low risk of recurrent CVT in women who have had previous extra cerebral venous thrombotic events, in the absence of hereditary or acquired thrombophilia, and if the previous venous thrombosis was associated with a temporary risk factor (e.g., oral contraceptives, immobilization due to a fracture, etc.). [6] In contrast, the risk of recurrence is increased if thrombophilia is present or if the previous thrombotic event was idiopathic. Women with a history of extra cerebral or cerebral CVT who are pregnant or planning to conceive should undergo screening for thrombophilia, which can help reduce the individual risk of recurrence in future pregnancies. [7] The clinical symptoms of CVT are varied, but some signs are frequently associated: headaches and seizures, which, although rare during pregnancy (complicating less than 1% of pregnancies), reveal CVT in 12 to 31% of cases, as was the case with our patient. [2] Lumbar puncture and electroencephalogram (EEG) can provide diagnostic clues. Lumbar puncture is abnormal in 80% of cases, showing varying degrees of increased pressure and changes in cerebrospinal fluid composition. [8] The EEG can be normal in 25% of cases or show diffuse abnormalities with no specific characteristics [9]. The definitive diagnosis is neuroradiological. Computed tomography (CT) is the first examination to request, and it is normal in only 10-20% of cases. [8] The most indicative sign is the delta sign, which is found in 20-30% of cases [9]. It represents the hyperemia of the dural sinus walls, which enhances the hypo density effect of the non-contrast-enhanced thrombotic lumen [9]. CT can also show an image of spontaneous hyper density from the thrombosis known as the "cord sign," images of diffuse or localized cerebral edema, and images of venous infarcts or non-hemorrhagic infarcts. The "cord sign" appears early within the first days of thrombosis and generally disappears within one to two weeks, whereas the delta sign is not described in the early days and is usually identifiable only from the second week, sometimes disappearing only in the second month. In our case, the CT showed bilateral cerebral edema. Demonstrating total or partial venous occlusion is essential for making the diagnosis [10]. The most common site is the superior longitudinal sinus, in 72% of cases, followed by the lateral sinuses in 26% of cases which was the case of our patient [8]. The key to diagnosis is imaging of the venous system itself, which can show the occluded vessel or

intravascular thrombus. The current gold standard is a combination of MRI to visualize the thrombosed vessel and magnetic resonance venography to detect the lack of visualization of the same vessel. [3] MRI alone is limited by flow artifacts that can lead to false positives and the absence of hyper intensity on T1 and T2-weighted images during the early stage of acute thrombosis. During the first 3 to 5 days, the thrombosed sinus is iso-intense on T1 and hypo-intense on T2, making it very difficult to distinguish from normal veins. The diagnostic yield of magnetic resonance venography alone is limited by the fact that, as with other angiographic techniques, differentiating between thrombosis and hypoplasia is a typical diagnostic dilemma for the lateral sinuses [3]. Even with the combination of MRI and magnetic resonance venography, diagnosis can still be challenging, particularly in isolated cortical venous thrombosis. In the absence of the characteristic cord sign on non-contrast CT or MRI, conventional angiography is sometimes required [11]. Some studies have highlighted the value of Echo Planar Imaging (EPI) MRI sequences, particularly T2*-weighted sequences, which, unlike T1 and T2, show thrombosis as a hypo intense signal associated with magnetic susceptibility, similar to that observed in intracerebral hemorrhages [12]. Measurement of D-dimer: Given the wide variety of clinical presentations in cerebral venous thrombosis (CVT), it would be of practical interest to have a test that is easy to perform in emergency settings and can reliably exclude CVT. Several studies have tested the value of D-dimer in deep vein thrombosis of the limbs, with a level (<500 ng/ml) showing a high negative predictive value. Indeed, in most patients with CVT, D-dimer concentrations are elevated. A negative D-dimer test can make the diagnosis very unlikely, although it cannot completely rule it out [13].

Antithrombotic treatment with low-molecular-weight heparin administered subcutaneously or adjusted-dose intravenous heparin is widely used as a first-line treatment based on evidence from three randomized trials and a meta-analysis [14]. Despite numerous case studies and small series investigating the benefits of thrombolysis in cerebral venous thrombosis (CVT), none provide a high level of evidence supporting the use of either systemic or local thrombolysis [15]. There is potential bias in the currently published studies, with possible underreporting of cases with poor outcomes and complications. The treatment and assessment were not blinded, leading to bias in evaluating the results. In the international study on cerebral vein and dural sinus thrombosis (ISCVT study), 13 patients were treated with local thrombolysis, and five (38.5%) were either dead or dependent 6 months after CVT. These outcomes are worse than those in other studies are but may guide clinical practice. However, if patients deteriorate despite adequate anticoagulation and optimized symptomatic treatment of complications, thrombolysis or thrombectomy may be considered in select centers with expertise in interventional radiology [3,14].

In patients suffering from isolated intracranial hypertension with papilledema threatening vision, a lumbar puncture to deplete cerebrospinal fluid is necessary before starting heparin. This procedure is generally followed by a rapid improvement in headaches and visual acuity. In cases where patients present with early signs of brain herniation due to extensive CVT or its complications, a DE compressive hemicraniectomy may be required as a life-saving measure [16]. This also leads to an improvement in functional prognosis. Patients who experience partial or generalized seizures should receive antiepileptic treatment as they are at risk of recurrence [17]. However, the risk of seizures occurring in patients without seizures at admission is very low, except for those who present with hemorrhagic parenchymal lesions at the time of admission [17].

The objective of continuing anticoagulation after the acute phase is to prevent recurrent CVT and other thrombotic events, including pulmonary embolism. CVT is very rare and difficult to document, especially if MRI follow-up is not available. Other thrombotic events, such as deep vein thrombosis of the limbs or pelvis and pulmonary embolism, occur in about 5% of patients. According to recommendations for systemic deep vein thrombosis, anticoagulation with warfarin for 6 to 12 months is recommended for survivors of acute CVT, targeting an international normalized ratio between two and three times the normal. Prolonged oral anticoagulation is reserved for patients with acquired or congenital thrombophilias, including those with antiphospholipid antibody syndrome [18]. Seizures occur in 11% of patients, and the incidence is higher if the patient had seizures during the acute phase or has hemorrhagic parenchymal lesions. [17]. These patients may receive antiepileptic drugs to prevent recurrent seizures. However, the optimal duration of antiepileptic medication treatment is unknown. Severe loss of visual acuity is fortunately a very rare event nowadays [18]. If visual acuity decreases during follow-up and no other obvious ophthalmological cause is found, a fundus examination should be performed. Increased intracranial pressure should be promptly ruled out and managed, if necessary, through cerebrospinal fluid (CSF) diversion and possibly optic nerve sheath fenestration to prevent optic atrophy. Pregnancy and the postpartum period are significant risk factors for cerebral venous thrombosis (CVT). An important question to consider is the risk of recurrent thromboembolic events in future pregnancies for women with a history of CVT. Six studies have addressed this issue, involving a total of 855 women under observation, of whom 83 became pregnant after their CVT (101 pregnancies) [18]. In these studies, the risk of complications in future pregnancies was low: 88% of pregnancies progressed normally to term, while the remainder were terminated prematurely due to voluntary or spontaneous abortion. There were no cases of recurrent CVT, and only two cases of deep vein thrombosis were reported. Therefore,

based on available studies, CVT, including those associated with pregnancy or postpartum, does not constitute a contraindication for future pregnancies. Women should be advised to use contraceptive measures to avoid pregnancy while on anticoagulant treatment with coumarins due to their teratogenic effects. Low molecular weight heparin (LMWH) is generally continued for at least six weeks postpartum or until vessel recanalization is achieved [3]. For pregnant patients with a history of cerebral venous thrombosis in previous pregnancies or with thrombophilia, prophylactic low molecular weight heparin (LMWH) is recommended [5]. The clinical course and prognosis of CVT are unpredictable on an individual basis. Some patients may initially be in a coma and survive without any sequelae, while others may present with minor symptoms, then deteriorate and suffer significant long-term consequences. The mortality rate in developed countries is approximately 10 to 20%. [19], While it was 30 to 50% in the 1960s, the functional prognosis for survivors is better than in arterial ischemia, with 10 to 20% of patients experiencing lasting sequelae [8]. (Epilepsy, focal deficits, optic atrophy). Several poor prognostic factors have been described: specific thrombosis locations (deep veins, cerebellar veins, and isolated cortical thrombosis); the nature of the underlying condition; the presence of focal signs, coma; the occurrence of hemorrhagic infarction or a delta sign on the CT scan; the association with pulmonary embolism; and finally, the speed of thrombosis progression.

Conclusion

The diagnosis of cerebral venous thrombosis (CVT) during pregnancy remains rare and challenging due to its clinical polymorphism. It is essential to consider it even with subtle or non-specific signs and to request neuroimaging to confirm the diagnosis. The current gold standard combines MRI with magnetic resonance venography. Treatment involves therapeutic anticoagulation, continued for at least 6 months postpartum. The prognosis is usually favourable, provided the diagnosis and anticoagulant treatment are initiated early. CVT, including those related to pregnancy or postpartum, does not constitute a contraindication for future pregnancies. For pregnant patients with a history of cerebral venous thrombosis in previous pregnancies, prophylactic low molecular weight heparin (LMWH) is recommended, continued for at least six weeks after delivery.

Conflicts of Interest Disclosure: The authors declare that they have no conflicts of interest.

Participants Consent: All participants have given their explicit consent for the publication of personal data concerning themselves and their colleagues as part of this study. They understand that this data may include information that could identify them in the context of the research findings. They have been informed about the purpose of this publication, the type of data that will be disclosed, and the potential implications. They acknowledge that this information will be publicly accessible after publication. They confirm that their consent is voluntary and that they have the right to withdraw it at any time prior to publication.

Authors Contributions: All authors contributed to the production of this article. They also declare that they have read and approved the final version of this manuscript.

References

1. Coriu L, Ungureanu R, Talmaci R, Uscatescu V, Cirstoiu M, ET AL (2014) Hereditary Thrombophilia and thrombotic events in pregnancy: single-center experience. J Med Life. 7:567-71.
2. Farzi F, Abdollahzadeh M, Faraji R, Chavoushi T. (2015) Seizure in Pregnancy Following Cerebral Venous Sinus Thrombosis. Anesth Pain Med.5:e26866.
3. Masuhr F, Mehraein S, Einhäupl K. (2004) Cerebral venous and sinus thrombosis. J Neurol. 251:11-23.
4. James AH, Bushnell CD, Jamison MG, Myers ER. (2005) Incidence and risk factors for stroke in pregnancy and the puerperium. Obstet Gynecol. 106:509-16.
5. Mehraein S, Ortwein H, Busch M, Weih M, Einhäupl K, ET AL (2003) Risk of recurrence of cerebral venous and sinus thrombosis during subsequent pregnancy and puerperium. J Neurol Neurosurg Psychiatry. 74:814-6.
6. Brill-Edwards P, Ginsberg JS, Gent M, Hirsh J, Burrows R, ET AL (2000) Recurrence of Clot in This Pregnancy Study Group. Safety of withholding heparin in pregnant women with a history of venous thromboembolism. Recurrence of Clot in This Pregnancy Study Group. N Engl J Med. 343:1439-44.
7. Deschiens MA, Conard J, Horellou MH, Ameri A, Preter M, ET AL (1996) Coagulation studies, factor V Leiden, and anticardiolipin antibodies in 40 cases of cerebral venous thrombosis. Stroke. 27:1724-30.
8. Ameri A, Bousser MG. (1992) Cerebral venous thrombosis. Neurol Clin. 10:87-111.
9. Roullet E, Offenstadt G, Vassal T. (1990) Thrombophlébites cérébrales. Réanimation et médecine d'urgence. Expansion scientifique française, Paris, 1990: 491-505.
10. Bonnar J, Green R, Norris L. (1998) Inherited thrombophilia and pregnancy: the obstetric perspective. Semin Thromb Hemost. 24:49-53.
11. Ahn TB, Roh JK. (2003) A case of cortical vein thrombosis with the cord sign. Arch Neurol. 60:1314-6.
12. Idbaih A, Boukobza M, Crassard I, Porcher R, Bousser MG, ET AL (2006) MRI of clot in cerebral venous thrombosis: high diagnostic value of susceptibility-weighted images. Stroke. 37:991-5.
13. Kosinski CM, Mull M, Schwarz M, Koch B, Biniek R, ET AL (2004) Do normal D-dimer levels reliably exclude cerebral sinus thrombosis? Stroke. 35:2820-5.
14. Stam J. (2005) Thrombosis of the cerebral veins and sinuses. N Engl J Med. 352:1791-8.
15. Canhão P, Falcão F, Ferro JM. (2003) Thrombolytics for cerebral sinus thrombosis: a systematic review. Cerebrovasc Dis. 15:159-66.
16. Petzold A, Smith M. (2006) High intracranial pressure, brain herniation and death in cerebral venous thrombosis. Stroke. 37:331-2.

17. Ferro JM, Correia M, Rosas MJ, Pinto AN, Neves G (2003) Cerebral Venous Thrombosis Portuguese Collaborative Study Group [Venoport]. Seizures in cerebral vein and dural sinus thrombosis. Cerebrovasc Dis. 15:78-83.

18. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F (2004) ISCVT Investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke. 35:664-70.

19. Rondepierre P, Hamon M, Leys D, Leclerc X, Mounier-Vehier F, ET AL (1995) Thromboses veineuses cérébrales: étude de l'évolution [Cerebral venous thromboses: study of the course]. Rev Neurol (Paris). 151:100-4.